The Cognitive Neuropsychological Profile of
Psychosis following Traumatic Brain Injury (PFTBI):
Comparisons with Traumatic Brain Injury, Schizophrenia, and Healthy Control Cohorts

A thesis submitted in fulfilment of the requirements for the degree of Doctor of Philosophy

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October 2012
Declaration

This is to certify that:

(i) Except where due acknowledgement has been made, this work is my own;

(ii) The work has not been submitted previously, in whole or in part, to qualify for any other academic award;

(iii) The content of this thesis is the result of work which has been carried out since the official commencement date of the approved research program;

(iv) Any editorial work, paid or unpaid, carried out by a third party is acknowledged;

(v) Ethics procedures and guidelines have been followed.

_________________
Rachel A. Batty
October 2012
Dedication

First, and above all else, this work in its entirety is dedicated to the Most High God and my saviour, Lord, and friend, his son Jesus; from whom, through whom, and for whom, is my every effort and success (Colossians 3:17; Romans 11:36).

Thank you for your fiercely persistent love and limitless generosity, in this and everything else.

I love you.
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“Sometimes a great wound or concussion of the head, especially which happens by falling headlong from an (sic) high place, brings a prejudice and weakness to the animal faculty, dulling the understanding.”

-Thomas Willis
(English physician, January 1621-November 1675)

“It is in the brain that the poppy is red, that the apple is odorous, that the skylark sings.”

- Oscar Wilde
Publications, Presentations, and Grants during PhD Candidature

Peer-Reviewed Publications


Forthcoming Publications


Oral Presentations

*Denotes presenter where Batty, R.A. is not first author.


**Poster Presentations**

*Denotes presenter where Batty, R.A. is not first author.


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Summary of Research

Traumatic insanity has been acknowledged since Meyer (1904), yet the relationship between traumatic brain injury (TBI) and psychosis remains poorly understood and under-researched. Patients who are dually-diagnosed with psychosis following traumatic brain injury (PFTBI) suffer significantly as a result of both their injury and illness, however systematic and standardised neuropsychological research of PFTBI has not been undertaken. Instead, a relatively small amount of work relying on retrospective chart reviews, case studies, and loosely defined self-reported TBI has been conducted. Such data is often inconsistent, and reports of intact neurocognition in PFTBI have been made despite substantial evidence of deficits in the literature on TBI and psychosis.

Patients with PFTBI (N=10), injury-matched patients with TBI without psychosis (TBIWP) (N=10), patients with schizophrenia (N=23), and a healthy cohort (N=23), were administered a comprehensive battery of standardised cognitive neuropsychological tests. The data were examined for group-wise differences, relationships with mediating variables identified in the existing TBI and psychosis literature, and the correct classification of the cohorts according to two prominent features of the battery (i.e., RBANS Total [overall neurocognition] and Stroop Colour Trial [processing speed]).

Patients with PFTBI were characterised by a neuropsychological profile that appeared to be cumulative in the degree of impairment relative to their single-diagnosis counterparts, while comparable to schizophrenia with respect to their pattern of deficits. This was further supported by discriminant function analysis (DFA), where the greatest misclassification of the PFTBI cohort was as a schizophrenia patient, and vice versa. In addition, language-specific deficits were uniquely shared by the brain injured cohorts, partially driven by the laterality of language processing. Statistical matching of patient demographics further established that reduced neurocognition in PFTBI is not attributable to mediating characteristics of the injury or illness, however these factors were associated with performance for all patient cohorts.

As the first empirical investigation of the cognitive neuropsychological profile of PFTBI, this research provides a novel and valuable contribution to the existing PFTBI literature, particularly with regard to diagnosis and treatment. The assessment of verbal learning and verbal memory may be an essential diagnostic tool, while the extent of overall impairment indicates that treatment programs should focus on adjunctive therapy, beginning with cognitive remediation as a supplement to the usual antipsychotic treatment.
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<th>Full Form</th>
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<th>Full Form</th>
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<tr>
<td>ABI</td>
<td>Acquired brain injury</td>
<td>HMO</td>
<td>Health Management Organization</td>
</tr>
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<td>ANCOVA</td>
<td>Analysis of covariance</td>
<td>ICD</td>
<td>International Classification of Diseases</td>
</tr>
<tr>
<td>ANOVA</td>
<td>Analysis of variance</td>
<td>IQ</td>
<td>Intelligence quotient</td>
</tr>
<tr>
<td>BA</td>
<td>Brodmann’s area</td>
<td>JTC</td>
<td>Jumping to conclusions</td>
</tr>
<tr>
<td>C1</td>
<td>Condition one</td>
<td>LOC</td>
<td>Loss of consciousness</td>
</tr>
<tr>
<td>C2</td>
<td>Condition two</td>
<td>MANOVA</td>
<td>Multivariate analyses of variance</td>
</tr>
<tr>
<td>CBT</td>
<td>Cognitive brain therapy</td>
<td>MAPrc.</td>
<td>Monash Alfred Psychiatry Research Centre</td>
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<tr>
<td>CHRP</td>
<td>Copenhagen High-Risk Project</td>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence interval</td>
<td>Ms</td>
<td>Milliseconds</td>
</tr>
<tr>
<td>COWAT</td>
<td>The Controlled Oral Word Association Test</td>
<td>MVPT</td>
<td>Motor-Free Visual Perception Test</td>
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<tr>
<td>CPT</td>
<td>Continuous Performance Test</td>
<td>mTBI</td>
<td>Mild traumatic brain injury</td>
</tr>
<tr>
<td>CPZ-e</td>
<td>Chlorpromazine equivalent</td>
<td>MVA</td>
<td>Missing value analysis</td>
</tr>
<tr>
<td>CRT</td>
<td>Cognitive remediation therapy</td>
<td>MVA</td>
<td>Motor vehicle accident</td>
</tr>
<tr>
<td>CT</td>
<td>Computerised tomography</td>
<td>NART</td>
<td>National Adult Reading Test</td>
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<td>CWIT</td>
<td>Color-Word Interference Test</td>
<td>NIMH</td>
<td>National Institute of Mental Health</td>
</tr>
<tr>
<td>DA</td>
<td>Dopamine</td>
<td>NMDA</td>
<td>N-methyl-D-aspartate</td>
</tr>
<tr>
<td>DAI</td>
<td>Diffuse axonal injury</td>
<td>NS</td>
<td>Not significant</td>
</tr>
<tr>
<td>DFA</td>
<td>Discriminant function analysis</td>
<td>OCD</td>
<td>Obsessive-compulsive disorder</td>
</tr>
<tr>
<td>DLPFC</td>
<td>Dorsolateral prefrontal cortex</td>
<td>PANSS</td>
<td>Positive and Negative Syndrome Scale</td>
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<tr>
<td>DoD/DVA</td>
<td>Department of Defense and Department of Veterans Affairs</td>
<td>PET</td>
<td>Positron emission tomography</td>
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<tr>
<td>DSM</td>
<td>Diagnostic and Statistical Manual of Mental Disorders</td>
<td>PLS</td>
<td>Plain language statement</td>
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<td>DTI</td>
<td>Diffusion tensor imaging</td>
<td>PPI</td>
<td>Prepulse inhibition</td>
</tr>
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<td>ECT</td>
<td>Electroconvulsive therapy</td>
<td>pSCZ</td>
<td>Paranoid schizophrenia</td>
</tr>
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<td>EEG</td>
<td>Electroencephalography</td>
<td>PFTBI</td>
<td>Psychosis following traumatic brain injury</td>
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<td>EHI</td>
<td>Edinburgh Handedness Inventory</td>
<td>PTA</td>
<td>Post traumatic amnesia</td>
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<tr>
<td>ERP</td>
<td>Event-related potential</td>
<td>PTSD</td>
<td>Post traumatic stress disorder</td>
</tr>
<tr>
<td>FA</td>
<td>Fractional anisotropy</td>
<td>RBANS</td>
<td>Repeatable Battery for the Assessment of Neuropsychological Status</td>
</tr>
<tr>
<td>fMRI</td>
<td>Functional magnetic resonance imaging</td>
<td>rCBF</td>
<td>Regional cerebral blood flow</td>
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<tr>
<td>GCS</td>
<td>Glasgow Coma Scale</td>
<td>RT</td>
<td>Reaction time</td>
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<td>GECIT</td>
<td>Gabor Elements Contour Integration Task</td>
<td>SAC</td>
<td>Supervisory attentional control</td>
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<td>HADS</td>
<td>Hospital Anxiety and Depression Scale</td>
<td>SaLP</td>
<td>Schizoaffective-like psychosis</td>
</tr>
<tr>
<td>HC</td>
<td>Healthy control</td>
<td>SANS</td>
<td>Scale for the Assessment of Negative Symptoms</td>
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<th>Description</th>
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<td>SAPS</td>
<td>Scale for the Assessment of Positive Symptoms</td>
<td>TBIWP</td>
<td>Traumatic brain injury without psychosis</td>
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<tr>
<td>SCID</td>
<td>Structured Clinical Interview for DSM-IV Axis I Disorders</td>
<td>TD</td>
<td>Thought disorder</td>
</tr>
<tr>
<td>SCZ</td>
<td>Schizophrenia</td>
<td>TLC</td>
<td>Thought, Language, and Communication Index</td>
</tr>
<tr>
<td>SCZf</td>
<td>Schizophreniform</td>
<td>TLE</td>
<td>Temporal lobe epilepsy</td>
</tr>
<tr>
<td>SLP</td>
<td>Schizophrenia-like psychosis</td>
<td>TMT</td>
<td>Trail Making Test</td>
</tr>
<tr>
<td>SNK</td>
<td>Student-Newman-Keuls</td>
<td>ToM</td>
<td>Theory of mind</td>
</tr>
<tr>
<td>SOA</td>
<td>Stimulus onset asynchrony</td>
<td>TWFT</td>
<td>Thurston Word Fluency Test</td>
</tr>
<tr>
<td>SPECT</td>
<td>Single-photon emission computed tomography</td>
<td>WAIS</td>
<td>Wechsler Adult Intelligence Scale</td>
</tr>
<tr>
<td>sTBI</td>
<td>Severe traumatic brain injury</td>
<td>WRAT-R</td>
<td>Wide Range Achievement Test-Revised</td>
</tr>
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<td>TBI</td>
<td>Traumatic brain injury</td>
<td>Ψ</td>
<td>Psychosis</td>
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Chapter 1: Psychosis and Traumatic Brain Injury: An Introduction

1.1 An Introduction to Psychosis in Australia

The term *psychosis* refers to an abnormal condition of the mind (i.e., from the Greek; ‘psyche’ meaning mind/soul, and ‘osis’ meaning abnormal state or condition). Psychotic disorders, including schizophrenia, are characterised by distorted cognition and perception, blunted or inappropriate affect, unusual behaviour, and a decline in socio-occupational function (Fusar-Poli, McGuire & Borgwardt, 2011; Morgan et al., 2011; Pantelis et al., 2003; WHO, 2010). Hallucinations and delusions are most common, both of which are experienced by approximately four out of five Australians with a psychotic illness (Morgan et al., 2011; SANE Australia, 2011).

An Australian Government report based on the second Australian national survey estimated that approximately 63,533 people sought mental health services during 2010 for a psychotic disorder, the most common of which was schizophrenia (47% of all cases) (Morgan et al., 2011). This equates to 3.1 Australians for every 1,000 diagnosed with a psychotic disorder according to ICD-10 criteria. The same report found that more males than females (~61.2%), and more middle aged individuals (i.e., 35-64 years of age, 60.4%) were diagnosed. True to existing epidemiological studies, however, the mean onset of age was between 23-24 years, with the majority experiencing their first psychotic episode before the age of 25 (64.8%) (Morgan et al., 2011; SANE Australia, 2011).

A number of other comorbid psychiatric and health issues were highlighted by the report, including comorbid depression and/or anxiety in more than fifty per cent of individuals. Poor life skills, such as inadequate self-care, was reported by approximately one third (32.3%), as well as a predominance of distress related to socio-economic and socialisation problems (i.e., loneliness), even over and above the profound physical and mental health aspects of their illness (Morgan et al., 2011). Impaired cognition influences many aspects of patients’ lives, with several studies showing a relationship between poor cognition and quality of life (McGurk & Meltzer, 2000; McGurk, Twamley, Sitzer, McHugo, & Mueser, 2007). The cognitive profile of psychosis, and schizophrenia in particular, is discussed in detail in *Chapter Three*. 
An Introduction to Traumatic Brain Injury (TBI) in Australia

The Australian Department of Human Services and Health broadly defines acquired brain injury (ABI) as an: “injury to the brain which results in deterioration in cognitive, physical, emotional or independent functioning, … can occur as a result of trauma, hypoxia, infection, tumour, substance abuse, degenerative neurological diseases or stroke, … may be either temporary or permanent, and cause partial or total disability or psychosocial maladjustment” (Department of Human Services and Health, 1994, as cited in Fortune & Wen, 1999, p. xii). Traumatic brain injury (TBI) is an ABI that is characterised by external assault of blunt or penetrating impact, and/or from acceleration/deceleration forces (Fortune & Wen, 1999; Helps, Henry, & Harrison, 2008; Ponsford, Sloan, & Snow; 1995). Contusions can be both coup (i.e., tissue damage directly below the site of external impact with the skull) and contrecoup (i.e., damage loci diametrically opposite to the impact site, where the brain has moved rapidly within the skull in response to the force of impact and caused damage to tissue absorbing the force; effectively, the linear translation of the impact, see Figure 1.1) (Asha’Ari, Ahmad, Rahman, Kamarudsin, & Ishlah, 2011; Besenski, 2002; Hardman & Manoukian, 2002). Contrecoup contusions can occur without direct impact, and are common, for example, following the rapid acceleration/deceleration of the brain within the skull during high speed motor vehicle accidents (Besenski, 2002; Hardman & Manoukian, 2002; Weninger & Hertz, 2007).

TBI is typically defined as mild, moderate, or severe according to a range of criteria (Fortune & Wen, 1999; Helps et al., 2008; Ponsford et al., 1995). The standard criteria and their parameters for the determination of injury severity are contained in Appendix A; Table A.1. Consideration is normally given to the duration of both loss of consciousness (LOC) and post-traumatic amnesia (PTA) in the determination of injury severity.

In Australia during 2004-2005¹ an estimated 22,710 cases were hospitalised with traumatic brain injury (Australian Institute of Health and Welfare [AIHW], 2010; Helps et al., 2008). Approximately 4.3 per cent (n =976) of these cases were fatal (Helps et al., 2008), and direct hospitalisation costs were reported at $184 million (Helps et al., 2008). TBI-based hospitalisation rates are higher in males relative to females (2-2.5:1) and in youth/young adults (i.e., 15-24 year olds), as well as people aged 75 years and over (AIHW, 2010; Helps et al., 2008). According to the AIHW, the most common causes include falls, transportation-

¹ These are the latest figures tallied by the AIHW specific to traumatic brain injury in Australia.
related accidents, and assaults. This reflects records from previous years in Australia and internationally, perhaps with the exception of the United States where gunshot wounds represent a substantial aetiology (AIHW, 2010; Hardman & Manoukian, 2002; Helps et al., 2008; Fujii & Ahmed, 2002; Weninger & Hertz, 2007).

![Image 1.1](image1.jpg)

Figure 1.1. a) Severe contrecoup traumatic cortical laceration and haemorrhage of the right frontal pole following a blow in the left occipital region. Note. Injury exacerbated by right craniotomy and removal of “pulped” (sic) brain tissue prior to patient death. b) Horizontal section through the cerebral hemispheres illustrating the injury depth and severe oedema of the right cerebral hemisphere. Arrow indicates the left occipital site of impact, notice the larger size relative to the right, indicative of swelling. Taken from Goggio (1940).

Even where the injury is not life threatening, substantial and lifelong consequences of brain tissue damage may result. Research from various disciplines has indicated physical, cognitive, psychological, behavioural, and social impairments, the scopes of which are too great to list here. One famous case is that of Phineas Gage, who demonstrated in 1848 that pronounced personality change can follow damage to the frontal lobes of the brain (see Figure 1.2).

---

2 The cognitive neuropsychological profile of traumatic brain injury is a major focus of this thesis and is, thus, covered in extensive detail in Chapter Four.
Figure 1.2. a) Cabinet-card portrait of Phineas P. Gage (1823-1860), holding the tamping iron that injured him (left frontal lobe). b) Gage’s actual skull, photographed for his treating physician, Harlow, in Woburn, 1868. Taken from Jackson (1870).

Personality change described by his treating physician, John Martyn Harlow (1868, as cited in MacMillan, 2000):

The equilibrium or balance, so to speak, between his intellectual faculties and animal propensities, seems to have been destroyed. He is fitful, irreverent, indulging at times in the grossest profanity (which was not previously his custom), manifesting but little deference for his fellows, impatient of restraint or advice when it conflicts with his desires, at times pertinaciously obstinate, yet capricious and vacillating, devising many plans of future operations, which are no sooner arranged than they are abandoned in turn for others appearing more feasible. A child in his intellectual capacity and manifestations, he has the animal passions of a strong man. Previous to his injury, although untrained in the schools, he possessed a well-balanced mind, and was looked upon by those who knew him as a shrewd, smart businessman, very energetic and persistent in executing all his plans of operation. In this regard his mind was radically changed, so decidedly that his friends and acquaintances said he was “no longer Gage”. (p.13)

1.3 Neuroanatomical Potential for Organic Psychosis

The major theme of this thesis is psychosis following TBI (PFTBI). Given that the emergence of psychotic symptoms following a traumatic injury to the brain are taken to reflect neuroanatomical changes precipitated by the injury, a short review of the known neuroanatomical changes associated with both psychosis and TBI follows.
1.3.1 The neuroanatomy of psychosis.

Evidence of biochemical abnormalities have long been established in schizophrenia, with a particular focus on dopamine (DA) neurotransmission, and consensus regarding the general overactivity of DA systems; referred to as the DA hypothesis (Carlsson & Lindovist, 1963; Emanuele, Martinelli, Abbiati, Fusar-Poli, & Politi, 2012; Epstein, Stern, & Silbersweig, 1999; Rao, Kellom, Reese, Rapoport, & Kim, 2012; Sotovama et al., 2011). The advancement of magnetic resonance imaging (MRI) has also introduced substantial evidence for abnormal brain structure in major psychotic disorders (Fusar-Poli et al., 2011; Lawrie & Abukmeil, 1998; Pantelis et al., 2003; Velakoulis et al., 1999). Structural and functional cerebral abnormalities in psychotic patients have typically been demonstrated in frontal and temporal brain regions (Bachus & Kleinman, 1996; Borgwardt et al., 2007; Ellison-Wright, Glahn, Laird, Thelen, & Bullmore, 2008; Friston, Liddle, Frith, Hirsch, & Frackowiak, 1992; Honea, Crow, Palssingham, & MacKay, 2005; Horn et al., 2010; Lawrie & Abukmeil, 1998). Cortical white (frontal) and grey matter loss, with reduced medial and middle frontal, medial and superior temporal gyri, and dorsolateral prefrontal cortex, are considered characteristic of schizophrenia (Borgwardt et al., 2007; Ho et al., 2003; Honea et al., 2005; Mathalon, Sullivan, Lim, & Pferrerbaum, 2001; Pantelis et al., 2003; Pridmore & Bowe, 2010).

Studies have shown further that such reductions in grey matter may be associated with ‘at risk’ healthy individuals, as well as the onset and course of psychotic symptoms (Elkis, Friedman, Wise, & Meltzer, 1995; Lawrie et al., 1999; Mathalon, Sullivan, Lim, & Pferrerbaum, 2001; Pantelis et al., 2003; Roy, Zipursky, Saint-Cyr, Bury, & Langevin, 1998; Videbech, 1997; Velakoulis et al., 1999). Pantelis et al. (2003) investigated individuals at ultra high-risk of psychosis according to a combination of trait and state factors (see Yung et al., 1998 for ultra-high-risk classification). Those who transitioned showed reduced grey matter in the right prefrontal cortex, insular, and temporal cortex, basal ganglia, and the cingulate cortex, relative to those who did not (see Figure 1.3).

In the same study, Pantelis et al. (2003) rescanned the patients approximately twelve months after they had transitioned and reported further grey matter abnormalities particular to the left fusiform, parahippocampal, orbitofrontal, and cerebellar cortices. Accordingly, ongoing grey matter changes following symptom onset are apparent, and these changes appear to be isolated from the potential effects of antipsychotic medications, which may themselves alter grey matter volume; significant cortical reductions have been demonstrated
in medication-naïve patients (e.g., Pridmore & Bowe, 2010; Steen, Mull, McClure, Hamer, & Lieberman, 2006).

Others have shown that grey matter abnormalities may be linked to symptom profile. Empirical evidence has identified greater rates of cortical grey matter loss in patients with greater symptomatology and longer durations of hospitalisation (e.g., Mathalon, Sullivan, Lim, & Pferrerbaum, 2001), and according to isolated symptoms of thought disorder (e.g., Horn et al., 2010). Schaufelberger et al. (2011) reported more recently that initial grey matter differences between first episode patients and controls at baseline may actually be reversible in patients with a remitting course. Such findings substantiate a direct structural-functional relationship, whereby regenerative plasticity changes are linked with the remittance of symptoms, and vice-versa.

Figure 1.3. Grey-matter probability maps for baseline comparison of at risk individuals who developed psychosis versus those who did not. Red regions denote areas of reduced grey-matter volume in people who developed psychosis. Images are presented in standard radiological fashion, where right is left and vice versa. Z coordinate shows position of each slice with respect to the Talairach atlas. Clusterwise probability of type I error, $p < 0.004$, meaning less than one false-positive test is expected over the whole map. Taken from Pantelis et al. (2003).
While this is not an exhaustive discussion of the neuroanatomy of psychosis\(^3\), the intention here is to highlight important findings. Very generally, psychosis, and proneness to psychosis, has been consistently associated with cortical changes involving white and grey matter in the frontal and temporal lobes.

1.3.2 The neuroanatomical vulnerabilities of the brain to TBI.

Delicate brain tissue (e.g., neurons, axons, and dendrites) may be irrevocably damaged following even mild cerebral trauma. Tearing, stretching, bruising, bleeding, and swelling are likely to occur, especially in contrecoup injury where brain and bone collide (Bigler, 2007; Goggio, 1940). Because of the internal structure of the skull, the frontal lobe (posterior base) and temporal lobe (anterior pole) have an increased vulnerability to injury in instances of trauma. The brain sits within the anterior and cranial fossa of the skull, and in this position, the sphenoid bone (i.e., butterfly shaped bone forming part of the base of the skull, behind the nasal cavity and in front of the temporal bone) and tentorium cerebelli (i.e., extension of the dura matter, separating the cerebellum from the occipital lobes) are aligned with the frontal and temporal lobes respectively. These hard surfaces are thus perfectly positioned to absorb impacts and/or swift movements of the head that have propelled the brain forward or backward within the skull, invariably leaving the brain tissue that has come in contact with them damaged.

A range of intracranial lesions can occur, including extradural (between dura matter and skull), and subdural injury (between dura matter and the arachnoidal layer covering of the brain), as well as cortical contusion (bruising), and laceration (a contusion accompanied by tears in the pia-arachnoid). Depending on the severity of the injury, intracranial haemorrhage (ruptured blood vessel/s) is also likely, and significantly life threatening, and can be intra- and extra-axial (within the brain tissue, and within the skull but outside of the brain tissue, respectively) (Besenski, 2002; Goggio, 1940). Neuronal damage causes axons to swell, detach from the cell body, and release toxic levels of neurotransmitter into the synapse, causing the further cell death of neighbouring neurons\(^4\). This process is exacerbated in diffuse

\(^3\) For instance, other common brain changes in schizophrenia, not discussed here, include ventricular enlargement and reduced cortical folding (Cahn et al., 2002; DeLisi et al., 1997; DeLisi, Sakuma, Maurizio, Relja, & Hoff, 2004; Lieberman et al., 2001; Mane et al., 2009; Vita, De Peri, Silenzi, & Dieci, 2006).

\(^4\) The resilience of brain tissue has also been demonstrated, where neurons sprout new fibres and attempt to reconnect with undamaged neighbouring cells (Gravel, Weng, & Kriz, 2011). However, this is a delicate process
axonal injury (DAI), where damage occurs to widespread white matter tracts, rather than one or more isolated sites. Widespread neuronal cell death translates to the loss of connections between networks, disrupting the transfer of information within brain circuitry, and accounting for deficits in functionality in any given domain.

Again, rather than providing an exhaustive discussion, the intention of this overview is to highlight cortical areas with the greatest vulnerabilities to injury. The locus of injury following TBI depends on many factors, not least of which are the location and propelling or rotational force of the blow/acceleration/deceleration, as well as secondary injury as a result of haemorrhage, cell death, and/or swelling. Nonetheless, frontal and temporal lobe injuries appear to be chief among the findings, generally accounted for by the position of the brain within the skull.

1.3.3 Fronto-temporal association and example case study.

To say that traumatic brain injury and psychosis are causally linked simply because they both predominantly implicate fronto-temporal regions ignores the complexity of human brain structure and function. It also ignores empirical and clinical evidence. Psychosis following TBI is not as commonplace as psychiatric and neuropsychological sequelae (for instance, depression, anxiety, memory loss, and general cognitive deficits) (Lezak, 1979; Ponsford et al., 2011; Tate, Fenelon, Manning, & Hunter, 1991). It has already been shown that the degree of injury to a particular structure(s) of the brain with demonstrated specialised functionality does not necessarily predict neuropsychological outcome in that functionality, for instance, damage to hippocampal structures and memory impairment (e.g., Bigler, 2007). Nonetheless, in light of the preceding review, fronto-temporal commonalities appear to offer the best explanation for organically generated psychoses. However, this is not to say that other factors, such as heritability, environmental, and psychological/emotional stressors, are not involved in determining the vulnerability of any given individual for the development of psychotic symptoms (Bourque, van der Ven, Fusar-Poli, & Malla, 2012; Must, Janka, & Horvath, 2011).

The following is an excerpt taken from Bamrah and Johnson (1991). It is a case report detailing the injury, and subsequent pathology, of a young adult male over his lifetime. The and can be disrupted by multiple factors, including neuroexcitation which is prominent post injury given the elevated levels of neurotransmitter in the synapse.
case report illustrates, among other sequelae, the onset of psychosis following traumatic brain injury. Note that he had no prior personal or family history of psychosis, his first symptoms of psychosis were experienced thirteen years post injury, and generalised bilateral frontal lobe atrophy was later demonstrated on a computerised tomography (CT) scan.

The patient was involved in a car accident at the age of 27 years and sustained multiple fractures, including closed head injury involving fractures of the right skull bones. He was unconscious for over 12 hours, and had retrograde and anterograde amnesias upon recovery. Before the accident, he had worked as a busy salesman and was described by his wife as being a “very able” man. He had no previous history of psychiatric illness, alcoholism or any illness suggestive of cerebral disorder, and no psychiatric illness or epilepsy are reported in the family. Following the accident, he developed an amnestic syndrome, headaches, anxiety, tearfulness, and was unable to work. In fact, he never regained employment, and although according to his wife he remained fairly well between relapses while on medication, he lived a restricted life, in the extremely caring atmosphere of his family. His symptoms gradually worsened, and two years after the head injury he had his first attack of severe depression, with insomnia, hypochondriasis, and suicidal ideation, which responded to a course of electroconvulsive therapy (ECT).

At age 31, he developed focal epilepsy, associated with Jacksonian fits spreading from the left hand to the left arm, and occasional generalised tonic-clonic seizures with incontinence and unconsciousness lasting 10 minutes. The fits were controlled with phenobarbitone and phenytoin, which were discontinued 20 years later with no recurrence.

Between the ages of 32 and 35, he had three further episodes of depressive illness associated with three suicidal attempts; on each occasion he improved with ECT and antidepressants. At 40, he developed auditory hallucinations which subsided spontaneously; a year later he took a further overdose of drugs in response to commanding auditory hallucinations. He was convinced the voices were transmitted to him via a broadcasting device, and that thoughts were being removed from and inserted into his mind. He had thought disorder, persecutory delusions, and believed that his body had been programmed by a computer. In addition, his affect was depressed. His IQ (Wechsler Adult Intelligence Scale) was 99, and on the Wechsler Memory Scale and Williams Memory Tests, results were in line with the IQ estimate,
delayed recall was well preserved, and there was impairment of the verbal learning of new material. Bender Gestalt drawings were accurately reproduced. On the Eysenck Personality Inventory, his neuroticism score was high, his extraversion score low, compatible with a ‘dysthymic personality type’. Physical examination, routine blood tests, lumbar puncture and electroencephalography (EEG) were all normal. A course of chlorpromazine relieved his psychotic symptoms.

At the age of 48, he presented with similar symptoms associated with a depressive state which responded to trifluoperazine and amitriptyline. At 57 years, he again developed delusions of being controlled by a computer and of thoughts being removed from his mind by beams emitted by the computer, persecutory delusions, and third-person auditory hallucinations. Although routine investigations and EEG were again normal, a computerised tomography (CT) brain scan showed a generalised atrophy, predominantly in the frontal region.

Depot flupenthixol decanoate failed to control his symptoms but he responded to trifluoperazine which he continued until he was 58, when he presented with a manic psychosis. On admission, he was elated, sexually disinhibited, insomniac, and had loud, pressured speech. He believed he was exceptionally gifted, and described grandiose plans on space travel. He showed a copy of a poem he had sent to President Reagan about the space race, and thought his exploits would make his whole family rich. No schizophrenic first-rank symptoms were elicited. Flupenthixol decanoate (40mg every three weeks) and chlorpromazine (100mg per day) resolved his psychosis, allowing his discharge three weeks later. He was readmitted two weeks later in a hypomanic state. He was overfamiliar, elated, grandiose, had pressure of speech and, quite uncharacteristically, he had been drinking heavily. Lithium carbonate and thioridazine induced complete remission, with no recurrence of symptoms two years later. (pp.117-118)

1.4 Scope and Chapter Outline

This thesis is focused on the cognitive neuropsychological profile of psychosis following traumatic brain injury (PFTBI). The preceding sections of this chapter have established the neuroanatomical potential for the development of psychotic symptoms post cortical injury, and provided case study evidence of PFTBI. Chapter Two reviews the PFTBI
literature to date. Given that PFTBI is the chief focus of this thesis, and it has been relatively under-researched, a detailed review is provided of this literature. Chapters Three and Four provide an extensive review of the cognitive neuropsychological profile established in schizophrenia and TBI without psychosis (TBIWP) respectively. Chapter Five summarises these reviews according to the cognitive neuropsychological profiles of all three cohorts, identifies limitations in the existing literature, and the subsequent aims of this work. The study design of this research and a thorough description of the participant groups are contained in Chapter Six. Chapter Seven is an empirical chapter covering the hypotheses, methods, results, and discussion pertaining to each cognitive neuropsychological domain addressed in this thesis. Potential mediators of the reported cognitive neuropsychological performance are addressed in Chapter Eight, and Chapter Nine uses discriminant function analysis (DFA) to investigate whether cognitive neuropsychological performance can correctly classify participant group membership. Finally, Chapter Ten provides a general discussion and the overall conclusions arising from this work.
Chapter 2: Psychosis Following Traumatic Brain Injury (PFTBI)

2.1 Introduction

The relationship between traumatic brain injury (TBI) and psychosis has been reviewed a number of times in the past (David & Prince, 2005; Davison & Bagley, 1969; Kim, 2008). One of the earlier suggestions of this relationship was published during the seventeenth century when influential British physician Thomas Willis noted that “sometimes a great wound or concussion of the head, especially which happens by falling headlong from an (sic) high place, brings a prejudice and weakness to the animal faculty, dulling the understanding” (Willis, 1685, p.490). Two centuries later, empirical evidence arose from the analysis of substantial cohorts of brain injured patients following the Franco-Prussian War of 1870 (Davison & Bagley, 1969; Meyer, 1904). By the twentieth century, upon review of the work of his colleagues (prevalent German physicians at the time), and inspection of his own twenty-three cases, Meyer (1904) was convinced of the existence of what he referred to as “traumatic insanity”.

Today the relationship between TBI and psychosis remains poorly understood and relatively under-researched. Of the small number of cohort studies that exist ($N < 20$), conclusions are frequently tentative, or altogether lacking, due to considerable methodological limitations. For example, common empirical shortcomings are generated by constraints in recruitment, inconsistencies in diagnostic criteria, and reliance on patient recall (see Section 2.7 for full discussion). By contrast, substantial case study reports have been published, both of single (e.g., Bamrah & Johnson, 1991) and groups of cases (e.g., Rossell, Batty, & Hughes, 2010). However, the pooled analysis of single case studies compromises the comparability of assessment protocols, and small group case studies compromise statistical power, making it difficult to draw definitive conclusions with confidence. Generally researchers have instead opted to investigate the more prevalent, and in some ways more treatable, psychiatric sequelae post injury (e.g., depression and anxiety, Demakis, Hammond, & Knotts, 2010; Silver, Kramer, Greenwald, & Weissman, 2001; Whelan-Goodinson, Ponsford, Johnston, & Grant, 2009). Even so, the existing data strongly suggest that one of the consequences of traumatic insult to the brain can indeed be psychotic experiences and behaviour.

The common working reference in the field to psychosis thus induced is Psychosis Following Traumatic Brain Injury (PFTBI) (used throughout this thesis), or Psychotic
Disorder Due to Traumatic Brain Injury (PDTBI) (American Psychological Association; APA, 1994, p. 334). Persons who suffer with symptoms of psychosis following their injury live with a complex dual diagnosis that is often accompanied by substantial distress and disability. Along with the typically profound physical and cognitive effects of their injury, they represent a clinically complicated sample, often experiencing additional psychiatric comorbidities (e.g., depression and anxiety) (Fleminger, 2008; Koponen et al., 2002), drug and alcohol abuse/dependence (West, 2011; Westermeyer, 2006), and social isolation (Oddy, Coughlan, Tyermanz, & Jenkins, 1985; Xiang, Shum, Chiu, Tang, & Ungvari, 2010a).

This chapter provides a summarised review of PFTBI. Given the paucity of standardised research investigating this cohort, along with the considerable limitations of the published work to date, a generalised overview of PFTBI is provided from a number of perspectives germane to its phenomenology, including; prominent theories tackling the aetiology and nature of PFTBI, estimated prevalence, clinical assessments, cognitive neuropsychological data, neuroimaging and localisation data, and a discussion devoted to the substantial shortcomings of the work informing this information. The literature selected for review was principally confined to publications that have compiled and reported on a selection of case histories, rather than detailing the substantial number of available case histories individually here. Two large literature reviews were included, the first from Davison and Bagley (1969) because their work represented a novel and influential study at the time of publication, and the second from Corcoran and Malaspina (2007) because their review describes data from the four decades following. Work from Silver et al. (2001) was included as a stand-alone large epidemiological study. While epidemiological methodologies have their limitations, for instance, a reduced scope for the specificity of diagnostic criteria, they provide advantages in sample size ($N = 5034$). By contrast, the work from Buckley et al. (1993) was included because, due to their small sample ($N =5$), the authors were able to provide valuable neuroimaging data and clinical assessments obtained from standardised measures. They also restricted recruitment to a select group of cases where the development of psychotic symptoms clearly followed cerebral trauma. Finally, the case history published by Bamrah and Johnson (1991) was included, both to illustrate the experience of PFTBI from an individual case perspective (Chapter One presents this case in full), and because of the quality of information recorded for this patient, including clinical, cognitive, and neuroimaging data.
Other publications (i.e., Burg, McGuire, Burright, & Donovick, 1996; Fleminger, 2008; Koponen et al., 2002; 2006; Mainio et al., 2007), were not used where PFTBI trends were summarised because their psychotic sample were inadequately defined (i.e., psychiatric and psychotic cases formed one cohort). However, their work was referred to in discussion. Another large review of the literature from David and Prince (2005) was omitted from the summary of trends because the authors incorporated a number of studies reviewed here, including Davison and Bagley (1969), Achte, Hillbom, and Aalberg (1969), and Wilcox and Nasrallah (1986). The remaining studies were chosen for review on the basis that they made a contribution to one or more of the domains of interest, and were not already covered by existing reviews summarised here. Appendix B contains the full list of the publications used in this review.

2.2 Prominent Aetiological Theories

Theoretical attempts to define the aetiology of PFTBI have been made since the earliest suggestions of a relationship between head trauma and psychotic symptoms. Prominent figures as early as Kraepelin⁵, suggested that childhood head trauma might play a causal and/or supplementary role in the later development of schizophrenia (Kraepelin, 1913). While our understanding remains in its infancy, this idea is still favoured in the literature, with only a few exceptions.

Figure 2.1 illustrates five prominent theories that have been proposed to date in the explanation and conceptualisation of the relationship between traumatic brain injury and psychosis. First, it has been suggested that traumatic brain injury can lead to a phenocopy of schizophrenia (i.e., as the ‘stress’ component in stress-diathesis theory). That is, the brain injury activates an existent hereditary susceptibility for schizophrenia in an individual (Corcoran & Malaspina, 2007; Kim, 2008). The second theory denotes that traumatic brain injury can lead to psychotic symptoms that resemble the spectrum of psychoses (stress-diathesis relationship). In this model the injury initiates a genetic predisposition in the same way as the first, but this account allows for the conceptualisation of psychosis as existing on a continuum, where healthy personality traits that are indicative of psychosis-proneness exist at one end and diagnosable schizophrenia exists at the other (see Verdoux & van Os [2002] for

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⁵ Kraepelin was responsible for early conceptualisations of psychiatric disease as a consequence of biological and genetic sources.
Figure 2.1. Schematic depicting five prominent conceptualisations of the traumatic brain injury and psychosis/schizophrenia relationship.
review of the psychosis continuum). The genetic predisposition thus causes the individual to be liable to any condition along the continuum (Corcoran & Malaspina, 2007; Kim, 2008).

Third, it has been suggested that traumatic brain injury causes the development of a unique set of psychotic symptoms (Kim, 2008). Here, genetic liability is less influential. Instead, the injury is responsible for a chain reaction of structural and/or functional changes in the brain that instigate psychosis (i.e., organic psychosis). The psychosis may or may not resemble functional schizophrenia, but should be conceived of as unique given its origin. Current DSM-IV (APA, 1994) criteria allow for diagnosis of cases fitting this type under “psychotic disorder due to a general medical condition”.

Fourth, a case for “reverse causality” has been proposed, where the existence of psychosis increases the likelihood of trauma. This is simply an acknowledgement of the increased prevalence of injury in the psychotic population (not confined to head trauma), and does not explain neurological insult prior to the development of psychotic symptoms (David & Prince, 2005; Nielsen et al., 2002). This has not stopped researchers, however, from proposing this theory as an explanation for the observed PFTBI relationship (e.g., David & Prince, 2005), or looking to rates of injury in schizophrenia cohorts for PFTBI prevalence estimates (e.g., Nielsen et al., 2002, discussed in Section 2.3). Last, a spurious relationship has been suggested whereby TBI and psychosis share no actual relationship, rather psychosis-proneness (or genetic vulnerability) increases the likelihood of both psychosis and trauma (Corcoran & Malaspina, 2007). Here genetic proneness is the causal mediating factor that accounts for an erroneously observed relationship between brain injury and psychosis.

The first three theoretical models are fundamentally identical, differing only in their definition of the subsequent psychosis, and thus, the importance of genetic liability (i.e., DSM-IV diagnosed schizophrenia has an established genetic component which is not necessarily true for the manifestation of psychotic symptoms generally; e.g., Egan et al., 2001; McGuffin, Asherson, Owen, & Farmer, 1994). Essentially, the first three models propose that the brain injury acts to demonstrate some causality in the ensuing psychotic symptoms. However, genetic liability (at least with respect to heritability) cannot be discounted, nor should it be a necessary component of PFTBI. Whether the action of the injury is to trigger existing liability to psychosis, or to generate and/or initiate structural/functional liability should not be a defining aspect of the model, given that the existence of PFTBI has already been demonstrated in individuals both with (e.g.,
AbdelMalik, Husted, Chow, & Bassett, 2003) and without genetic liability (e.g., Fujii & Ahmed, 2001). Thus, a reasonable assumption from the existing literature would be that the injury can instigate the development of psychotic symptoms in both types of individuals, and this should be reflected in the model accordingly.

The move to define psychotic outcome by distinguishing between a collection of hypothetically “unique” psychotic symptoms, or schizophrenia as it is currently classified, is impractical. This is because the classification of psychotic outcome can only be informed by thorough and standardised clinical and neuropsychological assessment of cases with PFTBI in the first instance; either the demonstrated profiles will resemble profiles established in schizophrenia, or they will be unique. The fact that more than one theoretical model exists, each a proponent of a different conceptualisation of the ensuing psychosis, only provides evidence that the necessary empirical testing is yet to be undertaken\(^6\). As identified by the second model, the last decade of research has reconceptualised psychosis generally, where psychotic thoughts, experiences, and behaviour, exist on a continuum (i.e., a psychosis spectrum), rather than as categorical distinctions *per se* (Badcock & Dragovic, 2006; Myin-Germeys, Krabbendam & van Os, 2003; Verdoux & van Os, 2002). In this sense, the proposed categorisation of symptoms in the first model is somewhat theoretically out-dated.

Finally, as already discussed, claims of reverse causality offer an incomplete, and subsequently inadequate, picture of dually diagnosed patients. Similarly, the prospect of a spurious relationship relies on the genetic liability of a patient, and can therefore be discounted by PFTBI research that has recruited PFTBI cases without genetic liability (e.g., no familial or personal history of psychosis, for instance, Fujii & Ahmed, 2001). Accordingly, the most accurate reflection of the PFTBI literature to date appears to be the theoretical explanation offered by the second theory (Corcoran & Malaspina, 2007; Kim, 2008), provided the requirement for genetic liability is removed. Simply put, it appears that traumatic insult to the brain can instigate psychotic symptoms, possibly both temporary and lifelong, and that the mechanism of action may occur via both pre-existing genetic liability and/or changes in structural/functional brain neuroanatomy, along with the influence of any other risk factors established in the literature (e.g., environment, socio-economic status etc.) (see Figure 2.2).

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\(^6\) An aim of this thesis is to inform the psychotic conceptualisations of PFTBI primarily with regard to the neuropsychological profile, but also, as a secondary aim, with regard to the clinical profile.
2.3 Prevalence and Onset Latency

2.3.1 Prevalence.

Davison & Bagley’s (1969) influential review presents both the lowest (0.7%) and highest (9.8%) estimates of psychosis prevalence within a TBI cohort. The approximate ten per cent variability in their estimates probably indicates the influence of methodological inconsistencies across their chosen studies, and thus, the poor comparability of the studies generally. Nonetheless, in reviewing the available research between 1917 and 1964 the authors provided a valuable and novel contribution to the literature, estimating an increased risk for the development of schizophrenia somewhere between two to three times greater in the TBI population (Davison & Bagley, 1969). Elsewhere estimates range from 3.4 per cent (Silver et al., 2001) to 9.2 per cent (Fujii, Ahmed, & Hishinuma, 2004). Figure 2.3 summarises estimates from the currently available literature where authors have determined psychosis within a brain injured population.
Silver et al. (2001) determined a 3.4 per cent prevalence using data from a New Haven sample (portion of the National Institute of Mental Health [NIMH] Epidemiologic Catchment Area programme). Psychosis, specifically schizophrenia, was identified by the NIMH Diagnostic Interview Schedule which is based on DSM-III diagnostic categories. Rates of head injury, however, were determined by the yes/no response to one direct question; “Have you ever had a severe head injury associated with loss of consciousness or confusion?” It is possible that confinement to ‘severe’ head injury defined by loss of consciousness/confusion may be responsible for a reduced estimate in this research. While the likelihood of PFTBI is probably greater following a severe trauma, the risk post mild to moderate injury cannot be discounted (Fann et al., 2004). In fact, Achte et al. (1969) reported higher rates of schizophrenia in patients who had suffered mild compared with severe TBI. On the other hand, discounting medical confirmation and other usual definitive

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7 McKeon, McGuffin, and Robinson (1984) report the case of a sixteen year old girl who developed obsessive-compulsive neurosis the day after having been hit on the back of the head by her mother with a hair brush. At the time of the publication (eight years post), she had had ongoing symptoms for which she had been admitted to hospital. The girl had no noteworthy premorbid history. While this is not an illustration of psychotic disorder it serves as evidence of the vulnerability of the brain, in this case demonstrating almost immediate pathology following an extremely mild injury.
injury characteristics (e.g., localisation, duration of loss of consciousness, clear definition of severity etc.) may have led to inflated rates from the population in Silver et al.’s (2001) work. In addition, the authors failed to collect any temporal information, leaving both the direction of the PFTBI relationship (i.e., whether the TBI occurred before or after the emergence of psychotic symptoms), and the duration of the time period in between (i.e., onset latency) unclear.

Fujii et al. (2004) recruited hospital inpatients over a five year period. During this time, twenty-four of two hundred and sixty one (9.2 per cent) met the criteria for PFTBI. These were patients already identified for a follow up neuropsychological assessment after having illustrated poor performance on measures of attention, planning, and visual Gestalt during their intake screen. These domains are known to be affected in both psychosis (Evans, Chua, McKenna, & Wilson, 1997; Joshua & Rossell, 2009; Mitchie et al., 2000) and following traumatic brain injury (Brosseau-Lachaine, Gagnon, Forget & Faubert, 2008; Schmitter-Edgecombe, 1996). As such, the selection criteria employed by Fujii et al. (2004) may be responsible for an inflated estimate relative to Silver et al. (2001). However, the diagnostic criteria applied to both psychosis and traumatic brain injury was relatively more stringent in the Fujii et al. (2004) study; psychosis was determined by DSM-IV criteria and TBI severity by the duration of loss of consciousness, an excepted and typical yardstick in the literature (see Appendix A) (Buckley et al., 1993; Hoofien, Gilboa, Vakil, & Donovick, 2001).

Another reason for the discrepancies in prevalence estimates across studies may be differences in the conceptualisation of psychosis. Where some studies have included cases with one or more psychotic symptoms (e.g., Achte et al., 1969; Fann et al., 2004) others have confined their estimates to DSM-IV diagnosed schizophrenia (e.g., Silver et al., 2001). Additionally, those using broader definitions of psychosis may have included diagnoses not traditionally considered psychotic per se. For instance, Achte et al. (1969), who estimated a prevalence of 8.9% psychosis in men injured during the Finnish war, included diagnoses of Korsakoff’s syndrome, “grave dementia” and borderline psychotic cases (n =7) in their estimate. Such methodologies would increase prevalence estimates relative to those applying more stringent criteria.

Estimates on PFTBI prevalence must further consider possible shortcomings in diagnosis generally, especially where recruitment is driven by the identification of cases according to pre-existing diagnosis, and without further follow-up of patients. Given the greater prevalence of psychiatric sequelae post TBI, the misdiagnosis of PFTBI cases may
potentially occur where symptoms identified as psychiatric in TBI patients may actually be masking underlying psychosis. For example, negative psychotic symptoms and/or thought disorder may be mistaken for depression, and selected positive symptoms, such as grandiosity, for mania.

Where psychotic patients have instead been screened for their history of TBI the rates are generally much higher. This is because collecting lifetime TBI rates collapses data from both pre- and post-psychotic onset. Given that injury rates tend to be higher in psychotic populations when they are ill this method provides an inflated, and subsequently unreliable, estimate of PFTBI prevalence (e.g., Corcoran & Malaspina, 2007; Murrey, Starzinski, & LeBlanc, 2004). However, Wilcox and Nasralla (1986) assessed schizophrenia inpatients for childhood TBI, where incidents of trauma were restricted to injury that occurred before age ten, and reported a prevalence of 11%. By contrast, Nielsen et al. (2002), who restricted traumatic brain injury to the fifteen years prior to diagnosis, reported only 2.2% prevalence. This estimate is notably reduced compared with others assessing the history of TBI in psychotic cohorts (11%-17.05%, Figure 2.4), and is particularly interesting relative to the estimate provided by Wilcox and Nasralla (1986). With respect to the two estimates, the data may be indicative of a greater vulnerability to the development of psychosis following childhood TBI (e.g., before the age of ten; Wilcox & Nasralla, 1986), relative to teenage/adulthood injury (Nielsen et al., 2002). Fujii and Ahmed (2001) found an increased risk for PFTBI in patients who had experienced their injury prior to adolescence. However, Harrison et al. (2007) found an increased risk for non-affective psychosis, specific to those exposed to a head injury after the age of ten. On the other hand, the reduced estimates produced by Nielsen et al. (2002) may instead be explained by the authors’ stringent TBI criteria; cases must have been hospitalised with concussion or severe head trauma). By contrast, Wilcox and Nasralla (1986) incorporated any patient who had a lost consciousness for longer than one hour following their injury, likely to be classified as a moderate injury (see Appendix A). Figure 2.4 illustrates estimates of TBI prevalence taken from psychotic populations in the available literature.
2.3.2 Onset latency.

The literature also disagrees with regard to the onset latency of psychosis post TBI. Investigations have suggested that the greatest rates of psychosis onset occur in less than one year post TBI (Davison & Bagley, 1969; Fann et al., 2004), at the approximate five year mark (Fujii & Ahmed, 2001; Nielsen et al., 2002; Sachdev et al., 2004), and greater than ten years post injury (Achte et al., 1969; Bamrah & Johnson, 1991). Figure 2.5 summarises psychosis onset latency according to the reviewed publications reporting this information. From these data it appears that the onset of symptoms occurs at a comparable frequency for each latency band, with the exception of the five to ten year mark post TBI where the rates are approximately half. The apparent spread of onset latency may simply reflect individual differences in the development of psychotic symptoms where vulnerability is increased due to brain trauma. That is, the greatest predictor of the timing of onset may be a set of individual factors unrelated to the injury, such as, for example, familial support, environmental stressors, and resilience. Further, onset latency is likely to be mediated by injury variables, socio-environmental factors, resilience characteristics, and social/familial support have demonstrated influence in the onset of psychotic symptoms in prone individuals, and improved treatment outcome (e.g., Albert et al., 2011; Bourque et al., 2012; Must et al., 2011; Smieskova, Fusar-Poli, Riecher-Rossler, & Borgwardt, 2012).
such as the severity of the injury and lesion location. Fujii and Ahmed (2002) reported that significantly more cases with mild brain injury had a shorter time lag between their injury and the development of psychotic symptoms, relative to the severe cases that generally showed a longer latency before psychosis onset. Such a trend is somewhat counterintuitive, however, it should be noted that the majority of the cases they reviewed had unspecified injury severity, and thus, these findings were based on a small number of patients. In general, the data presented in Figure 2.5 should be considered cautiously given that it is drawn from the average of latency figures provided by studies with incompatible methodologies, especially with regard to defining their target (i.e., dual diagnosis) sample.

![Figure 2.5](image.png)

*Figure 2.5. Onset latency taken from the reviewed studies providing this information (see Table 2.1 for details). The percentage of patients within each latency band (collapsed across studies, i.e., mean value) is presented. The number of studies included in the equation for each latency band is indicated by “n”.*
Table 2.1 contains details of each publication reviewed in this section for their prevalence and onset latency estimates. In particular, the sample size, proportion of gender, onset latency data source, and diagnostic criteria employed for both TBI and psychosis are described in the table. These variables are likely to have had a substantial influence over the prevalence estimates made in each study, and the source for onset latency information is a vital determinant of the accuracy of this data (e.g., hospital records with documented standardised assessments versus patient recall). Accordingly, in review-based publications where the data sources are generally unknown, such as the one from Davison and Bagley (1969), the durations reported between injury and psychosis onset (i.e., onset latency) must be considered with some caution.

Given that such a large discrepancy exists between prevalence estimates using cohorts of TBI patients and those using cohorts of psychotic/schizophrenia patients, it is apparent that these two approaches are measuring different phenomena. Because the focus of this thesis is psychosis following traumatic brain injury (PFTBI), the lower estimates taken from TBI cohorts are most applicable. From the reviewed data then, it appears that the prevalence of PFTBI is in the order of 1.35 - 9.2% of individuals who experience a traumatic brain injury. It further appears, as already stated, that the onset of psychotic symptoms can occur anywhere from within the first year following injury, to more than ten years post injury. A number of other variables that may influence these estimates, and thus possibly warrant further investigation, include lesion location, injury severity, individual differences in post injury support, environment, and resilience characteristics, and the potential for the misdiagnosis of PFTBI cases.

2.4 Clinical Profile

Comprehensive and systematic assessment of the clinical presentation of PFTBI is yet to be undertaken. An overview of the clinical picture reported to date is contained in Table 2.2. In brief, the clinical profile in PFTBI appears indistinguishable from that of schizophrenia, in so far as all diagnostically salient symptoms characteristic of schizophrenia have also been reported in PFTBI. This includes, i) positive symptoms, which refer to abnormal thoughts and behaviours such as delusions, hallucinations, and disorganised behaviour and language; ii) negative symptoms, which refer to the absence of responses that are normally present in speech, emotion, and behaviour, and, iii) cognition, including
<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>N</th>
<th>Gender (%)</th>
<th>Estimated Prevalence % (n)</th>
<th>Onset Latency (%)</th>
<th>Diagnostic Criteria</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>TBI</td>
<td>Ψ</td>
<td>Data Source*</td>
</tr>
<tr>
<td>Achte et al.</td>
<td>1969</td>
<td>3552</td>
<td>100 M</td>
<td>100 M</td>
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<td>Hospital records</td>
</tr>
<tr>
<td>Corcoran &amp; Malaspina</td>
<td>2007</td>
<td>2732</td>
<td>-</td>
<td>-</td>
<td>17.05 (22)</td>
<td>-</td>
</tr>
<tr>
<td>Davison &amp; Bagley</td>
<td>1969</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.7-9.8 (median 1.35)</td>
<td>Multiple (literature review)</td>
</tr>
<tr>
<td>Fann et al.</td>
<td>2004</td>
<td>3756</td>
<td>51 F</td>
<td>-</td>
<td>3.6 (34)</td>
<td>HMO computerised records</td>
</tr>
<tr>
<td>Fujii &amp; Ahmed</td>
<td>2001</td>
<td>284</td>
<td>-</td>
<td>96 M</td>
<td>8.8 (25)</td>
<td>Retrospective chart review</td>
</tr>
<tr>
<td>Fujii et al.</td>
<td>2004</td>
<td>69</td>
<td>52.4 F</td>
<td>100 M</td>
<td>9.2 (24)</td>
<td>-</td>
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<tr>
<td>Murrey et al.</td>
<td>2004</td>
<td>3,133</td>
<td>59.6 M</td>
<td>-</td>
<td>16.73 (524)</td>
<td>-</td>
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</table>

*(continued)*
Table 2.1
Estimates of PFTBI Prevalence and Onset Latency (continued)

<table>
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<th>Author</th>
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<th>N</th>
<th>Gender (%)</th>
<th>Estimated Prevalence % (n)</th>
<th>Onset Latency (%)</th>
<th>Diagnostic Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>TBI Ψ</td>
<td>&lt;1yr 1-5yrs 5-10yrs &gt;10yrs</td>
<td>&lt;1yr 1-5yrs 5-10yrs &gt;10yrs</td>
<td>TBI Ψ</td>
</tr>
<tr>
<td>Nielsen et al.</td>
<td>2002</td>
<td>91,168</td>
<td>88.9 M -</td>
<td>2.2 (180)</td>
<td>27.2 36.1 36.7 (&gt; 5yrs)</td>
<td>Hospitalised concussion/s TBI; ICD-8 codes</td>
</tr>
<tr>
<td>Silver et al.</td>
<td>2001</td>
<td>5034</td>
<td>61.9 M -</td>
<td>3.4 (73) -</td>
<td>-     -     -     -</td>
<td>Solitary question - have you ever had a severe injury associated with loss of consciousness or confusion? SCZ inpatients; ICD-8 codes</td>
</tr>
<tr>
<td>Wilcox &amp; Nasralla</td>
<td>1987</td>
<td>659</td>
<td>- -</td>
<td>11.0 (22)</td>
<td>-     -     -     -</td>
<td>TBI &lt; 10yrs old LOC &gt; 1 hour Hospital charts</td>
</tr>
</tbody>
</table>

Note. M = Male; F = Female.
†represents mean value of all participants in years, SD = 4.4 (range 1-23 years).
*source pertaining to onset latency data only.
impairments in memory, the executive functions, and often a generalised intellectual deficit (APA, 1994; 2000). The symptoms of schizophrenia are described in detail in Chapter Three.

Preliminary work from Fujii and Ahmed (2002) has, however, highlighted the reduction of negative symptoms as a possible diagnostic distinction between PFTBI and schizophrenia. Using a retrospective chart review, the data collected by Fujii and Ahmed (2002) showed a small number of cases with negative symptoms (i.e., eight of fifty-five; 14.55%). Nonetheless, their hypothesis may be premature. First, because five of the seven publications reviewed here included data on the clinical assessment of negative symptoms in PFTBI, and in each case negative symptoms were evident (see Table 2.2). This may suggest that the data from Fujii and Ahmed (2002) reflects a sample bias, although the same could be said for any of the other five publications that have reported on negative symptoms, especially because sample sizes are relatively small.

Second, schizophrenia is notoriously heterogeneous in its clinical presentation, and negative symptoms are not a requirement for diagnosis. According to the DSM-IV-TR (APA, 2000) only two symptoms must be present from any one of the three categories; positive, negative, and/or cognitive (see Chapter Three for details). Thus, it is possible to receive a diagnosis of schizophrenia without the presence of negative symptomatology. As such, there is no real basis for the hypothesis that reduced negative symptoms offer a diagnostically distinct profile from that of schizophrenia as it is currently conceptualised.

It is imperative to acknowledge that because of intrinsic complexities in the identification, recruitment, and testing of PFTBI patients, the available literature on clinical symptoms is notoriously incomplete. Even where data exists for each of the symptom types, the data gathered from retrospective chart reviews typically summates fragmented information that is difficult to verify (three of the seven studies reviewed here fall into this category, see Table 2.2). As well as missing information, charts are often incompatible, even where standardised measures have been used. These gaps in the literature may, in fact, create an incomplete picture of the PFTBI symptom profile that is misleading in its current resemblance of the existing profile for functional schizophrenia. This would be compounded further by the fact that schizophrenia itself is diagnostically variable as already mentioned.

Accordingly, it is too early to compare symptom rates with any real clinical significance; the majority of work that has reported the phenomenological characteristics of
### Table 2.2
**Available Data on the Symptom Profile of PFTBI**

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>N (n(^{Ψ}))</th>
<th>Diagnosis</th>
<th>Method</th>
<th>Clinical Assessment</th>
<th>Positive Symptoms†</th>
<th>Negative Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achte et al.</td>
<td>1969</td>
<td>3552 (317)</td>
<td>SCZ (24%)</td>
<td>Retrospective chart review</td>
<td>Psychiatrist notes-unlikely standardised</td>
<td>Paranoid (22%)</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>pSCZ (22%)</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bamrah &amp; Johnson</td>
<td>1991</td>
<td>1</td>
<td>SCZf</td>
<td>Treating clinician</td>
<td>-</td>
<td>Persecutory</td>
<td>Auditory</td>
</tr>
<tr>
<td>Buckley et al.</td>
<td>1993</td>
<td>5</td>
<td>SLP SaLP</td>
<td>Research psychiatrist</td>
<td>DSM-III-R SAPS/SANS</td>
<td>80% positive symptoms</td>
<td>100%</td>
</tr>
<tr>
<td>Davison &amp; Bagley</td>
<td>1969</td>
<td>-</td>
<td>-</td>
<td>Literature review</td>
<td>-</td>
<td>Paranoid (80%)</td>
<td>-</td>
</tr>
<tr>
<td>Fujii &amp; Ahmed</td>
<td>2001</td>
<td>46 (25)</td>
<td>PFTBI</td>
<td>Retrospective chart review</td>
<td>DSM-IV</td>
<td>Paranoid (72%)</td>
<td>Auditory (60%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Visual (8%)</td>
<td></td>
</tr>
<tr>
<td>Fujii &amp; Ahmed</td>
<td>2002</td>
<td>69*</td>
<td>PFTBI</td>
<td>Retrospective chart review</td>
<td>DSM-IV</td>
<td>68.1%</td>
<td>Auditory (92.9%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Visual (32.2%)</td>
<td></td>
</tr>
<tr>
<td>Sachdev et al.</td>
<td>2001</td>
<td>90 (45)</td>
<td>SLP</td>
<td>Retrospective chart review</td>
<td>DSM-IV</td>
<td>100%</td>
<td>Auditory (84.4%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Visual (20%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Tactile (4.4%)</td>
<td></td>
</tr>
</tbody>
</table>

†Cognitive symptoms are reviewed in Section 2.5.

* N = 55 for data on negative symptoms.
PFTBI has relied on the compilation of available chart information, thus the likelihood for inaccuracies is substantial. In addition, most of the work has defined PFTBI grossly as “psychosis”, without recording individual symptom information (e.g., Burg et al., 1996; Koponen et al., 2002; 2006), and no work has provided a statistical comparison of the clinical profiles of matched PFTBI and schizophrenia patients. As such, there is currently a significant void in the literature. 9 Systematic examination of the clinical presentation of PFTBI using standardised clinical interviews and measures is vital for accurate diagnosis and treatment. Attempting to draw any definitive conclusions about the clinical presentation of PFTBI, and its similarities and differences compared to functional schizophrenia, is premature until this has been done.

2.5 Cognitive Neuropsychological Profile

Akin to the clinical profile, very little research has been published detailing the cognitive neuropsychological profile in PFTBI. A summary of the available data to date is contained in Table 2.3. From this work, it appears some common deficiencies in language and vocabulary (e.g., Fujii et al., 2002; 2004; Sachdev, Smith, & Cathcart, 2001), verbal memory (e.g., Fujii et al., 2004; Sachdev et al., 2001), and verbal learning (e.g., Bamrah & Johnson, 1991) may be paramount in PFTBI. Such deficits have been shown both in comparison to norms provided by standardised measures (e.g., Bamrah & Johnson, 1991; Fujii et al., 2004) and with matched injury groups (e.g., Sachdev et al., 2001). Studies that have used a comparison group, consisting of either healthy controls or TBI cases without psychosis, also suggest that PFTBI may be associated with a generalised IQ deficit (e.g., Fujii et al., 2004; Sachdev et al., 2001).

Work from Fujii et al. (2004) and Sachdev et al. (2001) may further provide preliminary evidence that the severity of the brain injury is less influential than the psychosis in determining neuropsychological performance. PFTBI and TBI control patient chart information was compiled in both of these research studies. Fujii et al. (2004) did not match injury severity across groups, in fact, the PFTBI group had substantially more mild injuries than the TBI group, who generally had more moderate to severe injuries (mild; 16/7 and

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9 As noted in Section 2.2, a secondary aim of this thesis is to perform statistical comparisons of the clinical profiles obtained for matched PFTBI and schizophrenia cohorts.
moderate to severe; 6/9 for PFTBI and TBI groups respectively)\(^\text{10}\). Despite their lesser injury, the PFTBI group performed more poorly than the TBI group on all neuropsychological tests, with the exception of the Trail Making Task (TMT, Forms A and B; Reitin & Wolfson, [1985], the list of tests are contained in Table 2.3). The TMT is a commonly used executive function task (i.e., processing speed, attention, and mental switching), and poorer performance would be anticipated by more severe brain injury as was shown. Unfortunately, the authors did not perform group-wise analyses on this data, instead choosing to compare each patient group with a set of norms. Nonetheless, this descriptive data provides an interesting indication of the relative influence of injury and psychosis on cognitive neuropsychological performance.

By contrast, while Sachdev et al. (2001) did match their injury groups on both severity and lesion location, the PFTBI cohort again showed significantly reduced performance on measures of verbal/nonverbal memory and executive function. Thus, because the groups were matched, it appears that the presence of psychosis in the PFTBI cohort accounted for their poorer neuropsychological performance. There was, however, a trend for the PFTBI cohort to have more left/bilateral temporal, and right parietal injury, differences that were no longer significant following Bonferroni correction. Given the established hemispheric laterality for language (i.e., the left hemisphere is dominant during verbal tasks, covered in detail in Chapter Four), the locus of injury in some PFTBI patients may also explain some of the reduced performance in verbal memory. Since, (i) this is the only study offering a group-based, analyses-driven indication of the role of lesion location in PFTBI cognitive performance and, (ii) lesion location was not statistically different across groups, this suggestion is, however, made very tentatively. By contrast, for instance, the case study presented by Bamrah and Johnson (1991) also showed deficits in verbal learning in particular, yet the CT scan taken of this patient’s brain indicated a generalised (and especially frontal) atrophy, rather than localised left hemisphere lesions (Figure 2.6).

The summary of trends presented in this section is done so with additional caution for two reasons. First, because it is based on only four publications, one of which is a single-sample case study, and second, because methodologically these publications contain serious empirical limitations. In particular, all of the existing cognitive neuropsychological data

\(^{10}\) Statistical comparisons were not run by the authors so it is unclear whether these differences in injury severity are significant.
<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>N</th>
<th>Diagnosis</th>
<th>Method</th>
<th>Assessment</th>
<th>Comparison</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bamrah &amp; Johnson</td>
<td>1991</td>
<td>1</td>
<td>PFTBI</td>
<td>Case study</td>
<td>WAIS (IQ), Wechsler Memory Scale &amp; Williams Memory Tests</td>
<td>Norms</td>
<td>Normal range IQ and memory/recall. Impaired verbal learning</td>
</tr>
<tr>
<td>Fujii &amp; Ahmed</td>
<td>2002</td>
<td>69*</td>
<td>PFTBI</td>
<td>Retrospective chart review</td>
<td>Various/inconsistent</td>
<td>Norms</td>
<td>88% impaired; 58.82% memory, 41.18% executive function, 41.18% visuo-spatial, 11.76% language, 11.76% attention</td>
</tr>
<tr>
<td>Fujii et al.</td>
<td>2004</td>
<td>69</td>
<td>PFTBI</td>
<td>Retrospective chart review</td>
<td>WAIS, Logical Memory (immed. recall), Vocabulary, Block Design &amp; Similarities subtests, Trail Making Test (A&amp;B), Verbal Fluency, Wisconsin Card Sorting Test.</td>
<td>Norms &amp; healthy control data from elsewhere</td>
<td>Lower IQ, impaired vocabulary, verbal memory (recall) and executive functioning (relative to controls after Bonferroni correction)</td>
</tr>
<tr>
<td>Sachdev et al.</td>
<td>2001</td>
<td>90</td>
<td>SLP</td>
<td>Retrospective chart review</td>
<td>Various/inconsistent</td>
<td>SLP v TBI</td>
<td>Lower IQ, verbal and nonverbal memory, and frontal executive function impairments</td>
</tr>
</tbody>
</table>

* N = 17 for cognitive neuropsychology data.
† Consists of 24 PFTBI and 24 schizophrenia patient charts (remainder = 21 TBI).
published to date has been based on case study or retrospective chart review alone. Thus, again, even where standardised assessments have been used the methodology is not consistent, and results are not necessarily complete or comparable across cases. Well conducted empirical studies using standardised research tools are required to further elucidate the cognitive neuropsychological profile of PFTBI\textsuperscript{11}. This information is vital in the creation and/or adaptation of treatment programs to best support this cohort.

2.6 Neuroimaging and Localisation

Comprehensive empirical event-related potential (ERP) investigations (i.e., averaged time-locked electroencephalographic [EEG] responses to specific stimuli that provide an

\textsuperscript{11} Standardised assessment of the cognitive neuropsychological profile in PFTBI is the major aim of this thesis.
indication of information processing, such as visual, auditory, somatosensory etc.) have not been published using PFTBI cohorts. Existing electroencephalograms in PFTBI (i.e., the recording of spontaneous electrical activity in the brain, that is, the voltage fluctuations that arise from ionic current flows within neurons) have typically been obtained for diagnostic purposes, for instance, where seizures are apparent, and/or the extent of injury is unclear. Hillbom (1960) reported that approximately 53% of his substantial collection of post-war cases (N=3552) had undergone EEG assessments of this kind, and the majority of these were obtained for patients with mild to moderate injury severity. According to Hillbom (1960), the excess of mild/moderate EEG recordings in his dataset likely reflect the use of EEG data as a tool of injury confirmation, given that ex-servicemen had an incentive to fabricate or exaggerate their condition in order to meet criteria for financial compensation at the time. Unfortunately, Hillbom (1960) did not detail EEG outcome according to case diagnosis and so findings particular to dually-diagnosed patients from his work are not available.

The work from Fujii and Ahmed (1996; 2002) has probably been the most informative by providing summarised indications of EEG abnormalities in PFTBI. In both case history reviews these authors reported a predominance of temporal lobe abnormalities, along with a history of seizures in the majority of the case histories studied in their 1996 review (Fujii & Ahmed, 1996; 2002). More than 70% of cases (i.e., 29 of 41) reviewed by them in 2002 illustrated evidence of EEG scan abnormalities. The majority of these showed slowing (i.e., reduced number of neural oscillations over time [termed frequency]; strictly a reduction in the number of sine waves recorded per second, which is often, but not confined to, a symptom of seizure). However, spiking (i.e., ‘bursts’ of high frequency sine waves shown in gamma [25-100Hz] and delta [0-4Hz] frequency bands, and also common in seizure patients) and dysrhythmia (i.e., a term for EEG abnormalities, usually rated in grades from I-V classifying various theta-delta intensity/frequency or rhythmic activity including spikes and seizure; Mayo Clinic [1991]) was also reported. While temporal abnormalities were chief (45.71%), Fujii and Ahmed (2002) also described instances of frontal (14.29%), parietal (5.71%), occipital (14.29%), central (2.86%), and diffuse (17.14%) impairment, with no differences in regard to the hemispheric location of EEG abnormalities across their sample. Their data provides an indication of the common neurophysiological abnormalities accompanying psychotic symptoms post traumatic brain injury. Due to the lack of empirical publications, however, it is unclear how these compare to neurophysiological function following TBI. Slowing, spiking, and dysrhythmia, especially as epileptiform (i.e., seizure)
activity, is characteristically shown on EEG scans from TBI patients (Ronne-Engstrom & Winkler, 2006; Wallace, Wagner, Wagner, & McDeavitt, 2001). Focal abnormalities are also commonly shown in frontal and temporal regions, and, less commonly, in the parieto-occipital regions (Ronne-Engstrom & Winkler, 2006; Wallace et al., 2001). On the other hand, normal EEG was reported on two occasions for the case study presented by Bamrah and Johnson (1991), where both substantial psychiatric and psychotic symptoms were experienced over the patient’s lifetime post TBI.

Alternative neuroimaging techniques (e.g., magnetic resonance imaging [MRI], computerised tomography [CT]) have shown that both left and right frontal and temporal lesions are most commonly associated with PFTBI (Achte et al., 1969; Fujii & Ahmed, 2002; Hillbom, 1960; Wilcox & Nasrallah, 1986). Reduced volume of these areas has been associated with schizophrenia for some time (McAllister & Ferrell, 2002). Yet, again, this data may be inconsequential given the scarcity of empirical research to date. Similar to the existing EEG publications, the majority of structural data identifying the locus of injury has not compared localisation rates across PFTBI and non-psychotic TBI groups, and thus, it is plausible that the current data reflects common injury localisation in TBI generally. This would seem likely given that frontal and temporal sites have an increased vulnerability to injury due to the position of the brain within the skull (discussed in Chapter One). Work by Hillbom (1960), Sachdev et al. (2001) and Wilcox and Nasrallah (1986), who did compare control non-psychotic TBI groups, also support this idea. No significant differences were shown in lesion location across comparison groups by any of these studies. Table 2.4 compiles current PFTBI imaging data and Figure 2.7 illustrates the percentage rates of localisation according to this data anatomically.

Of course, as discussed in Chapter One, the relationship between structural neuroanatomy and psychotic symptoms remains largely unclear in light of the patient heterogeneity reported in the literature. Because the regions implicated in schizophrenia are interconnected it is feasible that neuroanatomic disturbances originating from various and/or numerous locations may result in similar psychotic outcomes. However, it is interesting to note the absence of diffuse axonal injury (DAI, of comparable injury severity) in the PFTBI literature, perhaps a feature of PFTBI worth further investigation. The empirical neuroimaging data in PFTBI is, overall, extremely limited, and like other subjects of investigation in PFTBI, considerable further research is required.
Figure 2.7. TBI localisation rates in PFTBI according to the existing literature.

2.7 Existing Methodological Limitations and Future Recommendations

As discussed throughout this chapter, substantial methodological weaknesses are a frequent theme in the PFTBI literature. Data pooling, despite discordant information, represents one of the more flawed practices. Chart review-based studies, which constitute the majority of available research, tend to draw conclusions about symptom trends even where substantial amounts of data are missing on measures of interest (Burg et al., 1996; Fujii & Ahmed, 2002). Similarly, critical literature reviews have typically pooled data from studies with incompatible methodologies and attempted to draw meaningful conclusions about PFTBI cohorts as a whole (e.g., Davison & Bagley, 1969).

Recruitment is often confined to hospital inpatients or chart information taken from inpatient wards, and in one circumstance potential cases were sought from a list of TBI patients referred for further neuropsychological testing (Fujii & Ahmed, 2001). These are the worst cases and miss mild to moderate brain injured patients who may be experiencing mild psychotic symptoms (Burg et al., 1996; Fujii & Ahmed, 2001; Malaspina et al., 2001), or experiencing other psychiatric symptoms that are inadvertently concealing their symptoms of
<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>N (nΨ)</th>
<th>Diagnosis (%)*</th>
<th>Localisation method</th>
<th>Hemisphere</th>
<th>Lobe</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achte et al.</td>
<td>1969</td>
<td>3552 (317)</td>
<td>SCZ (24%)</td>
<td>Case record</td>
<td>Bilateral</td>
<td>Frontal (23.8%) Temporal (20.4%) Parietal (15.3%) Basal (14.3%)</td>
<td>Basal lesions most frequently psychotic</td>
</tr>
<tr>
<td>Bamrah &amp; Johnson</td>
<td>1991</td>
<td>1</td>
<td>SCZf</td>
<td>CT</td>
<td>Generalised atrophy</td>
<td>Frontal</td>
<td></td>
</tr>
<tr>
<td>Buckley et al.</td>
<td>1993</td>
<td>5</td>
<td>SLP (60%)</td>
<td>MRI</td>
<td>Left</td>
<td>Temporal</td>
<td>Left temporal lesions in SLP cleanly differentiated groups</td>
</tr>
<tr>
<td>Fujii &amp; Ahmed</td>
<td>1996</td>
<td>15</td>
<td>PFTBI</td>
<td>EEG/SPECT/CT/MRI</td>
<td>Bilateral</td>
<td>Temporal/Frontal</td>
<td>Right temporal lesions most common</td>
</tr>
<tr>
<td>Fujii &amp; Ahmed</td>
<td>2002</td>
<td>69</td>
<td>PFTBI</td>
<td>EEG/CT/MRI</td>
<td></td>
<td>Fontal (33.3%) Temporal (21.7%) Ventricles (15.9%)</td>
<td></td>
</tr>
<tr>
<td>Hillbom</td>
<td>1960</td>
<td>3552 (498)</td>
<td>TBI &amp; Ψ†</td>
<td>Case record</td>
<td>Bilateral</td>
<td>Temporal</td>
<td>Left (and bilateral) temporal lesions most frequently psychotic</td>
</tr>
<tr>
<td>Sachdev et al.</td>
<td>2001</td>
<td>90 (45)</td>
<td>SLP</td>
<td>CT</td>
<td>Bilateral</td>
<td>Temporal/Parietal</td>
<td></td>
</tr>
<tr>
<td>Wilcox &amp; Nasrallah</td>
<td>1987</td>
<td>659 (200)</td>
<td>PFTBI (11%)</td>
<td>Case record</td>
<td>Bilateral</td>
<td>Temporal</td>
<td></td>
</tr>
</tbody>
</table>

* The percentage value is provided in the ‘Diagnosis’ column where this number differs from (nΨ).
† Case histories of men injured during the war. Temporal order of psychosis and injury unclear.
psychosis (i.e., symptoms of depression co-occurring with affective flattening, Fleminger, 2008; Koponen et al., 2002; Mainio et al., 2007). There are a number of indications in the literature that mild injury can precede the development of psychosis. For example, higher rates of psychosis have been shown in patients who have suffered a mild injury when compared with those who have suffered a severe injury on two occasions; Achte et al. (1969) and Fujii et al. (2004). Further, Fujii and Ahmed (2002) reported that PFTBI patients with milder injury tended to have shorter onset latency (i.e., the period between injury and the development of psychotic symptoms).

Related to a bias in recruitment, a number of studies, particularly in the earlier research, have reported on servicemen/war veterans with penetrating skull injuries (Achte et al., 1969; Corcoran & Malaspina, 2007; David & Prince, 2005; Davison & Bagley, 1969). While these data are valuable because of their robust sample sizes, there are obvious limitations to their generalisability to later PFTBI populations, both because of the inflated rates of skull penetrating injuries, and the introduction of additional confounding psychopathology that may be specific to war injuries, for example, post-traumatic stress disorder.

Diagnostic criteria, concerning both the identification of a traumatic brain injury and the presence of psychosis, are often not standardised (e.g., Achte et al., 1969). A significant traumatic brain injury is commonly identified in research by self-report, and the relevant details are obtained from a patient’s recall of the prior injury. As noted earlier, in some instances this is drawn from a simple yes/no response to one question (Fann et al., 2004; Silver et al., 2001). Elsewhere however, there are strict criteria applied to determine the existence and severity of a traumatic brain injury (Deb, Lyons, Koutzoukis, Ali, & McCarthy, 1999; Max et al., 1997). Similarly, a number of different methods have been used to define TBI severity; Glasgow Coma Scale (GCS; Teasdale & Jennett [1974], e.g., Max et al., 1997), duration of loss of consciousness (Buckley et al., 1993; Hoofien et al., 2001), length of coma, duration of post-traumatic amnesia (PTA; Koponen et al., 2006), and ICD-10 codes (Fujii & Ahmed, 2002; Harrison et al., 2006). These are not necessarily compatible and thus make the task of determining a relationship between injury severity and psychotic outcome difficult.

Psychotic patients are also more likely to want to attribute their psychiatric disturbances to a physical cause, and thus, more likely to report a TBI. In some cases, diagnoses of psychosis have been made from available chart notes alone (Corcoran & Malaspina, 2007; Kim, 2008). As discussed in Section 2.2, disparity is also shown in the conceptualisation of the subsequent psychotic symptoms; some research has focused on elucidating the potential for organic schizophrenia (AbdelMalik et al., 2003; Corcoran & Malaspina, 2007; Kim, 2008; Malaspina et al., 2001; Nielsen et al., 2002), whereas others have conceptualised the link to psychotic symptoms along a continuum
(Buckley et al., 1993; David & Prince, 2005; McAllister & Ferrell, 2002; Wilcox & Nasrallah, 1986).

Retrospective recall bias is a further considerable issue in PFTBI investigations. Much of the work has relied on recall for a number of criteria, especially when collecting data relating to personal and family history (e.g., Burg et al., 1996). This is shown most in large community-based prevalence investigations where questionnaires are widely distributed (Fann et al., 2004; Silver et al., 2001). Generally, relying on recall is subject to potential inaccuracies, and this risk is exacerbated within brain injured and potentially psychotic populations who are known to carry cognitive and neuropsychological deficiencies, particularly in memory (Malaspina et al., 2001; Silver et al., 2001).

Further inconsistencies arise in the recording and assessment of personal and family history of psychosis. Research has both; (i) failed to assess personal history of psychosis in those presenting with PFTBI (Burg et al., 1996; Fujii & Ahmed, 2002), and (ii) collapsed groups with and without psychoses prior to a TBI in their investigations (Fann et al., 2004). It is essential that these are reliably recorded and separated in analyses to work toward understanding the nature and/or direction of the relationship between psychoses and traumatic brain injury. Because genetic liability in schizophrenia is well established (Kim, 2008; Kumar et al., 2010), family history should also be reliably ascertained to move toward assessing potential aetiological (i.e., genetic) similarities between PFTBI and schizophrenia.

Many of the limitations discussed here are at least partially a consequence of the inherent difficulties in the recruitment and assessment of a PFTBI cohort. If the existing prevalence estimates are accurate then prevalence appears to be between 0.7% and 9.2% of patients who sustain a TBI (Davison & Bagley, 1969; Fujii et al., 2004). This would explain the prominence of case study and retrospective chart or database reviews in the literature. Nonetheless, theorised conceptual models of the relationship between traumatic brain injury and psychosis are premature until substantial investigations, that are comprehensive and standardised, and that address the methodological confounds discussed in this review, are undertaken. This is required across all domains reviewed here. Only then can we begin to obtain a true picture of the PFTBI phenomenon.
Chapter 3: Cognitive Neuropsychological Deficits in Psychosis

3.1 Introduction

3.1.1 Schizophrenia.

Schizophrenia is a severe mental disorder characterised by a range of disturbances in thought, perception, emotion, and behaviour. It is diagnosed in approximately one per cent of the general population, typically becoming evident during adolescence or early adulthood and persisting for life (Breier & Berg, 1999; Loebel et al., 1992; Szymanski et al., 1995; Torrey, 1987). It is diagnosed in more men than women (i.e., with a male: female ratio as high as 1:4; McGrath, 2006), and commonly carries with it a range of comorbid mental health issues, particularly substance use and mood disorders (Baynes et al., 2000; Braga, Mendlowicz, Marrocos, & Figueira, 2005; Breier & Berg, 1999).

The symptoms of schizophrenia are generally categorised as positive, negative, and cognitive (Andreasen & Olsen, 1982; Kay, Fiszbein, & Opler, 1987; Liddle, 1987). Positive symptoms reflect the presence of abnormal thoughts and behaviours, and include delusions (i.e., false beliefs maintained in the face of overwhelming contradictory evidence), hallucinations (i.e., perceptual experiences similar to true perceptions but not resulting from the stimulation of a sense organ), and disorganised behaviour and language (e.g., motor immobility, stupor, excessive and apparently purposeless motor activity, or peculiarities of voluntary movement (APA, 2000; Colman, 2009). Disorganised language is most commonly referred to as thought disorder. As early as 1919, Kraepelin referred to the incoherence of thought and anomalous thought processes, and these are believed to be observable via patient language. For example, patients may demonstrate disorganised or incoherent speech and alogia (i.e., poverty of speech or poverty of content) (Andreasen & Grove, 1986; McGrath, 1991).

Negative symptoms reflect the absence of responses that are normally present, and include affective flattening (i.e., reduced expression of emotion), avolition (i.e., difficulty initiating or sustaining purposeful behaviour), alogia (i.e., poverty of speech or speech content), and apathy (APA, 2000; Colman, 2009). The cognitive symptoms of schizophrenia include deficits in memory, insight, and executive function, including attention and planning (Andreasen & Grove, 1986; Goldman-Rakic, 1994). A generalised intellectual impairment has also been established, and although a sub-group of patients with “normal” or above average IQ has also been illustrated, patients typically perform poorly across most cognitive domains (Henry & Crawford, 2005).

According to the DSM-IV-TR (APA, 2000) diagnostic criteria, any two symptoms must be present for a significant part of one month and interfere with one of three spheres of life: personal
hygiene, occupational functioning, or social interaction. These disturbances must continue for at least six months (although they may be attenuated for some of this time), and must not be better explained by a diagnosis of schizoaffective disorder, bipolar disorder, or personality disorder (APA, 2000). The symptoms of schizophrenia combine heterogeneously from patient to patient in both presence (absence) and severity (Andreasen & Olsen, 1982; Kay et al., 1987; Liddle, 1987). In acknowledgement of this, the DSM-IV-TR (2000) identifies five subtypes, including (i) paranoid schizophrenia (i.e., characterised by prominent delusions and hallucinations with relatively preserved intelligence), (ii) disorganised schizophrenia (i.e., the essential features of which are disorganised speech and behaviour, and affective flattening or inappropriate affect), (iii) catatonic schizophrenia (i.e., characterised by marked psychomotor disturbance manifested as physical immobility, excessive or peculiar movement, mutism, or echolalia), (iv) undifferentiated schizophrenia (i.e., featuring patterns of symptoms indicative of schizophrenia but not easily resembling the aforementioned subtypes), and (v) residual schizophrenia (i.e., at least one previous episode of schizophrenia but currently without prominent positive symptoms). Irrespective of subtype, irregular patterns of thinking, perceptual anomalies, variable emotions, and behavioural peculiarities combine to make schizophrenia particularly disturbing for individuals with the disorder (Braga et al., 2005; Breier & Berg, 1999).

A century of focused research has committed to investigating the cognitive neuropsychological domains that are deficient in schizophrenia. To date, the literature reflects a handful of broad domains for which consistent impairment has been shown. These include: visual-perceptual organisation (including visual Gestalt processing), language and memory (including verbal fluency and semantic processing), reasoning (including probabilistic reasoning), executive functioning (including attention, mental inhibition and switching, and processing speed), and generally reduced intelligence. A detailed review and discussion of the literature pertaining to each of these domains follows.

### 3.2 Visual-Perceptual Organisation

#### 3.2.1 Gestalt processing: A definition.

Visual *Gestalt* (German, meaning ‘figure’, ‘form’ or ‘structure’) processing refers to the perceptual organisation of visual stimuli into coherent and intelligible forms, rather than an array of unrelated visual elements (Chey & Holzman, 1997; Sternberg, 2003; Uhlhaas & Mishara, 2007). Gestalt theory offers an explanation for the human perception of form; how we perceive parts of objects as integrated wholes based on their configuration, pattern and/or context\(^\text{12}\) (Sternberg, 2003; Uhlhaas & Mishara, 2007). This tendency for perceptual organisation is explained by a number of Gestalt principles including; figure-ground, proximity, similarity, continuity, closure and the principle of symmetry, *See Figure 3.3.*

\(^{12}\) This tendency for perceptual organisation is explained by a number of Gestalt principles including; figure-ground, proximity, similarity, continuity, closure and the principle of symmetry, *See Figure 3.3.*
Uhlhaas & Mishara, 2007). In fact, the catchcry of Gestalt theory, “the whole is greater than the sum of its parts”, goes further to acknowledge the essentiality of perceptual organisation abilities in the facilitation of visual cognition (Cutting, 1989; Sternberg, 2003). For example, without this ability, Figure 3.1 is no more than an assortment of black dots. However, when seen as a Gestalt or whole image, a schematic ‘smiley face’ is perceived; two eyes and a mouth. A more complex example is shown in Figure 3.2. Perceived in parts, Figure 3.2 shows a series of white ‘blobs’ on a black background, yet, when these ‘blobs’ are perceptually organised into a whole or ‘Gestalt-based’ image an agitated male face is perceivable. Von Ehrenfels referred to this concept as ‘Gestaltqualität’ (form quality), where the unified pattern of elements creates an extra dimension that cannot be derived from the basic summation of its component parts (Cutting, 1989).

Considering Figure 3.1 once more, for example, the sum of the eleven black dots is meaningless; the face is apparent in the configuration of dots, perceivable only by applying Gestalt principles.

![Figure 3.1. Schematic ‘smiley’ face perceived via Gestalt processing.](image1)

![Figure 3.2. Mooney face (Mooney, 1957); Perceived via configural (Gestalt) processing.](image2)

### 3.2.2 In schizophrenia: A history.

Figureheads in the study of schizophrenia, for instance Kraepelin and Bleuler, failed to consider the role of perceptual processing in the symptomatology of schizophrenia (Kraepelin, 1913; Uhlhaas & Mishara, 2007). However, by the 1950’s (e.g., Conrad), and again in the 1980’s
(e.g., Matussek), links between symptoms and sensory processing abnormalities had been made (Conrad, 1954; John & Hemsley, 1992). Maher (1974) famously identified a fundamental anomaly in sensory input and perceptual processing in his cognitive account of delusion formation. More recently, cognitive neuropsychology has provided empirical evidence for deficiencies in the earliest stages of sensory processing in patients, especially the perceptual organisation of sensory stimuli (Parnas et al., 2001; Schwartz-Place & Gilmore, 1980; Silverstein, Kovacs, Corry, & Valone, 2000). In the tradition of Maher (1974), one line of research has concentrated on disruptions of visual processing in schizophrenia and potential pathways from impaired early visual processing to the development and maintenance of hallucinations and delusions (see Cutting, 1989; Uhlhaas & Mishara, 2007).

Figure 3.3. Examples of Gestalt principles: a) proximity b) similarity c) continuity d) closure e) symmetry. Images taken from Sternberg (2003).

\[\text{Figure 3.3. Examples of Gestalt principles: a) proximity b) similarity c) continuity d) closure e) symmetry. Images taken from Sternberg (2003).}\]

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\[\text{According to Maher (1974), delusions are the result of entirely normal and intact cognitive explanations sought to rationalise abnormal percepts.}\]
Perception involves the interaction of existing knowledge with incoming sensory input at all stages of processing. Changes in the organisation of the perceptual field are thus likely to impact perception and cognition (Uhlhaas & Mishara, 2007). Koehler (1947, as cited in Uhlhaas & Mishara, 2007p. 145) explained that “it is precisely the original organisation and segregation of circumscribed wholes which make it possible for the sensory world to appear so utterly imbued with meaning... in its gradual entrance into the sensory field, meaning follows the lines drawn by organisation.” That is, the ability to perceptually organise visual information in a way that facilitates the cognitive appreciation of that information within its context (i.e., via Gestalt processing) is vital to healthy perception. The identification of visual elements, objects, and parts seems to remain intact in schizophrenia (for example, patients readily identify a car, a bird, a house), but these are disjointed rather than parts of a scene (for example, of a neighbourhood home). This context (i.e., the neighbourhood home) is vital in the logical and meaningful assessment of otherwise fragmented objects in the environment (John & Hemsley, 1992).

3.2.3 Research in schizophrenia.

The disintegration of Gestalt processing has been shown in experimental paradigms (Joshua & Rossell, 2009; Parnas et al., 2001; Rief, 1991; Schwartz-Place & Gilmore, 1980; Silverstein et al., 2000), and in subjective phenomenological accounts related to the onset of psychosis (Cutting, 1989; Uhlhaas & Mishara, 2007). Cutting and Dunne (1986) reported that at least fifty per cent of patients could clearly remember a perceptual change relating to the onset of their illness. Accounts of this change unequivocally implicate disruptions to the essential Gestalt:

Everything I see is split up. It’s like a photograph that’s torn into bits and put together again. If somebody moves or speaks, everything I see disappears quickly and I have to put it together. (Uhlhaas & Mishara, 2007, p. 144)

I was surrounded by a multitude of meaningless details...I did not see things as a whole, I only saw fragments: a few people, a dairy, a dreary house. To be quite correct, I cannot say that I did see all that, because these objects seemed altered from the usual. They did not stand together in an overall context, and I saw them as meaningless details... My impressions did not flow as they normally do... (Cutting, 1989, p. 431)

She remembered that she could not look at the whole door. She could only look at the knob or some corner of the door. The wall was fragmented into parts. (Uhlhaas & Mishara, 2007, p. 144)
Paradigms have been designed to further elucidate the nature of specific perceptual organisation and Gestalt processing inabilities, should isolated inabilities exist (Knight, Manoach, Elliott, & Hershenson, 2000; Silverstein et al., 1996). For instance, patients have been shown to differentially process stimuli made up of non-contiguous (i.e., non-touching) non-configural (i.e., do not require holistic/Gestalt processing) elements relative to controls (Silverstein et al., 1996). This implicates a deficit at the initial stage of basic visual element organisation, and may be supported further by work showing that NMDA receptors, implicated in proficient perceptual organisation via glutamatergic excitation, may be hypoactive in schizophrenia (Olney, Newcomer, & Farber, 1999; Phillips & Singer, 1997). Additionally, although some literature is contentious (e.g., Chey & Holzman, 1997), processing of non-contiguous configural stimuli that relies on Gestalt principles to be perceived, such as the Mooney face (Mooney, 1957, Figure 3.2), seems to be fundamentally disrupted in patients (Buchanan et al., 1994; Joshua & Rossell, 2009; Rabinowicz, Owen, Opler, & Knight, 1996; Silverstein et al., 2000). On the other hand, there is some evidence to suggest that the perceptual organisation of visual elements to symmetrical stimuli, also requiring Gestalt processing, may be intact (Knight et al., 2000).14

Of course, poor performance by patients on tasks attempting to capture a breakdown in visual perceptual organisation may reflect, at least in part, other illness-related factors. Intelligence, reduced short term/working memory abilities, general medications effects (e.g., slowed reaction times), and negative symptoms such as apathy and reduced motivation would all be expected to influence task performance. However, in general, these factors have been discounted in this field and replicable visual organisation deficits are reported (see Parnas [2001] for example).

Schwartz-Place and Gilmore (1980) showed that the performance of patients with schizophrenia was reduced relative to healthy controls when they were asked to determine the number of lines (i.e., ranging from zero to six) amongst distracter stimuli (i.e., circles amongst the lines; circles create the “noise” condition, see Figure 3.4a for example stimuli). However, the opposite trend in performance (i.e., reduced accuracy from healthy controls instead) was shown when the orientation and proximity of the lines was manipulated, but no distracter stimuli/noise conditions were introduced (see Figure 3.4b). This is evidence of a deficit in the capacity of patients to perceptually organise visual features into perceptual wholes (i.e., Gestalt) based on similarities in their properties because, in the first experiment, which patients were unable to do well, the

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14 The degree to which perceptual organisation was necessary for the task used by Knight et al. (2000) is questionable. Their data may instead reflect the intact featural (i.e. objects, parts etc.) processing ability already established in schizophrenia.
Figure 3.4. Sample stimuli from Schwartz-Place & Gilmore (1980): a) experiment one, “noise” condition (p. 411), b) experiment two, orientation and proximity of stimuli manipulated, condition without “noise” (p. 414).

Figure 3.5. Sample card taken from the Gabor Elements Contour Integration Task (GECIT; Kovacs et al., 2000). The circular figure must be identified amongst the distracters (shown here in the bottom left corner). Illustrates the figure-ground Gestalt principle.
organisation of the stimuli into groups of lines and circles facilitates the speed and accuracy of the task. Thus, patients were at a disadvantage because, theoretically, they were visually processing the stimuli as individual lines (i.e., distinct “parts”). Conversely however, this strategy of processing gave them an advantage in the second experiment, where the habitual tendency to perceptually group the lines was not conducive to the task. These findings were later replicated by Wells and Leventhal (1984).

Further evidence comes from Silverstein et al. (2000) who showed reduced performance by patients on a contour integration task. Cards are presented to participants that contain non-contiguous dashes, where a select few of the dashes form a circle among the distracter dashes. Participants need to be able to apply Gestalt principles to detect the circular grouping (i.e., figure) amongst the distracters (i.e., ground, see Figure 3.5 for an example of this task; the Gabor Elements Contour Integration Task [GECIT]; Kovacs, Polat, Pennefather, Chandna, & Norcia, 2000).

Proficient Gestalt processing in schizophrenia has also been shown. Chey and Holzmen (1997) demonstrated Gestalt processing in patients with schizophrenia over two experiments. However, a closer look at their paradigm reveals that these data may be misleading. The authors requested that participants identify whether a certain stimulus ‘part’ presented on screen had come from the whole stimulus that they had been shown for five seconds prior. It stands to reason that both patients and controls could adequately complete this task given that both Gestalt processing strategies (presumably employed by controls) and featural/part processing strategies (presumably employed by patients) would be effective in the identification of matching parts to the original whole stimulus. If the breakdown in Gestalt processing in schizophrenia is accurate, patients may even have an advantage in a task of this nature, which may explain the faster reaction times reported by Chey and Holzmen (1997) for patients relative to controls.

Work from Rief (1991), however, showed that while global/Gestalt processing abilities are reduced in patients, this disadvantage may be relative according to the salience of the Gestalt properties in the visual image. Using the paradigm established by Schwartz-Place and Gilmore (1980), Rief (1991) found that where the salience of the Gestalt was strong, for example when all six non-contiguous lines in the shape of a hexagon were presented, patients did in fact perceive the global Gestalt. However, in the three line condition, where the hexagon shape is obscured, patients appeared to be processing the lines as local information (i.e., line by line). This is consistent with the proposal that rather than being unable to utilise Gestalt principles in visual processing, patients

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15 This task would further be confounded by reliance on working memory load. Schizophrenia patients have established deficits in working memory (Brebin, Bressan, Pollowsky, & David, 2011; Ehrlich et al., 2011), discussed in section 3.4 Memory.
are instead less influenced by the global features of visual displays (Chey & Holzman, 1997; Landgraf et al., 2011; Rief, 1991).

Attempts to trace the degradation of visual organisation over the course of the illness (i.e., cross-sectionally) have also been made. Parnas et al. (2001) administered three visual binding tests, (i.e., contour integration, the Müller-Lyer illusion, and the global/local letter test, see Figures 3.6a-c) to four groups; a group of chronic re-admitted schizophrenia patients, first episode patients, prodromal schizotypal disorder patients, and a group of hospital staff controls. Chronic patients illustrated the worst performance across all visual binding tasks, confirming reduced perceptual organisation in schizophrenia. Interestingly though, the prodromal patients exhibited superior performance, even relative to controls. Given the deterioration of perceptual organisation in schizophrenia, it may be that the prodromal phase is marked by an enhancement in Gestalt detection and processing. Theoretically then, the development of the illness into diagnosable schizophrenia would be accompanied by the development of enhanced Gestalt processing into Gestalt deterioration (Parnas et al., 2001). Just prior to illness onset and/or during their first episode of psychosis, individuals often describe symptoms that would support this interpretation (see Cutting, 1989). For example; “Out of these perceptions came the absolute awareness that my ability to see connections had been multiplied many times over” (Uhlhaas & Mishara, 2007, pg. 146). Further, there is evidence that the prodromal phase is associated with hyper-reactivity in the magnocellular visual pathway (Keri & Benedek, 2007). Such evidence may offer a biological basis for enhanced intensities of visual stimuli, and these are likely to facilitate superior Gestalt detection (Parnas et al., 2001). Of note, the prodromal patients in Parnas et al.’s (2001) investigation showed intermediate results (as anticipated) on a range of cognitive measures. This is an important indication that accurate evidence of superior Gestalt detection during the prodrome phase was shown, rather than a data-based inaccuracy specific to the prodromal group (Parnas et al., 2001).

The work from Parnas et al. (2001) provides some insight into illness chronicity and relative perceptual deficits, but in general the literature remains unclear. When compared with an outpatient group, the breakdown in visual perceptual organisation was observed in inpatients only (Silverstein et al., 2000). Such findings conflict with evidence of Gestalt processing deficits in (i) schizotypal personality (i.e., a healthy personality trait known to share the neurocognitive profile in schizophrenia, Goodarzi, Wykes, & Hemsley, 2000) and, (ii) healthy first degree relatives (Surguladze et al., 2011).
Figure 3.6. Example Stimuli from Parnas et al. (2001). a) Contour Integration; Some of the lines have the same orientation. The figure can be segregated from the ground because of the saliency of figure-defining contour elements. In this example, a square appears on the right of the figure. b) Muller-Lyer Illusion, The horizontal lines here are of equal length but the right one appears longer. c) Global vs. Local Processing; Participants have to focus either on the global (‘T’) or the local (‘F’) letter.

Where healthy but psychosis-prone individuals illustrate comparable deficits the implication is for a trait, rather than state, impairment. Yet, abnormalities in perceptual organisation have been associated with disorganised symptoms in particular (Knight & Silverstein, 1998; Silverstein et al., 2000; Uhlhaas, Phillips, & Silverstein, 2005; Uhlhaas, Phillips, Mitchell, & Silverstein, 2006), but not positive, negative, or general symptoms (Knight & Silverstein, 1998). Moreover, Uhlhaas et al. (2005) demonstrated that visual perceptual organisation improved significantly as disorganised symptoms were reduced in patients undergoing treatment, and this implicates state-related perceptual impairments instead.

Essentially, the literature points to a perceptual organisation deficit that may be somewhat heterogeneous in its degree. This is reflective of most aspects of the illness. It may be that alternative illness-related factors (e.g., intelligence, working memory etc., as mentioned) account quite nicely for some of the heterogeneity in findings, and/or that variation in perceptual organisation abilities across research studies are simply reflective of basic individual differences. Nonetheless, a preference for local information processing (i.e., over global/Gestalt processing) appears viable in schizophrenia.

3.3 Language

3.3.1 General language deficits.

Language is inextricably linked to the core communication-based characteristics of schizophrenia (Bellani, Perlini, & Brambilla, 2009; Covington et al., 2005; Crow, 1998; Kuperberg, 2010). Most noted is the language component of thought disorder, and the so far unsuccessful efforts to delineate the boundaries of thought, language and speech (Levy et al., 2010; Zegers, 2010). In fact, even Kraepelin, whose attention rested primarily on disordered thought, referred to
“derailments in the *expression* of thought in speech” (1896, p. 72, as cited in Levy et al., 2010, emphasis added). More recently Crow (1997) has gone so far as to ask whether “schizophrenia (is) the price *Homo sapiens* pays for language?” According to Crow (1997), because the genetic evolution of language in humans is relatively new, and thus failure-prone, one of its evolutionary ‘glitches’ may manifest as schizophrenia. Yet, even with its failures, language is preserved in the gene pool because it is so incredibly valuable (Crow, 1997; DeLisi, 2001).

Irrespective of its aetiological origin, a large body of work has established fundamental, and unusual, language deficits in patients (Crow, 1997; DeLisi, 2001; Zegers, 2010). Empirical studies of language have often focused on word generation and the meaning of utterances in patient populations (Bellani et al., 2009; Rossell, 2006; Rossell, Rabe-Hesketh, Shapleske, & David, 1999). Level by level assessments of linguistics including phonetics and phonology (i.e., speech sounds and their distribution/patterns and pronunciation rules), prosody (i.e., timing and intonation), morphology (i.e., word formation patterns, including inflection, derivation and composition), syntax (i.e., grammatical rules), semantics (i.e., meaning), pragmatics (i.e., situational context) and coherence (i.e., logical congruency and understandability) have revealed impairments at most linguistic levels, perhaps with the exceptions of phonological structure, morphology and syntax (Covington et al., 2005; DeLisi, 2001; Levy et al., 2010). The empirical study of abnormal semantics has by far received the most attention (e.g., Allen & Frith, 1983; Aloia, Gourovitch, Weinberger, & Goldberg, 1996; Elvevag, Weinstock, Akil, Kleinman, & Goldberg, 2001; Rossell et al., 2010; Rossell & David, 2006). Evidence from verbal fluency and semantic priming tasks points to the likely breakdown of access to the semantic memory store, as well as the disorganisation of semantic concepts within the network (Bozikas, Kosmidis, & Karavatos, 2005; Elvevag et al., 2001; Kremen, Seidman, Faraone, & Tsuang, 2003; Landro & Ueland, 2008; Rossell, Shapleske, & David, 2000; Vinogradov et al., 2002). The literature on semantics pertains to both language and memory. Verbal fluency (i.e., language) will be discussed next with references made to memory where necessary to provide a context, however a comprehensive discussion on semantic memory follows in *Section 3.4 Memory*.

### 3.3.2 Fluency, memory structure and strategy.

Assessments of verbal fluency require participants to generate as many words as they can from their inner lexicon while conforming to a given category (Chen, Chen, Chan, Lam, & Lieh-Mak, 2000; Vogel et al., 2009). They do this under time pressure, usually within 60 seconds, or over three minutes (Ojeda et al., 2010). Two types of fluency are typically assessed: (i) phonological (or letter) fluency, which refers to the generation of words that begin with a certain
letter, usually conducted over three trials using ‘F’ ‘A’ and ‘S’ (The Controlled Oral Word Association Test [COWAT]; Spreen & Strauss, 1998), (ii) semantic fluency, which requires words to be generated that belong to a specific semantic category (i.e., animals, fruits/vegetables) (Bowie et al., 2004; Rossell, 2006; Rossell, Rabe-Hesketh, Shapleske, & David, 1999). Both types are thought to demand a comparable amount of executive functioning, given that for both tasks verbal retrieval and recall needs to be efficiently organised, responses need to be self-initiated, self-monitored, and inhibited when inconsistent with the task (Henry & Crawford, 2005; Ojeda et al., 2010). However, semantic fluency is considered easier than phonological fluency to perform because, theoretically, it reflects the network model of memory (i.e., close storage and connection of concepts that are similar in meaning, allowing for faster retrieval). By contrast, phonological fluency asks for the retrieval of concepts based principally on their lexical representations, and thus, these concepts are more likely to be stored at a considerable (theoretical) distance from each other (i.e., ‘food’ ‘front’ ‘fumble’ ‘fly’) (Landro & Ueland, 2008; Rossell et al., 1999) (see Figure 3.7). This is reflected in the performance data, whereby a greater number of semantic, compared to phonemic, category words tend to be generated by healthy individuals (Harrison, Buxton, Husain, & Wise, 2000).

Semantic fluency is also thought to rely on specific cognitive strategies; clustering (i.e., the production of words from within a particular semantic category), and switching (i.e., the ability to switch efficiently to a new subcategory or ‘cluster’ once the present cluster is exhausted (Bozikas et al., 2005; Landro & Ueland, 2008; Moore, Savla, Woods, Jeste, & Palmer, 2006; van Beilen et al., 2004). For example, within the category ‘animals’ several clusters can be formed such as farm animals, birds, marine animals, wild animals, and zoo animals. The participant would actively switch from one cluster (e.g., farm animals) to another (e.g., birds) once they were unable to retrieve any further farm animals from memory. Thus, verbal fluency tasks have been used to assess, and presented as evidence of, various competencies and/or deficiencies in cognitive domains including executive function (Moore et al., 2006), verbal intelligence, language and vocabulary/lexicon size (Moore et al., 2006; Sumiyoshi et al., 2001), processing speed (Henry & Crawford, 2005; Ojeda, Pena, Sanchez, Elizagarate, & Ezcurra, 2008; Vinogradov et al., 2002), psychomotor speed (van Beilen et al., 2004) and semantic memory structure (Rossell et al., 1999; Sumiyoshi et al., 2005).
Figure 3.7. a) Schematic representation of a semantic network for the concept fish according to network models of memory. The diagram illustrates the network of concepts that are linked to fish and held permanently in semantic memory. The arrows represent mental pathways and these vary in length to indicate the salience of meaningful relationships between concepts. Shown is the superordinate category of aquatic animals, and superordinate to this, the category of animals. Example subordinate categories (i.e., tuna, seahorse, etc.) are also shown. Interconnections of horizontal and vertical semantic associations provide the concept fish with its meaning. b) Theoretical illustration of the semantic distance between concepts where the search is lexically-driven. The example maps words beginning with the letter ‘F’ (in red) over the original concept of fish. c) Adaptation of (a) illustrating the theorised semantic memory network in schizophrenia. The basic structure of the semantic memory store is intact; however, patients may have (i) less accurately related concepts available to them and (ii) more idiosyncratic relations available. Thus, hypothetical mental pathways between concepts such as fish and horse, or fish and numbers, may underlie poor performance on semantic memory tasks. Replicated from Rossell, Batty and Hughes (2010).
3.3.3 Research in schizophrenia: Access versus storage.

It is well established that patients with schizophrenia show a deficit on verbal fluency tasks (Bozikas et al., 2005; Elvevag et al., 2001; Kremen et al., 2003; Landro & Ueland, 2008; Prescott, Newton, Mir, Woodruff, & Parks, 2006; Vinogradov et al., 2002). Patients generally show a reduced number of total words, clustered categories of words, and switches across categories (Henry & Crawford, 2005; Landro & Ueland, 2008; Troyer, Moscovitch, & Winocur, 1997). Given that semantic fluency is considered less demanding on memory retrieval processes than phonological fluency, it is interesting that patients consistently and overwhelmingly demonstrate disproportionately impaired performance on semantic, relative to phonemic, tasks (Bokat & Goldberg, 2003; Henry & Crawford, 2005; Kremen et al., 2003; Landro & Ueland, 2008; Rossell et al., 1999). This is true even where intelligence quotient (IQ) (Kremen et al., 2003), medication effects, executive functioning deficits (Kremen et al., 2003) and processing speed (Ojeda et al., 2008; Vinogradov et al., 2002) are taken into account in data analyses. Only the rare exception has appeared in the literature and these may point to other factors (i.e., aging effects) rather than a consequence of schizophrenia sequelae (see Kosmidis et al., 2005).

It is reasonable to conclude that a semantic memory deficit exists in schizophrenia because the fluency and clustering of semantically related words depend intrinsically on the integrity of semantic associations within the network (Ojeda et al., 2010; Prescott et al., 2006; Sumiyoshi et al., 2005; Vinogradov et al., 2002). There is some contention in the literature as to whether the demonstrated deficits in fluency equate to (i) the inefficient retrieval of, or access to, stored concepts or, (ii) a disorganisation of the semantic memory store itself (Henry & Crawford, 2005; Rossell & David, 2006). Some authors have argued for the disruption of both (e.g., Henry & Crawford, 2005).

Henry and Crawford (2005) presented a meta-analysis of 84 studies published between 1981 and 2002 which pooled verbal fluency data from 2947 patients with schizophrenia and 2469 healthy controls. As expected, patients were worse at both fluency tasks compared to controls, and significantly worse on semantic versus phonological fluency. Because reduced performance was shown to both measures of fluency, the authors argued for

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17 Other authors have suggested that patients do create a comparable amount of both clusters and switching during word production by applying the same cognitive strategies as controls, but that they use these strategies less effectively, and thus, simply generate fewer words per cluster (Bozikas et al., 2005; Kosmidis et al., 2005; Van Beilen et al., 2004).
a general retrieval deficit in patients, and, given excessively reduced performance on the semantic task, an additional semantic store anomaly. They drew this conclusion in spite of their data showing no differential deficits on either measures of fluency once the influence of psychomotor speed (i.e., symptoms of blunted affect, emotional withdrawal, passive/apathetic social withdrawal, lack of spontaneity and flow of conversation; Vogel et al., [2009]) and general intelligence were statistically removed in analysis. As such, the findings from Henry and Crawford (2005) actually suggest intact fluency. Other meta-analyses have, however, provided evidence of the typical disproportionate semantic impairment in schizophrenia (e.g., Bokat & Goldberg, 2003).

A significant correlation between the duration of illness and semantic, but not phonemic, fluency was also shown by Henry and Crawford (2005). This is a noteworthy relationship, particularly from a dataset of this size, and instead points to a semantic-specific deficit in schizophrenia that may be influenced by the progression of the illness. Their data is in keeping with other investigations that have demonstrated a relationship between fluency abilities and symptom profile. For instance, patients with delusions exhibit poorer performance on fluency tasks (Rossell, 2006; Rossell et al., 1999), usually because currently deluded patients produce more idiosyncratic, and therefore, more category inappropriate words relative to non-deluded patients (Rossell et al., 2010). These findings support the hypothesis that the semantic store becomes more idiosyncratically organised over the duration of the illness (this hypothesis is discussed in the following section of this chapter; 3.4.4 Research in schizophrenia: Semantic memory abnormalities). Poor semantically-driven clustering in schizophrenia is also cited in support of this hypothesis. Patients have demonstrated semantic, but not phonemic, impairments in clustering, and this implies that the access and retrieval of concepts from memory are relatively intact, whereas the storage of concepts in the network appear disrupted (Bozikas et al., 2005).

Specific deficits in the retrieval of semantic information in patients have also been hypothesised. Vogel et al. (2009) gave patients a comprehensive battery of language-related tasks (i.e., measures of verbal fluency, semantic matching, naming and sentence generation) and, as expected, patients performed poorly relative to controls. The Pyramids and Palm Trees Test (Howard & Patterson, 1992) was administered as a semantic matching task and the data used as evidence of retrieval deficits. However, while the task was originally developed to measure access to semantic memory (Gudayol-Ferre et al., 2008), there is no reason why poor performance on this task is not equally as likely to be indicative of an
idiosyncratically organised semantic network. Therefore, the interpretation of these findings as evidence of deficient retrieval-based processes may not be justified. This would be especially true if the patients tested were chronically unwell and/or currently deluded (Rossell, 2006; Rossell et al., 1999). However, other than the mean duration of illness ($M = 8.42$, $SD = 5.66$), Vogel et al. (2009) did not provide clinical information, and thus the influence of symptoms on task performance is unclear.

3.3.4 Alternative explanations.

A number of other interpretations have been offered as an explanation for verbal fluency deficits including a fundamental deficit in lexicon size (Chen et al., 2000), the result of impaired psychomotor speed (van Beilen et al., 2004), and the influence of working memory (Ojeda et al., 2010). Generally the effects of these variables remain inconclusive in light of inconsistencies across studies and instances where likely confounds are ignored. For example, Chen et al. (2000) estimated lexicon size for both patients ($M = 90.6$, $SD = 49.9$), and controls ($M = 185.7$, $SD = 87.1$). Because patients showed an average lexicon less than half the size as that estimated for controls, the authors identified lexicon as the chief impairment (Chen et al., 2000). Primarily, their work ignores the differential impairment to semantic versus letter fluency established in the literature (Bokat & Goldberg, 2003; Henry & Crawford, 2005). Moreover, while Chen et al. (2000) controlled for age, education, and illness duration in their analysis, lexicon size is likely to reflect any number of other known deficits in schizophrenia, particularly those related to intelligence, cognition, and a poor social environment, of which they took no measurement. Thus, while it is likely that patients may in fact have a reduced lexicon relative to controls, a range of established impairments in executive function, poor concentration, attention, and/or working memory are at least equally as likely to explain these data.

Ojeda et al. (2010) split their patient group according to fluency performance and found that working memory was only predictive for patients in the poorer performance group. Processing speed was instead predictive of fluency scores from the better performers, a pattern that matched that of the healthy control group. They argued, thus, that neuropsychological data from patients may not always reflect the same underlying mechanisms, where less impaired patients are utilising cognitive strategies akin to those shown by healthy controls. However, both Ojeda et al. (2008) and Vinogradov et al. (2002) have shown the influence of processing speed on fluency performance, regardless of the level
of impairment. In fact, Ojeda et al. (2008) illustrated this relationship in chronic hospitalised patients, which is contradictory to their later work (i.e., Ojeda et al., 2010), and suggests that processing speed is influential for all task performers.

Not even the relationship between impoverished verbal fluency and symptoms of alogia (poverty of speech) is straightforward. Rossell (2006) demonstrated the expected relationship whereby deficient verbal fluency is related to alogia, but this is inconsistent with evidence from others (e.g., Bowie et al., 2004; Sumiyoshi et al., 2005). There is some indication, however, that patients with alogia have a larger degree of semantic disorganisation (Sumiyoshi et al., 2005) and that the presence of negative symptoms in schizophrenia significantly reduces fluency performance (Bowie et al., 2004). Together then, this literature illustrates that poverty of speech alone does not account for poor fluency in patients.

3.3.5 Age of onset, age of testing, and psychobiology.

The later onset of symptoms may protect against the substantial degradation and/or disorganisation of the semantic store seen in patients with a typical onset and course. Sumiyoshi et al. (2001), for instance, demonstrated that semantic fluency was relatively less impaired in late onset schizophrenia. By contrast, investigations in early onset psychosis have shown both semantic only impairments (e.g., Phillips, James, Crow, & Collinson, 2004) and equally impaired semantic and phonemic fluency (Landro & Ueland, 2008). These impairments appear to then continue into middle (e.g., Moore et al., 2006) and older age (e.g., Bowie et al., 2004; Kosmidis et al., 2005; Moore et al., 2006). Given their finding of an isolated semantic impairment in adolescent patients, Philips et al. (2004) suggested further that semantic and phonemic fluency processes may have distinct neurocognitive geneses. This complements data from Kosmidis et al. (2005) who demonstrated that elderly patients were differentially impaired in phonological fluency alone, however this finding has not been replicated (Bowie et al., 2004; Kosmidis et al., 2005; Moore et al., 2006).

Functional magnetic resonance imaging (fMRI) data has provided some further indication that distinct underlying cognitive mechanisms may explain disproportionate fluency performance. While the underlying neural networks overlap considerably, phonological fluency is generally associated with frontal lobe functionality implicating the executive processes required by this task, such as attention, concentration, effortful retrieval, and working memory. The same is true for semantic fluency, reflecting the executive demand of semantic tasks, however semantic fluency is also associated with temporo-parietal
function (Henry & Crawford, 2005; Kircher et al., 2009; Kremen et al., 2003; Spence et al., 2000; Takizawa et al., 2008). Kircher et al. (2009) showed that reduced activation in these areas correlated with NRG1, a susceptibility gene for schizophrenia, which was also significantly related to reduced semantic, but not phonological, fluency. Verbal fluency deficits have also been related to reduced grey matter volume and reversed asymmetry of the pars triangularis (generally, inferior parietal and Heschl’s gyri) in patients, and in their first degree relatives (i.e., at high genetic risk for schizophrenia) (Bhojraj et al., 2009).

In summary, a verbal fluency deficit in patients with schizophrenia has been established, although the underlying mechanisms that contribute to this deficit are less clear. Whether the problem reflects the disrupted access to networks, retrieval of stored concepts, inherent differences in the organisation of stored concepts, or the combined effect of these is uncertain. Existing data overwhelmingly suggests a greater semantic impairment where semantic and phonemic performance has been compared, even where other factors that are renowned for reducing performance in schizophrenia (for example, processing speed, working memory and IQ), have been ruled out as an explanation for poor performance. Empirical findings of this nature theoretically implicate the organisational structure and/or integrity of the semantic network, which has traditionally been measured via semantic priming paradigms.

3.4 Memory

3.4.1 General memory impairments.

Impaired memory is generally considered a neuropsychological feature of schizophrenia (Broome et al., 2010; Silver et al., 2001). Memory deficits have been demonstrated across both verbal (Bartholomeusz et al., 2011; Hofer et al., 2011; Nieto & Castellanos, 2011), and visual modalities (Hofer et al., 2011; Kalkstein et al., 2010; Nieto & Castellanos, 2011), and in the context of both short- (i.e., working), and long-term memory (Cannon et al., 2005; Nieto & Castellanos, 2011). This is especially true at the stage of information encoding (Dias et al., 2011; Zierhut et al., 2010). Deficits are also well established for specific types of memories, including episodic memories (i.e., memory relating to personally experienced past events, or episodes; Girard, Christensen, & Rizvi, 2010; Grillon, Krebs, Gourevitch, Giersch, & Huron, 2010; Leavitt & Goldberg, 2009; Wang, Metzak, Honer, & Woodward, 2010), and semantic memories (discussed in detail in Section
3.4.2), with data suggesting that recognition is less impaired than recall (Beatty et al., 1993; Kalkstein et al., 2010)\textsuperscript{18}.

In a meta-analysis of twelve studies investigating early onset schizophrenia Nieto and Castellanos (2011) indicated that memory capacities appear to be relatively stable. Further evidence of this comes from deficits shown in first episode patients (Bartholomeusz et al., 2011), and in schizotypy (Kerns & Becker, 2008). While impairment is shown in early onset patients (e.g., Girard et al., 2011; Nieto & Castellanos, 2011), data from Girard et al. (2011) suggested further that, along with some executive functions, memory may be preserved in late onset schizophrenia. The authors reported that no differences between late onset patients and controls were observed once age and education were considered in analysis (Girard et al., 2011). Further work has shown that the degree of working memory capacity may predict psychosis in individuals in the prodromal phase (Pukrop et al., 2007), that haplotypes (i.e., a set of alleles, or formations of a gene) associated with schizophrenia are also associated with reduced short- and long-term memory performance (Cannon et al., 2005), and that spatial working memory deficits may be linked to increased genetic risk for schizophrenia, shown in studies of monozygotic and dizygotic twins (Broome et al., 2010; Cannon et al., 2000).

Together this work suggests that memory deficits may exist as a persistent and heritable trait in schizophrenia, as opposed to being state (i.e., symptom) related.

There is some contention in the literature as to which memory modality is most impaired. Kalkstein et al. (2010) concluded that verbal memory is disproportionately impaired relative to other memory faculties in patients, whereas Palmer et al. (2010) showed visual memory to be differentially impaired, over and above some commonplace deficits considered characteristic of schizophrenia (i.e., working and episodic memory). Importantly, Palmer et al. (2010) conducted intra-patient comparisons which account for patient heterogeneity by assessing the cognitive deficits of each patient against a normal comparison group. While this analysis may give their data additional credence, replicable findings are necessary in this area in light of the substantial body of work showing working and/or episodic memory deficits (Cannon et al., 2005; Girard et al., 2010; Grillon et al., 2009; Leavitt & Goldberg, 2009; Nieto & Castellanos, 2011; Wang et al., 2010).

\textsuperscript{18} This is likely to be true for all individuals given that recall is intrinsically more difficult without the memory cues provided during recognition tasks.
More recently evidence has suggested that reduced processing speed may underlie the impairments shown in verbal and visual memory in patients. For instance, a regression analysis has implicated processing speed in both the superficial and deep encoding required for memory tasks (Brebion et al., 2011). Slowed information processing is characteristic of the disorder and is likely implicated in most aspects of cognition (see Section 3.6.7: Processing Speed). The contribution of this deficit to memory impairment in schizophrenia, however, requires much further investigation.

Finally, functional neuroimaging has provided additional indication of impairment by offering disparate brain-based correlates of memory function in patients. First, Ehrlich et al. (2011) reported the differential activation of brain regions in patients during the recall and manipulation of verbal working memories. Verbal working memory was associated with cortical thickness in the lateral prefrontal cortex in controls, yet for patients the right middle and superior temporal lobe regions were active (Ehrlich et al., 2011). Second, graded activation of the medial frontal cortex and right precuneus in response to memory load has been reported in individuals at different stages of the theorised continuum of psychosis. Broome et al. (2010) demonstrated that first episode patients showed the least amount of activation, followed by psychosis-prone individuals, and finally healthy controls with the most activation, especially during the most demanding level of the memory task. Last, decreased cingulum bundle (i.e., association fibres allowing for limbic system communication) integrity has been linked to working memory in schizophrenia (Kubicki et al., 2009; Nestor et al., 2010). This evidence of disrupted connectivity, along with attenuated and disparate activation in patient samples, may at least partially explain memory deficits illustrated in the literature.

3.4.2 Semantic memory.

Semantic memory refers to memory for general, factual, and conceptual information. The term semantic memory was originally used to describe memory for language (e.g., meanings of words), as distinguished from memory for personally experienced events (i.e., episodic memory) (Tulving, 1972). Subsequent theorisation and experimentation extended the concept to include knowledge of facts (including language), objects, information about the self (i.e., personal semantic memory), complex social rules (i.e., schemas, frames, and scripts), and abstract theoretical and moral concepts (Tulving, 1983, 1985). As such, semantic memory is currently conceptualised as the system by which cognitive
representations of this information are stored and linked according to their meaning (Baddeley, 1990; Surprenant & Neath, 2009).

The semantic memory store is currently considered to incorporate cognitive representations by way of a hierarchical network of interconnected concepts (Collins & Loftus, 1975; Collins & Quillian, 1969; McClelland, 1981; McClelland & Rumelhart, 1985; Quillian, 1967, 1969). According to network models of semantic memory, a link (i.e., mental pathway) between concepts represents a meaningful relationship (Hollan, 1975). Meaningfully related concepts are stored closer together in semantic memory than less related or unrelated concepts (Hollan, 1975), and this meaning is accumulated via experience and semantic associations (Baddeley, 1990; Baddeley, Eysenck, & Anderson, 2009; Collins & Loftus, 1975; McClelland, 1981; McClelland & Rumelhart, 1985). For example, the concept fish is associated with particular items of knowledge relating to its defining features, such as having gills, fins, and an elongated body covered with scales, as well as its characteristic behaviours, such as being able to swim. Fish is also linked upwards to the superordinate category of aquatic animals, and upwards again to animals, as well as downwards to specific examples of fish, both typical, such as tuna and salmon, and atypical, such as seahorse and mudskipper. Similarly, the examples of fish are linked to more specific subordinate information (e.g., bluefin tuna, Atlantic salmon, etc.). Concepts such as bait, boat, farm, and ocean are also related to fish, however, the location of these concepts in the semantic memory network relative to fish varies (i.e., semantic distance varies). This interconnected network of horizontal and vertical semantic associations provides the concept fish with its meaning (see Figure 3.7a).

The spreading-activation theory of semantic processing introduced by Collins and Loftus (1975) is prominent in the literature. Based on the network model of memory, they explained consciousness of the contents of semantic memory as the result of activation and interaction of interconnected concepts (see McClelland, 1981; McClelland & Rumelhart, 1985, for connectionist model of memory). Stimuli activate related concepts and this activation propagates through the semantic memory network to other concepts via excitatory or inhibitory, and direct or indirect, connections (Anderson, 1983; Collins & Loftus, 1975; McNamara, 2005). The extent to which adjacent concepts become activated is proportional to the semantic distance from the initiating concept (Anderson, 1983; Lorch, 1982; McNamara, 2005). For instance, the word tuna would rapidly activate the concept fish and its related features, alternative examples of fish (i.e., seahorse) would be activated to a lesser extent, and
unrelated concepts (i.e., car) not at all. Thus, spreading activation allows the most salient features associated with a particular concept to be accessed and retrieved from semantic memory in a timely manner (Lorch, 1982; McNamara, 2005), and this is vital for accurate and efficient comprehension and interaction with the world.

### 3.4.3 Semantic priming.

The structure and integrity of the semantic memory network is typically investigated using the semantic priming paradigm. Differentially related, paired stimuli (e.g., words and nonwords for the *lexical decision* task) are presented for brief periods and in rapid succession over numerous trials. Pairs consist of a *prime* followed by a *target* stimulus, and participants are required to read the prime and then indicate whether the target is a word or a nonword (see *Figure 3.8*). It is well established that responses are faster and more accurate to targets preceded by a semantically related prime, relative to targets preceded by an unrelated prime (Perea, Gotor, & Nacher, 1997; Sperber, McCauley, Ragain, & Weil, 1979), referred to as the *semantic priming effect*.

The priming effect thereby aligns with the hierarchical model of memory and spreading activation theory of semantic processing (Anderson, 1983; Collins & Loftus, 1975; McNamara, 2005). An initiating stimulus activates a particular item of knowledge and this activation propagates to, and therefore *primes*, related concepts. If one of these partially activated related concepts appears as a target stimulus, the prior activation (i.e., priming) will facilitate its retrieval from memory, resulting in a faster and more accurate response (Lorch, 1982; McKoon & Ratcliff, 1992). Spreading activation within the network is theoretically rapid and automatic, and therefore contributes to the semantic priming effect chiefly when the time between prime and target stimuli is short (Neely, 1977; Posner & Snyder, 1975; Rossell, Price, & Nobre, 2003).
Figure 3.8. Schematic of the speeded lexical decision semantic priming task. Example prime-target word pairs are shown across three categories: related, unrelated, and nonwords. A fixation cross (500 ms) is presented followed by a prime (200 ms), interstimulus interval (ISI; 50 or 500 ms) and target (200 ms). Participants decide if the target is a word or nonword (lexical decision). Lexical decision responses are typically faster and more accurate when the target is semantically related to the prime. Short stimulus onset asynchronies (SOAs; i.e., the time from presentation of the prime to presentation of the target; e.g., 250 ms) are thought to capture automatic processing, whereas long SOAs (e.g., 750 ms) allow for controlled processing.

At least two other processes may contribute to the semantic priming effect: semantic expectancy and semantic matching (Neely, 1991; Neely, Keefe, & Ross, 1989). Expectancy refers to a pre-lexical, controlled process by which individuals actively generate a set of expected target items (e.g., semantically or associatively related words) in response to the prime (McNamara, 2005; Neely, 1977; Posner & Snyder, 1975; Shiffrin & Schneider, 1977). Using the established example, in response to the prime ‘fish’, expected targets such as ‘ocean’, ‘gills’, ‘fins’ and ‘tuna’, among others, may be activated. These concepts are partially activated (i.e., primed), and thus, if one of them appears as the target its retrieval is facilitated (i.e., the semantic priming effect is shown) (McNamara, 2005). By contrast, if one of these expected concepts does not appear as the target then processing of information outside the expectancy-generated set will be required, and semantic processing may subsequently be inhibited (McNamara, 2005; Morgan, Bedford, & Rossell, 2006).

19 The process of semantic expectancy is most relevant to situations where there is a long interval between stimuli because controlled processing is temporally demanding (Shiffrin & Schneider, 1977).
Semantic matching is a post-lexical process involving the detection of semantic relationships between prime and target words (Balota, Black, & Cheney, 1992; Lorch, Balota, & Stamm, 1986; McNamara, 2005). Responses during a lexical decision task may be facilitated where the identification of a semantic relationship provides an immediate indication that the target must be a word (rather than a nonword). Likewise, failure to detect a relationship may be facilitatory where the target is a nonword. However, in circumstances where the target is a word but a semantic relationship has not been detected, responses are likely to be inhibited (Chwilla et al., 1998; McNamara, 2005). Automatic spreading of activation, semantic expectancy, and semantic matching are together considered key underlying processes of the semantic priming effect.

### 3.4.4 Research in schizophrenia: Semantic memory abnormalities.

As discussed in section 3.3.2 Fluency, Memory Structure and Strategy, abnormalities in the semantic memory store have been hypothesised in response to poor performance on verbal fluency tasks by patients with schizophrenia. Research has also sought to investigate this hypothesis directly and shown semantic deficits across a wide variety of tasks, including categorisation (Chen, Wilkins, & McKenna, 1994; Rossell & David, 2006), sentence verification (Rossell, Shapleske, & David, 1998), semantic fluency (Rossell et al., 1999), semantic priming (Rossell, Shapleske, & David, 2000), and detection of word associations (Rossell & David, 2006). As such, semantic memory abnormalities are predicted to underlie the disturbances in thought and language observed in people with schizophrenia (e.g., thought disorder; Gouzoulis-Mayfrank et al., 2003). Furthermore, semantic memory abnormalities may underlie the deficits observed in other cognitive domains (e.g., reasoning; Joyce, Collinson, & Crichton, 1996), as well as provide a cognitive explanation for other symptoms of schizophrenia, such as delusions (Rossell et al., 2010; Rossell et al., 1999).

Also mentioned previously, there continues to be contention in the literature regarding hypothesised deficits in the access/retrieval of stored concepts, and/or the idiosyncratic semantic organisation of the network. Both hypotheses have been used to explain poor performance on semantic memory tasks (Allen & Frith, 1983; Aloia, Gourovitch, Weinberger, & Goldberg, 1996; Ellevag et al., 2001; Rossell et al., 2010; Rossell & David, 2006). However, recent research has suggested that the idiosyncratic storage of semantic information may provide a basis for the development and maintenance of
delusions in schizophrenia and in other disorders (see Figure 3.7c, Figure 3.9, and Rossell et al., 2010 for full discussion).

**Figure 3.9.** Schematic of hypothetical formation and maintenance of delusional beliefs, adapted from Rossell, Batty & Hughes (2010).

As with the empirical literature investigating perceptual organisation and verbal fluency, priming investigations have also shown inconsistencies. Minzenberg, Ober, and Vinogradov (2002) reviewed 23 “single-word” semantic priming studies and found that increased, normal, and reduced semantic priming has been shown in patients to date. Interestingly however, the variation was confined to semantic priming effects investigated at short onset asynchronies (SOAs; i.e., the time from presentation of the prime to presentation of the target, for example, 250ms), which are considered to capture automatic processing. The seven studies using long SOAs (e.g., 750ms) consistently reported poor performance from patients, suggesting significant impairments in controlled semantic processing in schizophrenia.

Research involving schizophrenia patients with thought disorder complicate matters further. Approximately half report an association between thought disorder and *increased* semantic priming, whereas the other half report an association between thought disorder and *decreased* semantic priming. Manschreck et al. (1988) illustrated semantic priming in chronic schizophrenia patients with and without thought disorder at a short SOA (i.e., 250ms). Interestingly, healthy controls and patients without thought disorder performed comparably...
(i.e., reaction time priming effects of 37ms and 36ms, respectively), whereas the schizophrenia patients with thought disorder showed a significantly greater degree of semantic priming (i.e., 83ms). Of note however, the thought disordered patients showed faster reaction times to both semantically related and unrelated words, suggesting that the observed facilitation may not have been related to the semantic properties of the prime. Instead, the faster reaction times may be better explained by an alternate hypothesis in the literature, that is, a theorised wider and less discriminate spreading of activation to other concepts in semantic memory (see Niznikiewicz et al., 1997; Niznikiewicz, Spencer, Salisbury, & McCarley, 2004).

3.4.5 Methodological concerns.

Concerns have been raised in the literature regarding the influence of a number of variables, including SOA, the calculation of reaction time effects, and, most commonly, artefacts characteristic of patient populations (e.g., such as slowed processing speed, already discussed). For example, a further meta-analysis incorporating thirty-six studies reported that semantic priming effects are moderated by both short and long SOAs, as well as the general slowing of reaction times (Pomarol-Clotet, Oh, Laws, & McKenna, 2008). On the other hand, research in schizotypy (effectively removing the influence of confounding symptomatology such as slowing) has revealed decreased semantic priming at the short SOA only (Morgan, Bedford, & Rossell, 2006). The findings from Morgan et al. (2006) highlight the potential for artefact when symptomatic patient populations are investigated. Certainly the relevance of automatic and controlled processing, that is believed to be captured by short and long SOAs respectively, remains largely unclear. Both SOA-based meta-analyses reviewed here have reported inconsistencies across findings, especially with regard to patient differences at the short SOA. However, it is imperative to acknowledge that these meta-analyses have incorporated studies with inconsistent definitions of a “short” and “long” SOA, and with unique patient groups that were invariably experiencing different sets of symptoms at the time of testing. This is problematic because there is no clear distinction in milliseconds between automatic (i.e., short SOA) and controlled (i.e., long SOA) processing, and a short SOA of 64ms for instance, (i.e., Passerieux et al., 1995) may be very different from a short SOA of 260ms (i.e., Ober, Vinogradov, & Shenaunt, 1997) in terms of cognitive processing. Yet these studies were compared head to head in Minzenberg et al. (2002). Given that controlled processing is more likely to be state rather than trait related, it also stands to reason that controlled processing would be affected by current symptom profile. For instance, a
patient with prominent negative symptoms is likely to be slower in their response time than one without negative symptomatology. Much further work that systematically controls for such confounds is needed in this area.

In addition, early semantic priming studies calculated the semantic priming effect as the difference in reaction times to unrelated versus related stimuli (McNamara, 2005). However, this yields spuriously large values for patient semantic priming effects. For instance, if group A obtained average reaction times of 600ms and 540ms, and group B obtained average reaction times of 750ms and 675ms, for the unrelated and related conditions, respectively, the priming effect would be calculated as 60ms for group A and 75ms for group B, which suggests greater semantic priming for group B. Yet, the proportional reduction in reaction time across groups A and B is the same (i.e., 10%), and thus, no group differences in priming are actually shown. As such, some literature may erroneously report greater semantic priming in patients relative to controls (McNamara, 2005; Niznikiewicz et al., 2004). Spitzer, Braun, Maier, Hermle, and Maher (1993) examined direct (e.g., doctor-nurse) and indirect (i.e., word pairs that are connected via a mediating associated word; e.g., black-white chalk) semantic priming effects in patients with and without thought disorder and healthy controls. Using a lexical decision task they showed greater semantic priming in schizophrenia patients with thought disorder at a short SOA (i.e., 200ms; trend level) and long SOA (i.e., 700ms; significant). However Spitzer et al. (1993) noted that group differences had been inflated due to the traditional calculation method. When the effect was recalculated as the percentage reduction in reaction time from the unrelated condition to the related condition the differences were no longer significant at either SOA (Spitzer et al., 1993).

Finally, in a review from Rossell and Stefanovic (2007) two additional methodological concerns were highlighted: relatedness proportion and the relationship type between prime and target stimuli. Relatedness proportion refers to the percentage of related prime-target pairs relative to all prime-target pairs (including pairs with nonwords), and relationship type refers to direct versus indirect word relationships (defined previously). Rossell and Stefanovic (2007) revealed that lower relatedness proportions result in reduced or normal semantic priming in individuals with schizophrenia, whereas higher relatedness proportions result in increased semantic priming, presumably because participants become aware that prime-targets are related in meaning. Interestingly, indirectly related word pairs (i.e., such as black chalk, related by the mediating word, white) typically increase semantic
priming in schizophrenia (Rossell & Stefanovic, 2007). This trend may reflect existing hypotheses in the literature such as increased idiosyncratic storage in schizophrenia and/or the wider activation of concepts following the presentation of a prime. Of course much further work is needed to confirm these speculations (see Rossell & Stefanovic, 2007, for review).

In sum, while semantic memory deficits are well established in the literature the manifestation of these deficits as captured by the semantic priming paradigm are less clear. Despite substantial research in priming, the influence of patient-related characteristics (i.e., such as the effects of medication, as well as other influences related to the disorder, such as slowed processing) have not been adequately elucidated. In addition, parameters of the priming task itself (i.e., SOA), along with the calculation of recorded effects, have been shown to mediate results and accordingly warrant careful attention in study designs.

3.5 Probabilistic Reasoning

3.5.1 Reasoning with beads and the Jumping to Conclusions (JTC) bias.

To “jump” to a conclusion is the act of making a decision based on “insufficient” or poor evidence (Garety & Freeman, 1999; Langdon, Ward, & Coltheart, 2010). As early as Jaspers (1913, as cited in Huq, Garety, & Hemsley, 1988) faulty reasoning and judgments by patients were posited in the development and maintenance of delusional beliefs. Given that a delusion is defined in the DSM-IV (APA, 1994) as “a false belief based on incorrect inference about external reality that is firmly sustained despite what almost everyone else believes and despite what constitutes incontrovertible and obvious proof or evidence to the contrary” (p. 765, emphasis added), reasoning biases in the development of delusional beliefs are already theoretically implicated. Indeed, when required to collect information before making a decision, patients with delusions have been shown to request less information than healthy control groups before reaching a confident judgement (Averbeck, Evans, Chouhan, Bristow, & Shergill, 2010; Lincoln, Ziegler, Mehl, & Rief, 2010). This was most famously shown by Huq et al. (1988) with the use of their now classic probabilistic inference (or “beads”) task.20

The task was developed using a framework of Bayesian probability and hypothesis (or belief) testing; a formal approach to probabilistic inferences when the information is based on

20 The Probabilistic Inference Task was actually initially conceived by Phillips and Edwards (1966) using poker chips.
knowledge/beliefs rather than frequency statistics alone. In essence, Bayesian theorem provides a model of logical inferential style against which clinical populations can be compared. Correct/incorrect conclusions are assessed in light of an existing belief and the adjustment of that belief according to new information. Replicated from Huq et al. (1988, p.803), the stages involved in probabilistic and belief testing according to a Bayesian framework are as follows:

1. the identification of the data sources that are most useful for discriminating between competing hypotheses;
2. the assessment of the implications of an observed datum vis-à-vis the truth of competing hypotheses;
3. an aggregation of the implications of different data with an overall appraisal of the relative likelihood of the truth of the hypothesis;
4. the selection, based on that appraisal, of the appropriate course of action

The Huq et al. (1988) beads task sought to assess this model in deluded relative to nondeluded patients. It consisted of eight jam jars, organised into four pairs. Each jar contained 100 beads of two different colours at a ratio of 85:15. Each pair contained the same colours, but these were complementary in ratio. For example, Jar A contained 85 pink beads and 15 green, whereas Jar B contained 85 green beads and 15 pink (see Figure 3.10). Each set was identical except for the colours used. A bead is drawn from one of the two jars (blind to the participant) and then returned to the same jar and another is drawn. The sequence of bead colours is predetermined according to the 85:15 ratio however participants are under the impression that beads are drawn randomly. Initially, either jar is equally as likely to be chosen, and thus, the probability is 50:50. The participant is to decide which jar the beads are being drawn from based on the ‘random’ selection of colours, while keeping the jar’s ratio in mind. Huq et al. (1988) administered four conditions. Condition one required participants to request another bead be drawn until they thought they had determined which jar the beads were coming from. Condition two was identical, except that participants were also required to estimate the probability of a particular colour being drawn before each draw. In condition three, participants were first shown the drawn beads and then asked to indicate, at each draw, the probability that this bead had come from one, and then the other, jar. Condition four combined conditions two and three. Subsequent studies manipulated task difficulty by adding other various bead ratios to their protocol, such as 60:40, 75:25, and 90:10 ratios (e.g., Dudley, John, Young, & Over, 1997; Young & Bentall, 1997).
Figure 3.10. Example of stimuli commonly used in Probabilistic Reasoning tasks. Ratio 85:15 is shown in the foreground (pink and blue beads). Ratio 60:40 is shown in the background (red and yellow beads).

Huq et al. (1988) showed that their deluded patients requested the least amount of draws to decision (i.e., on average 2.22) and had higher levels of certainty attached to their decision compared with the other two groups. Their healthy controls had the next least amount of draws to decision, with nondeluded patients being the most conservative in their judgements. The response pattern recorded by Huq et al. (1988) is therefore inconsistent with the theorised continuum of psychopathology, where healthy controls exist at one end and chronic psychotic patients at the other (see van Os et al. [2009] for discussion on the psychosis continuum; Badcock & Dragovic, 2006; Johnstone, Gleeson, & Rossell, 2009). In fact, according to the Bayesian model, the data recorded by Huq et al. (1988) actually identified the deluded patients as most ‘rational’ on both accounts; draws to decision and initial certainty, and the other two groups as overconservative in their decision making.

3.5.2 Reasoning anomalies?

There are robust discussions of probabilistic reasoning impairment in the literature (e.g., Dudley & Over, 2003; Garety & Freeman, 1999; McKay, Langdon, & Coltheart, 2007). It remains unclear whether the JTC bias reflects impairment in probabilistic reasoning abilities, or alternatively, a general data gathering bias such as a lowered threshold for decision making. Of course, the bias may result from the separate, or combined, effect of these anomalies. Notwithstanding altered performance on the beads (or “probabilistic reasoning”) task, however, there is actually very little evidence for an underpinning

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21 This is because 2.22 draws equates to the first two beads on any given trial, and these were always the same colour. As such, the objective probability that the bead had been drawn from the jar containing 85 beads of that colour is actually 97%, and thus, represents a rational decision.
disturbance in reasoning per se. For example, even in Huq et al.’s (1988) original study the higher estimates of probability made by the deluded group were not statistically different from the responses of the comparison groups. Furthermore, the conceptualisation of reasoning anomalies in schizophrenia is actually in conflict with Maher’s (1974) well-known hypothesis for the formation and maintenance of delusions. As mentioned in Section 3.2.2 In Schizophrenia: A History, Maher (1974) argued that patients suffer primarily from perceptual anomalies that are rationalised through normal cognitive mechanisms. Maher’s (1974) theory thus relies on intact reasoning abilities. In fact, Maher (1992) countered hypothesised reasoning anomalies with the argument that Bayes theorem identifies the JTC bias in patients as inherently rational (explained in Section 3.5.1 Reasoning with beads and the Jumping to Conclusions (JTC) bias).

An explicit assessment of probabilistic judgement/inference is also rarely taken by those who have replicated Huq et al.’s methodology (1988). A review from Garety and Freeman (1999) showed that only one of seven studies had asked participants for a probability estimate, and the study that did (i.e., Peters, Day, & Garety, [1997]), did not report the result. Probability estimates may complement performance on the beads task and thereby provide an additional indication of the reasoning capacities of patients. However, without supplementary evidence of this or any other kind a patient’s altered performance on the task is often taken as a sufficient indication of underlying reasoning impairment.

Similarly, given that the decision is theoretically based on the ratio of beads in the jar, the level of certainty expressed by patients once they have made their decision (zero to one hundred per cent) may provide a further indication of their reasoning capacities. However, this too is rarely tested and/or reported (e.g., Averbeck et al., 2010; Colbert & Peters, 2002; Lincoln et al., 2010; van Dael et al., 2006; Woodward, Munz, LeClerc, & Lecomte, 2009), and where certainty level has been reported the pattern is inconsistent (e.g., Langdon et al., 2010; McKay, Langdon, & Coltheart, 2006; 2007). For instance, Langdon et al. (2010) found no differences in the level of certainty attached to each draw by deluded versus nondeluded patients, yet in spite of this the response pattern of the groups varied significantly. Other studies have demonstrated both reduced confidence in patients compared to controls (McKay et al., 2007) and greater confidence in those with higher delusion-proneness (McKay, Langdon, & Coltheart, 2006). Figure 3.11 presents an example of the extreme tendency of one patient to shift in confidence level based on the new information provided by one bead. This is an example of the kind of pattern expected to be shown by patients should they have
an underlying deficit in reasoning. Because of the aforementioned limitations in the existing literature it is impossible to say just how closely patients illustrate a pattern of this kind. Given the tendency for a lack of group differences however, (such as in Huq et al. [1988] and McKay et al. [2007]), the available data would suggest that a pattern like the one shown in Figure 3.11 represents a pronounced exception, rather than the norm.

![Figure 3.11](image.png)

Figure 3.11. Certainty ratings from trials 1 to 20 on the Probabilistic Reasoning task for one of the most extreme patients and a cautious healthy control. Taken from Langdon et al. (2010).

While it is true that reasoning is likely to feature in the decision making required by the JTC task, Averbeck et al. (2010), along with Moritz, Woodward, and Lambert (2007), and Moritz et al. (2009), have proposed a “lowered threshold” or “liberal acceptance” hypothesis as an explanation for patient response patterns. These authors hypothesise that, instead of reasoning deficiencies per se, patients require less information to reach confidence in data gathering, assessment, and belief formation (see Figure 3.12). This lowered threshold is hypothesised as an underlying cognitive mechanism of the disease.

According to Averbeck et al. (2010) this provides a better explanation of reasoning behaviour in schizophrenia. Their patients illustrated problems on a second decision making task that required them to incorporate positive and negative feedback into their choices, but did not involve probability-based reasoning. A JTC bias was shown in patient choices, as well as a reduced tendency to adjust their decisions in response to positive feedback. In fact,
these were related, where those who adjusted the least in response to feedback also made the earliest decisions on the beads task. Data of this nature supports a more general deficit in decision making behaviour in schizophrenia.

Figure 3.12. Bayesian belief estimates of an ideal observer, and two possible hypotheses for why patients jump to conclusions; either i) they make their decision based on a lowered threshold, or ii) they believe more strongly than they should on the basis of limited feedback. Dashed lines indicate the threshold; solid lines indicate belief estimates for a sequence of six beads in the same colour (e.g., six pink beads drawn in a row). Red lines indicate hypotheses for patient performance; blue lines indicate possible control values. Taken from Averbeck et al. (2010).

On the other hand, Lincoln et al. (2010) reasoned that the lack of salience attached to the original beads task made it impossible to judge the decisions made by patients as premature. The authors increased the relevance of the patients’ decision by incorporating a financial loss/gain to their choice and hypothesised that if the observed JTC bias is not primarily a reflection of inefficient probabilistic reasoning, then patients should be able to incorporate positive and negative feedback (i.e., motivated by a potential loss/gain) and adjust their choice accordingly. Unlike the data from Averbeck et al. (2010), patients showed the hypothesised adjustments to their decisions according to feedback provided by the researchers. However, the JTC bias was evident in patient responses until the effect of intelligence and negative symptoms were accounted for in analyses. Van Dael et al. (2006) have reported the same mediators, although Langdon et al. (2010) indicated that the bias was not attributable to intelligence or memory in their dataset. Again, the importance of accounting for a range of mediating factors inherent in patient populations is illustrated here.
3.5.3 Neurocognitive underpinning.

Some efforts have been made to place the JTC bias alongside other theoretical explanations for delusion formation in an attempt to identify a common neurocognitive template in patients. It has been proposed elsewhere that patients are unable to appreciate the mental states of others; a “theory of mind” (ToM) deficit (Corcoran, Mercer, & Frith, 1995; Frith, 1992; Frith & Corcoran, 1996), and that they display an attributional style that is self-serving (i.e., “self-serving bias”), which refers to the explanation given to life events. That is, patients with delusions are more likely to attribute a negative event to a source other than themselves (Aakre, Seghers, St-Hilaire, & Docherty, 2009; Bentall, Kinderman, & Kaney, 1994; Moritz et al., 2010). These can all be considered reasoning anomalies of some kind, and some research has logically sought to determine whether they overlap in patients to provide a platform for the formation and maintenance of delusions (Garety & Freeman, 1999; Langdon et al., 2010; Moritz et al., 2010).

There is some face validity for all three, particularly in paranoid/persecutory delusions: i) less evidence is required for a belief to be accepted (i.e., JTC bias); ii) an inability to appreciate the perspectives/feelings of others allows for a “fill in the gaps” approach regarding their motivations and thoughts (i.e., ToM deficit); iii) attributing events to external sources, especially other people, is easily theoretically aligned with persecution (i.e., attributional style). To date, it appears that cognitive mechanisms for delusions only partially overlap. JTC and attributional style tend to be revealed as independent mechanisms (Langdon et al., 2010; Moritz et al., 2010), while ToM and JTC have been shown to be related in correlational analyses (Langdon et al., 2010), but independent in principal component analyses (Woodward, Mizrahi, Menon, & Christensen, 2009). Additionally, Woodward, Mizrahi et al. (2009) found that the biases related only to negative symptoms, whereas Langdon et al. (2010) reported significant correlations between JTC and ToM biases, but not attributional biases, in delusion prone individuals (although the self-serving bias was associated with paranoia). Garety and Freeman’s (1999) review concluded that none of the three anomalies had unequivocal support in the literature. More than a decade on, this appears to remain an accurate reflection of the existing literature.

3.5.4 Delusions versus schizophrenia.

While, theoretically, the link between reasoning biases and delusion formation is intuitive, it is also still unclear whether the bias is specific to, or more pronounced in, patients
with delusions, or an epiphenomenon of schizophrenia generally. There are suggestions that the bias is related to i) the formation of delusions (e.g., Bentall & Taylor, 2006; Freeman, 2007; Lincoln et al., 2010), ii) the severity of the delusion (e.g., Woodward, Munz et al., 2009), iii) the type of delusion, especially persecutory (e.g., Bentall & Swarbrick, 2003), although this is disputed by McKay et al. (2007), iv) the maintenance of the delusion (e.g., Dudley & Over, 2003), and v) a stable characteristic in patients who develop delusions (McKay et al., 2006). Those who score highly on measures of delusion proneness illustrate signs of the bias (Colbert & Peters, 2002; Linney, Peters, & Ayton, 1998; Warman, Lysaker, Martin, Davis, & Haudenscheid, 2007). In contrast, both Young and Bentall (1997) and Colbert, Peters, and Garety (2010) failed to find a JTC bias in patients with delusions, current or remitted. Another study found no differences between delusional and nondelusional patients, yet a clear JTC bias was shown by these patients as a group (Menon, Pomarol-Clotet, McKenna, & McCarthy, 2011). Taken together, this data instead suggests that the bias may exist as an epiphenomenon of schizophrenia (Averbeck et al., 2010; Menon et al., 2006; Moritz et al., 2007; Woodward, Mizrahi et al., 2009). Signs of the JTC bias have also been shown in healthy first degree relatives of schizophrenia patients, implicating heritability (van Dael et al., 2006). Accordingly, such data supports a trait (i.e., schizophrenia proper, including proneness) rather than state (i.e., currently deluded) association.

Of course patient and control comparisons need to be considered carefully. In Averbeck et al. (2010), for instance, the influence of clinical variables were not explored within their patient group (i.e., deluded versus nondeluded patients). As such, it is unknown whether their data is evidence of a general cognitive characteristic in schizophrenia, or specific to delusions but masked by the patient group analysis. This is especially relevant given that the mean PANSS positive score was quite high for their sample ($M =13.6, SD =5.9$). Moreover, the established influence of intelligence in existing data (e.g., Lincoln et al., 2010; van Dael et al., 2006) suggests that it would have been fruitful to determine the IQ effect in Averbeck et al.’s (2010) dataset. While a measure of IQ was taken for their sample, highlighting the usual tendency for a reduced mean IQ in patients relative to controls, this data was not subjected to analyses. These factors would need consideration across all existing datasets.

In summary then, the existing work has been unable to provide a definitive conclusion about the nature of the JTC bias in schizophrenia. Reasoning anomalies are clearly shown, but the underlying impairment, whether particular to probabilistic reasoning, part of a set of
wider reasoning impairments, or perhaps a lowered threshold for decision making, is unclear. There is evidence both for and against a delusion-specific and schizophrenia-in-general impairment, and to date these are lacking in comparable and thorough analyses that account for common influential factors such as intelligence.

3.6 Executive Function

3.6.1 Executive dysfunction.

Executive functioning (often referred to as “higher order functioning”) is a broad term used to describe cognitive processes involving control, flexibility, inhibition, regulation, planning, and execution of goal-oriented behaviour (Zayat et al., 2011). Neuroimaging has indicated that the executive processes involve abilities mediated by frontal areas generally, and the prefrontal cortex specifically (Fuster, 2008; Robbins, Weinberger, Taylor, & Morris, 1996). Deficient executive abilities are well established in schizophrenia (Evans, Chua, McKenna, & Wilson, 1997; Morice & Delahunty, 1996). Similar to other cognitive domains, deficits are also apparent during first episode psychosis (Hutton et al., 1998), in first degree relatives (Groom et al., 2008), and in schizotypal personality types (Laws, Patel, & Tyson, 2008). A number of measures have been used to capture aspects of executive function, with the most typical being the Digit Symbol Substitution Test (Lezak, Howieson, & Loring, 2004) or Digit Symbol Coding Test from the Wechsler Adult Intelligence Scale – III (WAIS-III; Wechsler, 1955; 1997), the Trail Making Test (TMT; Reitan & Wolfson, 1985), and the Stroop test (Stroop, 1935). Discussion pertaining to mental inhibition and switching, attention, and processing speed follows. Note that these executive abilities, especially attention and processing speed, have been found to influence the measurement of the other cognitive domains already reviewed in this chapter. Moreover, the executive abilities themselves are generally considered to be interlinked, made evident by tasks that capture more than one faculty (e.g., such as the Trail Making Test that measures both processing speed and mental switching).

3.6.2 Mental inhibition and switching.

Inhibition refers to the wilful suppression of automatic responses (Manoach et al., 2002). Patients with schizophrenia have illustrated comparably less control over prepotent responses on a range of tasks, including, stroop interference (explained in detail below) (Barch, Carter, & Cohen, 2004; Henik & Salo, 2004), prepulse inhibition (PPI) of the
acoustic startle response, shown both in schizophrenia (Braff, 2010; Braff, Geyer, & Swerdlow, 2001) and psychosis-proneness (Kumari, Antonova, & Geyer, 2008), and antisaccades (i.e., the wilful inhibition of reflexive movement of the eye toward a stimulus in the periphery) (Fukumoto-Motoshita et al., 2009; Kang, Dionisio, & Sponheim, 2011).

Task switching is the change from one attentional focus and/or behaviour to another in response to task demands, and requires significant cognitive flexibility (Manoach et al., 2002; Smith et al., 1998). Empirical research has shown that task switching abilities are also deficient in schizophrenia, at least as early as first episode, and generally culminate in delayed response times and increased errors (Hermens et al., 2010; Ravizza, Keur Moua, Long, & Carter, 2010; Smith et al., 1998; Wylie, Clark, Butler, & Javitt, 2010). This is especially true where contextual information is important, such as adherence to the changing rules/goals of a task (Ravizza et al., 2010). Switching impairments have also been shown neurophysiologically in patients at the P3a, an event related potential (ERP) index of early attention switching (Fisher, Labelle, & Knott, 2010).

3.6.3 The colour Stroop paradigm.

Current colour Stroop paradigms assess both cognitive inhibition and switching. The Stroop task typically involves three conditions: (i) a congruent speeded trial which serves as a control task for the participant’s ability to identify colour (i.e., the word ‘red’ written in the colour ‘red’ (Barch et al., 2004), or patches of colours where the participant is required only to name the colour); (ii) a neutral word trial (i.e., words of colours written in black ink) which serves as a control task for the participant’s ability to read the words; and (iii) the incongruent task where colour and word are in conflict (Barch et al., 2004; MacLeod, 1991). Words of colours written in incongruent ink colour are presented (i.e., the word ‘red’ written in the colour blue, the word ‘blue’ written in the colour green, and so on, see Figure 3.13c), and participants are to name the colour of the ink and ignore the word under time pressure. To do this, they must inhibit the prepotency of word reading over ink colour naming. The control conditions also serve as measures of attention and processing speed. Cognitive inhibition (or Stroop Interference control) on the incongruent condition is calculated against

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22 Some studies instead use noncolour words written in colour ink as the neutral condition, such as ‘dog’ written in the colour red, where participants are to name the colours (i.e., Barch et al., 2004). This condition instead retains the colour paradigm but is neither congruent nor incongruent, and is likely to be used when investigators are interested in looking at a measure of Stroop facilitation, the subtraction of ‘congruent’ trial reaction times (RT’s) from ‘neutral’ trial reaction times.
these control conditions (see Appendix C for calculation) (Albus et al., 1996; Ben-David et al., 2011; Dimoska-Di Marco et al., 2011; Barch et al., 2004; Cohen, Servan-Schreiber, & McClelland, 1992; Kaplan & Lubow, 2010; MacLeod, 1991). A fourth condition not always utilised measures switching, where the inhibition task is repeated but with additional word stimuli presented within a box; the Color-Word Interference Test (CWIT; Delis, Kaplan, & Kramer, 2001a; 2001b). The boxed stimuli are scattered throughout the unboxed words. Here, participants have to switch from ignoring the word and naming the ink colour, to ignoring the ink colour and reading the word when they come to a boxed word (see Figure 3.13d).

![Figure 3.13. The Stroop Task.](image)

**Figure 3.13.** The Stroop Task. a) Colour identification condition. Participants identify each colour patch from left to right under time pressure. b) Word reading condition. Identical to (a) except that participants read the word. c) Stroop interference condition. Participants are required to ignore the word and identify the ink colour under time pressure. d) Interference-switching condition. Identical to (c) except that participants are required to switch rules when they come to a boxed word and instead read the word for that stimulus only; they must switch back to identifying the ink colour for every unboxed word. Each condition contains 50 stimuli.

J.R. Stroop first published the initial variant of the task in 1935, a simplified card version aimed at elucidating observable interference from competing cognitive processes in healthy individuals (MacLeod, 1991). There have since been some 400 studies incorporating various changes to the original paradigm (MacLeod, 1991). The task continues to be used as a measure of mental inhibition and switching, as well as a measure of attention, and general cognitive flexibility (Abramczyk, Jordan, & Hegel, 1983; Fine et al., 2008; Perlstein, Carter, Barch, & Baird, 1998). Stoop administration to patients with schizophrenia is discussed in the following section.
3.6.4 Research in schizophrenia.

Cognitive impairment in schizophrenia has been demonstrated by Stroop data. Patients typically show slower reaction times (RTs) and reduced accuracy (Barch et al., 2004; Brenton et al., 2011; Ferchiou, Schurhoff, Bulzacka, Leboyer, & Szoke, 2010). Similar Stroop performance has been illustrated in delusion proneness (Orem & Bedwell, 2010), but not yet in schizotypal personality (i.e., psychosis proneness) (Kaplan & Lubow, 2010).

In addition to slower RTs and reduced accuracy, some research has highlighted the pattern of results in schizophrenia (Barch et al., 2004; Henik & Salo, 2004; Kubicki et al., 2009). Compared to healthy control groups it appears that patients with schizophrenia often show increased facilitation (i.e., faster RTs to congruent versus neutral trials), and increased errors in the incongruent trial, but they show equivalent interference (i.e., an equivalent increase in RTs to incongruent compared with neutral trials) (Barch et al., 2004; Henik & Salo, 2004). First, increased facilitation can be explained by particularly poor RTs to the neutral stimuli. According to Barch et al. (2004) this may reflect the greater difficulty patients have in ignoring the word more generally, which is necessary in some neutral versions of the task (not shown in Figure 3.13), but not in congruent trials. However, findings of equivalent interference appear to be inconsistent with established deficits in cognition more generally (e.g., attention and executive function). Barch et al. (2004) sought to determine if the interference effect in patients was being under-calculated due to their higher proportion of errors. That is, given that a greater number of errors are illustrated on words where the patient is having the most difficulty inhibiting their natural word-reading response, the extent of this reduced inhibition (i.e., RT interference) may be lost once errors are eliminated from analysis (Barch et al., 2004). However, Barch et al (2004) found no evidence of this.

There have been some instances of increased RT interference in schizophrenia and, in contrast to Barch et al. (2004), Henik and Salo (2004) have suggested that these patterns might simply reflect the delivery of the task. For instance, patients tend to show increased RT interference relative to controls when the task is given using the traditional card version. Here, words are shown individually thereby reducing attentional demands. This version of the task may match patient attentional resources, allowing for the true extent of their poor inhibition to be measured (Henik & Salo, 2004). The patterns of performance recorded when current versions of the task are used (i.e., Figure 3.13), may thus reflect a reduced ability to negotiate the task given the multiple attentional demands (Henik & Salo, 2004). This would
include reduced RTs and increased errors shown to all conditions, and particularly those shown even to the neutral condition (leading to an increased measurement of facilitation). Alternate task delivery might also explain some other inconsistencies in this literature; for example, Orem and Bedwell (2010) versus Kaplan and Lubow (2010). However, Perlstein et al. (1998) critically evaluated both delivery methods and argued instead that the single card version may not be sensitive enough to capture impairments. The authors suggested that current versions should instead be used, especially where an instrument sensitive to selective attention is preferred (Perlstein et al., 1998).

3.6.5 Evidence in imaging.

During cognitive tasks more generally, attenuated activation in the dorsolateral prefrontal cortex (DLPFC) has already been shown in schizophrenia and unaffected first degree relatives (Becker, Kerns, MacDonald, & Carter, 2008). During Stroop inhibition reduced activation of frontal regions has been reported (e.g., anterior cingulate gyrus, left precentral gyrus, medial and middle frontal gyrus, inferior frontal junction) (Krabbendam et al., 2009; Ungar, Nestor, Niznikiewicz, Wible, & Kubicki, 2010), as well as increased activation in medial parietal regions (i.e., posterior cingulate gyrus/precuneus) (Ungar et al., 2010). These data suggest differential and underactive networks (particularly frontal) during effortful inhibition and switching in schizophrenia. Furthermore, there are suggestions that this attenuation may be negatively correlated with positive symptoms; that is, increased activation of these areas (which would resemble control participants in functionality during Stroop inhibition) may be associated with the reduction of positive symptoms (Krabbendam et al., 2009).

3.6.6 Attention.

Extensive research has long established attention deficits in schizophrenia. In fact, along with memory and processing speed, poor attention was noted during the early observations of schizophrenia (i.e., Bleuler [1911] and Kraepelin [1919]), and impairments in attention are currently considered a core cognitive feature of the disease (Benton et al., 2011; Kumar et al., 2010; Mitchie et al., 2000). Attention deficits are identified as a key risk marker for schizophrenia, where such impairments are considered a stable enduring trait of the disorder, independent of clinical presentation (Benton et al., 2011; Mitchie et al., 2000). For example, deficient attention has been demonstrated in patients during their first presentation of psychosis when they are free from medication (Wang et al., 2007), in early onset
schizophrenia (i.e., late adolescence/early adulthood) (Jepsen et al., 2010), in chronic patients
where impairment does not correlate with symptomatology (Kurtz et al., 2001), in healthy
first-degree relatives, where relatives tend to show intermediate attentional resources between
patients and controls (Birkett et al., 2007; Brenton et al., 2011) and in schizotypal personality
types (Gooding et al., 2006).

Attention has been conceptualised as incorporating three organised networks; alerting
(i.e., vigilant sustained alert state), orienting (i.e., ability to identify, select and focus on
stimuli of interest) and executive attentional control (i.e., surveying and governing attentional
processes, allowing for decision making among distracters) (Brenton et al., 2011; Posner &
Peterson, 1990). Impairments are shown on all of these, with accounts of poor vigilance,
selective attention, switching attention, and sustained attention being commonplace in the
literature (Egeland et al., 2003; Heinrichs & Zakzanis, 1998). Furthermore, these are apparent
in both auditory and visual modalities (Baerwald et al., 2001; Kumar et al., 2010), and across
a wide range of tasks considered to tap various aspects of attention; including digit-symbol
coding (Dickinson et al., 2007), Stroop tasks (discussed previously at length) (Perlstein et al.,
1998), backward masking (Saccuzzo et al., 1974), the Trail Making Task, span of
apprehension tasks (Asarnow & MacCrimmon, 1982; Chan, Yip, & Lee, 2004), and, most
commonly used, the Continuous Performance Test (CPT) (Kurtz et al., 2001; Wang et al.,
2007).

Attentional impairments in schizophrenia have also been indicated
neurophysiologically. For example, Cullum et al. (1993) revealed that increased P50
amplitudes (i.e., indexing the gating of sensory auditory responses) was correlated with
performance on the digit cancellation test (i.e., a measure of sustained attention), but not with
measures of learning and memory. More specifically and more recently, attenuated P300
amplitudes and longer peak latencies to Nd, N2b, and P300 (i.e., reflecting selective
attention, voluntary attention, and cognitive context updating respectively) have been shown
in schizophrenia (Itagaki et al., 2011).

Neuroimaging evidence suggests differential activation patterns in the executive core
of the brain’s attentional system in schizophrenia patients compared to controls (Diwadkar et
al., 2011; Weiss et al., 2007), and in offspring of patients (Diwadkar et al., 2011). In general,
patients have demonstrated reduced activation in dorsolateral prefrontal, anterior cingulate,
and parietal regions, and increased activation in temporal and posterior cingulate regions
More recently, some inconsistencies in imaging patterns have been explained by the likelihood of a fundamental deficit in the modulation of brain activity in these areas, particularly in response to variations in attentional demands across task and non-task blocks of experimental paradigms (Carter et al., 2010). Carter et al. (2010) showed that patients actually displayed a greater percentage of active voxels relative to controls overall, but that during transient periods of the paradigm (i.e., those most important to task performance), patients instead showed a reduced percentage of active voxels, aligned with their poor performance (Carter et al., 2010).

Finally, reduced cingulum bundle integrity (i.e., poorer anatomical connectivity between regions known to be imperative during attentional control) has also been offered as an additional neuroanatomical explanation for the deficits shown (Kubicki et al., 2009). Some of these neuroanatomical differences reflect those established in the memory literature, for example, prefrontal and temporal activation, along with diffusion tensor imaging evidence of decreased connectivity via condensed cingulum bundle fibres (see Section 3.4: Memory). This may suggest common brain-based counterparts for various cognitive deficits (e.g., memory and attention in this case) and/or may indicate the neuroanatomical correlates of attention, which would be equally utilised during memory tasks.

### 3.6.7 Processing speed.

Processing speed refers to the rate at which cognitive operations are executed (i.e., the number of correct responses in a given amount of time or the total time taken to complete a standard task) (Dickinson et al., 2007; Morrens et al., 2008). The speed of information processing is typically measured by the Digit Symbol Coding (Lezak et al., 2004; Wechsler, 1955) Trail Making (Reitan & Wolfson, 1985), and Stroop tasks (Stroop, 1935), although there is some evidence to suggest that the Digit Symbol Coding task may be a better measure, probably because it incorporates the largest cognitive component (Brebion et al., 2007).

Patients with schizophrenia consistently show marked reductions in processing speed relative to control comparisons (i.e., Brebion et al., 1998; Egeland et al., 2003; Ojeda et al., 2008; Savla et al., 2010), and this deficit appears to be fairly stable overtime. For example, in a rare longitudinal study that spanned 20 years, Bonner-Jackson et al. (2010) assessed patients with schizophrenia (N=84), patients with other psychotic disorders, and a group diagnosed with depression. Using the Digit Symbol-Coding subtest of the RBANS the authors reported that patients with schizophrenia showed reduced processing speed relative to
both comparison groups over all seven testing points during the course of the project. Their data suggested further that processing speed may be particularly slowed during the acute phase of illness and that improvements shown following this phase remain relatively stable (Bonner-Jackson et al., 2010).

As already mentioned, a deficit of this nature is likely to have a bearing on the measurement of other cognitive domains, especially where tasks are speeded and/or reaction times constitute the outcome measure (see Section 3.4.1: General memory impairments). Slowed information processing may therefore exacerbate the extent of cognitive impairments in schizophrenia. Brebion et al. have conducted multiple studies in this area and, along with evidence that processing speed is able to predict both superficial and deep encoding (2000), they have shown that various other memory measures are consistently correlated with processing speed, including; efficient encoding (1998), verbal memory (2006), recall and recognition of low frequency (i.e., effortful memory encoding) but not high frequency words (i.e., relatively automatic encoding, 2007), and both superficial and deep verbal and visual memory (Brebion et al., 2011). Similar findings have been shown elsewhere, with some additional indication of comparable effects in the measurement of verbal fluency (Ojeda et al., 2008; Savla et al., 2010).

As also mentioned previously, rather than simply mediating the measurement of other areas of cognition, speculations that slowed processing speed has been mistaken for deficits in otherwise intact neuropsychological domains have also been made. That is, some established deficits in the literature, such as memory impairments, are now predicted to have primarily reflected poor information processing. Throughout their series of work, Brebion et al. showed more than once that the significance of diagnosis (i.e., schizophrenia versus control participants) across a number of memory measures was eliminated once processing speed was incorporated into the regression equation as a predictor (2007; 2011).

In further support of this idea, Dickinson et al. (2007) conducted a meta-analytic investigation incorporating forty studies and reported that effect sizes were larger to processing speed than to other cognitive measures, including episodic memory and executive function. The authors concluded that inefficient information processing constituted a central feature of the cognitive aspect of schizophrenia. However, in response to this work, Knowles et al. (2010) re-examined the same forty studies, along with an additional eleven that had since been published. Their goal was to investigate potential mediators in this research that
would help to explain the prominence of a processing speed deficit. They found that three variables significantly moderated the processing speed effect size, (i) the year of the published work under review, (ii) unmatched IQ in patient relative to control participants, and (iii), most significantly, the daily dosage of antipsychotic medication (chlorpromazine). Specifically, they reported that the smaller the daily dose the smaller the processing speed effect size (see Figure 3.14).

Thus, while the literature points to a primary deficit in the speed of information processing, current claims that this deficit accounts for some already established in other cognitive neuropsychological domains require further systematic investigation. The work from Knowles et al. (2010), for example, highlights that intelligence and medication may have an influential role.

![Figure 3.14](image-url)  
* Figure 3.14. The association between mean Chlorpromazine equivalent daily dose and Coding Task effect size. Taken from Knowles et al. (2010).

3.7 Intelligence

According to David Wechsler, the man responsible for the most commonly employed intelligence scales to date, intelligence is “the global capacity of a person to act purposefully, to think rationally, and to deal effectively with his environment” (Wechsler, 1939, p. 22). In the tradition of Wechsler, intelligence has classically been conceptualised as comprising two components; (i) a verbal and (ii) a performance (i.e., visual-motor) component, and these
incorporate verbal comprehension, perceptual reasoning, working memory, and processing speed faculties.\textsuperscript{23}

Intellectual deficits are well established in schizophrenia, both from the results of general intelligence tests (commonly including scores from the Wechsler Adult Intelligence Scale, WAIS; Wechsler, 1955) and/or composite test battery scores (Jespen et al., 2010; Kalkstein et al., 2010; Xiang, Shum, Chiu, Tang, & Ungvari, 2010b). Research has also identified a relationship between lower premorbid intelligence and the later development of schizophrenia (Cannon et al., 1999; Crawford et al., 1992). Moreover, a reduction in intelligence quotient (IQ) from premorbid to post-onset of the illness has been indicated (David, 1998; David, Malmberg, Brandt, Allebeck, & Lewis, 1997; Sheitman et al., 2000), and the literature has traditionally supported a fluid IQ decline as the illness progresses (Bilder et al., 1992; Caspi et al., 2003; Hoff, Svetina, Shields, Steward, & DeLisi, 2005; Seidman, Buka, Goldstein, & Tsuang, 2006).

Yet reports using estimates of premorbid intelligence for large cohorts of high-risk individuals have refuted the effectiveness of premorbid intelligence in the prediction of schizophrenia. For example, a total sample of 355 individuals in the New York High-Risk Project (Ott et al., 1998), and 311 Danish participants (99 at low risk, 155 at high risk, and 57 at super-high risk) in the Copenhagen High-Risk Project (CHRP; Carter, Parnas, Urfer-Parnas, Watson, & Mednick, 2010), showed no predictive relationship. Some data suggests further that patients may in fact advance intellectually overtime, and to the same degree as healthy individuals. In a meta-analysis of fifty-three studies ($n = 2476$ patients) investigating the course of cognitive faculties in schizophrenia, Szoke et al. (2008) showed that patients improved on a range of cognitive tasks between test and retest, with a mean of twelve months between each assessment. Four of their measures were subtests from the WAIS-IV; similarities, vocabulary, digit symbol substitution and block design. With the exception of vocabulary, improvement was shown at retest by patients on all of these. This finding provides additional evidence for the well-established premise that vocabulary represents a stable aspect of intelligence, independent of symptomatology, and thereby supports further the continued use of reading tests to obtain a measurement of premorbid intelligence, such as the National Adult Reading Test (NART; Nelson, 1981).

\textsuperscript{23} The current version of the Wechsler Adult Intelligence Scale (i.e., WAIS-IV), released in 2008, transitioned from dual verbal/performance IQ to an index score structure; Full Scale IQ, and four indices (Pearson, 2008).
Moreover, recent work has produced evidence of patient heterogeneity on intelligence measures that may suggest the preservation of intelligence in some cases (Badcock et al., 2005; Mercado, Johannesen, & Bell, 2011; Palmer et al., 1997), and/or the potential for a “high-functioning” subgroup in schizophrenia (Badcock et al., 2005; MacCabe et al., 2012). This is a relatively novel concept given the longstanding assumption that intelligence underlies the patient’s capacity for neuropsychological performance, which has consistently been shown to be poor (Karageorgiou et al., 2011; Lewandowski, Cohen, & Ongur, 2011; Nieto & Castellanos, 2011). More recently research has begun to dispel this myth, showing that patients continue to perform consistently below healthy controls on a range of neuropsychological measures, despite being matched in IQ (Badcock et al., 2005; Wilk et al., 2005). Wilk et al. (2005), for instance, matched patients and healthy controls within three Full Scale IQ points on the WAIS (Wechsler, 1997), yet their respective neuropsychological profiles were significantly different; patients showed a pronounced memory and speeded visual processing deficit.24 However, while Wilk et al. (2005) have shown neuropsychological deficits in patients over and above the influence of intelligence, this is not necessarily evidence of intact or preserved intelligence in schizophrenia. The data from Wilk et al. (2005) shows that the mean WAIS IQ for both groups was within the WAIS classification of average intellectual functioning ($M = 99.2$ for both groups, $SD = 12.4$ and 12.2 for patients and controls respectively). It therefore remains unclear whether patient cohorts that would fit into the above average and/or superior WAIS ranges actually exist.

Elsewhere, reports suggest that the acquisition of new intellectual information may be slowed during the first five years of illness onset (Jespen et al., 2010). Interestingly, rather than a cross sectional IQ assessment, Jespen et al. (2010) followed patients over the trajectory of the first five years following full clinical presentation of their first episode. This methodology accounts for the heterogeneous dynamic brain changes across individuals during the first five years of their illness, which is discounted when assessed cross-sectionally, and thus may offer an incomplete picture (Pantelis et al., 2009). While their sample sizes were relatively small (early onset schizophrenia, $n = 10$, non-affective psychosis, $n = 8$, healthy controls, $n = 35$), significantly reduced scores on intelligence measures were shown by the patients compared to control participants, however, no differences were shown between early onset and non-affective patient groups.

24 Their patients did, however, illustrate superior verbal comprehension and perceptual organisation, which is inconsistent with most literature.
Overall, despite some minor inconsistencies in the literature, and perhaps with the exception of vocabulary, there appears to be substantial evidence for generally reduced intelligence in schizophrenia. Recent suggestions of the autonomy of intelligence and neuropsychological performance probably warrant additional investigation, but the concept of preserved intelligence must be confirmed by longitudinal research that follows the same individuals over the trajectory of their illness, and to date, this has not been done.

### 3.8 Chapter summary

This chapter has reviewed a number of deficits that are generally considered to be established in the manifestation of schizophrenia. An assessment of the work conducted to date highlights the considerable inconsistencies related to some aspects of the larger phenomenon (e.g., variable priming effects at short versus long SOAs in an established semantic priming impairment). As has been discussed throughout, two main explanations may account for these discrepancies. First, the existing data reflects overarching impairments related to certain cognitive neuropsychological domains that can be considered core aspects of the disease, but the heterogeneity shown throughout, particularly to the finer nuances of the domain, might well be expected to arise from individual differences. Second, the existing data offer an incomplete picture of these impairments at each domain, given the high rate of failure to incorporate, and account for, significantly influential factors inherent in patient populations (e.g., the effects of medication). In general, future work should adhere to addressing these factors before drawing conclusions about cognitive neuropsychological domains that are likely to be influenced by them.

As early as 1913, Kraepelin’s “dementia praecox” incorporated deficiencies in memory and general intelligence as a defining feature of the disease (Badcock et al., 2005; Kraepelin, 1913). Another prominent issue raised by this review is the (perhaps still unclear) effect of these, and additional executive functions (i.e., processing speed and attention) on measurements of cognitive neuropsychological domains. These are invariably implicated in, and hypothesised to underpin, performance on a range of cognitive neuropsychological functions (Wilk et al., 2005). The preceding review has indicated that much of the reported data to date has failed to account for the influence of general factors such as these, possibly a significant oversight that might account for inconsistencies.

At least two decades of research has recorded widespread impairments in cognition and on neuropsychological measures in patients with schizophrenia, including, but not
limited to, the faculties discussed in this chapter. Overall, there is satisfactory evidence to suggest that patients with schizophrenia have impairments in aspects of perceptual (i.e., visual) organisation, language and memory, executive function and intelligence. In most cases, both substantial behavioural and neurophysiological/functional neuroanatomical data has been reported as evidence of impairment across each of these domains.
Chapter 4: Cognitive Neuropsychological Deficits following Traumatic Brain Injury (TBI)

4.1 Introduction

4.1.1 Traumatic brain injury.

As discussed in detail in Chapter One, traumatic brain injury (TBI) describes brain injury occurring as a result of external trauma to the head, which may or may not penetrate the skull. Focal TBI refers to brain tissue damage (i.e., a lesion) that is isolated to one (or many) particular cerebral location(s) of the brain, usually in response to blunt external trauma proximal to the resulting lesion. Diffuse axonal injury (DAI) consists of extensive and widespread damage to white matter tracts caused by shearing injury, typically following a sudden high-velocity acceleration and/or deceleration of the brain within the skull (Felmingham, Baguley, & Green, 2004; Johnson, Bigler, Burr, & Blatter, 1994). Depending on the cause of injury, focal lesions and DAI may occur together. As a result, cortical and subcortical regions may be damaged, including white and gray matter, and white matter tracts responsible for the connection between cortical regions (i.e., association fibres), such as the hippocampus, amygdala, corpus collosum, and cerebellum (Beauchamp et al., 2011b; Felmingham et al., 2004; Johnson et al., 1994; Nass, deCoudres Peterson, & Koch, 1989; Rios, Perianez, & Munoz-Cespedes, 2004).

The human brain is an intricate and complex structure, facilitating our capacity for sensation, perception, awareness, cognition, emotion, and behaviour. The brain is broadly mapped for functionality, and thus, injury to a particular cerebral location may result in damage to the associated functionality. For example, frontal lobe injury is commonly associated with a wide range of deficits in executive function (Lipton et al., 2009). Sequelae post TBI are vast, and include, but are not limited to; cognitive deficits, sensory deficits, mood symptoms (e.g., depression, mania, and apathy), anxiety, psychosis (discussed in Chapter Two), speech defects, and behaviour or dyscontrol disorders (LeBlanc, de Guise, Feyz, & Lamoureux, 2006; McAllister et al., 1999; Rao & Lyketsos, 2000; Sarno et al., 2000).

Post TBI outcome relies on several injury-related factors such as injury type (focal versus diffuse), severity, lesion location, and time since the trauma (Johnstone, Hexum, & Ashkanazi, 1995; Ponsford, Draper, & Schonberger, 2008). Injury severity has been determined in a number of ways in the literature and is currently most commonly classified
by the length of loss of consciousness (LOC) or coma, Glasgow Coma Scale (GCS) score (Teasdale & Jennett, 1974), and duration of post traumatic amnesia (PTA) (See Appendix A for classifications) (Schonberger, Ponsford, Reutens, Beare, & O'Sullivan, 2009; Vakil, 2005). In very general terms, worse injury is usually associated with worse outcome. However, focused investigations of the relationships between these injury demographics and cognitive neuropsychological domains have been relatively scarce, and are often inconsistent in both methodology and findings. Accordingly, associations between the range of injury variables and neuropsychological outcome remain unclear. For instance, it has been reported that childhood TBI may leave the child at greater risk given that damage may disrupt the developing brain (Beauchamp et al., 2011a). On the other hand, injury in adulthood and older age may increase the impact of trauma on the brain due to decreased neuroplasticity as we age (Schonberger et al., 2009).

This chapter provides a review of the cognitive neuropsychological literature pertaining to traumatic brain injury (TBI). Domains identified in Chapter Three as impaired in psychosis are covered in detail; visual-perceptual organisation, language and memory (verbal fluency and semantic processing), reasoning (probabilistic), executive function (including attention, mental inhibition and switching, and processing speed), and general intelligence. Some additional contextual literature is provided where necessary.

### 4.2 Perceptual Organisation and Visual Gestalt Processing

#### 4.2.1 Visual pathways.

As discussed in Chapter Three, visual perception involves the interaction of existing knowledge with incoming sensory input at all stages of processing. Visual information must be received, organised, and assimilated to facilitate a healthy perception of the environment (McKenna, Cooke, Fleming, Jefferson, & Ogden, 2006). While impaired perceptual organisation is paramount in psychosis, it appears that various disruptions to vision and visual processing pathways may occur as a consequence of traumatic brain injury, also resulting in perceptual deficits in this cohort.

In brief, the primary visual pathway extends from photoreceptive cells on the retina of the eye to the dorsal lateral geniculate nucleus in the thalamus, and on to the primary visual cortex (striate cortex/V1) of the ipsilateral hemisphere in the occipital lobe (Gray, 1989; Purves et al., 2001) (see Figure 4.1). Visual information then passes forward along a visual
hierarchy, from V1 via two routes, the dorsal and the ventral, gaining processing complexity as it goes. The dorsal route extends from V1 to V2 and onto V5 (or middle temporal area, MT), and the parietal cortex, while the ventral route extends from V1 to V2 and V4, and the temporal cortex (Purves et al., 2001; Ungerleider & Mishkin, 1982) (see Figures 4.2 and 4.3). Neurons in V1 encode the basic properties of a visual image (e.g., luminance, orientation), whilst the dorsal route adds spatial and motion information, and the ventral route facilitates form recognition, object identification, and categorisation of visual stimuli (Purves et al., 2001; Ungerleider & Mishkin, 1982). Information at each stage must be integrated to support vision, along with higher order visual attention, memory and visual cognition (Purves et al., 2001; Warren, 1993).

Both the afferent and efferent pathways (relaying information to, and from, the cortex respectively) can be affected by traumatic brain injury. Direct trauma may occur to the occipital cortex, and in a minority of cases to the optic nerve, and/or to the eye. More commonly, indirect trauma may occur to the brainstem and oculomotor nerves, usually the result of posttraumatic oedema of the nerve or surrounding tissues, and/or interruption of the
Figure 4.2. Localisation of multiple visual areas in the human brain using fMRI. (A,B) Lateral and medial views (respectively) of the human brain, illustrating the location of primary visual cortex (V1) and additional visual areas V2, V3, VP (ventral posterior area), V4, MT (middle temporal area), and MST (medial superior temporal area). (C) Unfolded and flattened view of retinotopically defined visual areas in the occipital lobe. Dark grey areas correspond to cortical regions that were embedded in sulci; light regions correspond to regions that were located on the surface of gyri. Taken from Purves et al. (2001).

Figure 4.3. The ventral (toward the temporal lobe) and dorsal (toward the parietal lobe) pathways extending from V1 (striate cortex). The ventral route (purple) facilitates object recognition while the dorsal route (yellow) facilitates spatial vision. Taken from Purves et al. (2001).
blood supply to the nerve itself (Kelts, 2010; van Stavern, Bioussé, Lynn, Simon, & Newman, 2001). Thus, damage at the lesion site, resultant swelling, and/or neuronal shearing may result in a perceptual consequence. In fact, given the proportion of the brain devoted to visual processing (i.e., almost the entire posterior half of the cerebral cortex), it is unsurprising that visual-perceptual impairment is common following TBI (Brosseau-Lachaine, Gagnon, Forget, & Faubert, 2008; Ripley & Politzer, 2010). For instance, one study identified deficits in more than fifty per cent of patients (van Stavern et al., 2001).

### 4.2.2 Disruptions to vision.

Of course intact visual perception relies first on accurate incoming visual information. The effects of trauma have been shown to compromise vision in a number of ways, including:

- (i) most typically, the loss of visual acuity (i.e., blurred vision) and visual field (i.e., spatial array of visual input available to each eye);
- (ii) diplopia (i.e., double vision, where the brain perceives two images of the same object, often displaced horizontally and/or vertically, and can result from either the misalignment of the fovea of each eye relative to one another and/or cranial nerve damage, particularly to the third and sixth cranial nerve);
- (iii) homonymous hemianopia (i.e., loss of half of the visual field on the same side in both eyes due to damage in one hemisphere of the brain, see Figure 4.4) (Brosseau-Lachaine et al., 2008; Kelts, 2010; Niemeier, 2010; Ripley & Politzer, 2010). Visual efficiency skills are also often compromised, and result in the further distortion of incoming visual stimuli. This is typically shown in reduced oculomotor function (i.e., eye movements necessary to identify and track objects), poor eye teaming (i.e., convergence), and reduced visual accommodation (i.e., change in focus to accommodate the distance of visual stimuli) (Hulse & Dudley, 2010; Niemeier, 2010).

In such cases, where visual input is likely to be incomplete and distorted, visual acquisition is insufficient for adept visual processing (Hulse & Dudley, 2010; Niemeier, 2010). Yet visual processing assessments, and neuropsychological assessments more generally, typically rely on visual stimuli, and thereby intact vision, to obtain their measurement. Thus, where known post injury visual dysfunction exists, data is likely to be confounded.²⁵ Cate and Richards (2000) have argued that the assessment of visual processing

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²⁵ Equivalent verbal versions of the various neuropsychological tests have been recommended in such cases (Cate & Richards, 2000; Niemeier, 2010). Of course, this does not resolve the problems inherent in the measurement of visual processing.
must begin with a measurement of basic visual function in patients. Their data illustrated a positive correlation between visual functionality and perceptual skills measured by the Motor-Free Visual Perception Test (MVPT; Colarusso & Hammill, 1972). One French case study reported that although visual acuity had improved enough to support reading by six years post injury, the patient continued to suffer with pronounced prosopagnosia (i.e., severely disrupted face perception and subsequent identity recognition) (Pradat-Diehl, Masure, Lauriot-Prevost, Vallat, & Bergego, 1999). Hence visual input and visual processing have clear implications for visual perception, and its measurement, following brain injury.

Figure 4.4. A homonymous hemianopia is the loss of half of the visual field on the same side in both eyes. Visual images seen on the right travel from both eyes to the left side of the brain, while images on the left travel to the right side of the brain. Therefore, damage to the right side of the posterior portion of the brain can cause a loss of the left field of view in both eyes, and damage to the left posterior brain can cause a loss of the right field of vision (images source at http://en.wikipedia.org/wiki/homonymous_hemianopsia).

4.2.3 Visual processing and perceptual deficits.

Visual-perceptual abilities are wide ranging in support of our interaction with the environment, providing proficient visual discrimination, visual memory, visual-spatial relations, visual figure-ground, visual closure, and visual-motor integration (Hulse & Dudley, 2010). To date, a number of studies have identified perceptual impairment following TBI (e.g., Kersel, Marsh, Havill, & Sleigh, 2001; Malina, Regan, Bowers, & Millis, 2001; McKenna et al., 2006; Shum, Harris, & O’Gorman, 2000). However, some published research has offered evidence of disrupted perception without considering the effects of basic visual
impairment in their sample. For example, Kersel et al. (2001) used the Block Design task of the WAIS-R (Wechsler, 1939) to show that forty per cent of patients with severe TBI \((N = 65)\) had some form of impairment in visual *processing* at six months post injury. The authors made no reference to the assessment of visual acuity.

Elsewhere research has shown that perceptual deficits remain even where visual impairment is excluded as an explanation, instead implicating damage to processing pathways (Brosseau-Lachaine et al., 2008; McKenna et al., 2006; Shum et al., 2000). Brosseau-Lachaine et al. (2008) ensured normal or corrected-to-normal vision (including binocular vision) and ocular health, assessed by an optometrist in children following mild TBI (mTBI). In spite of this, complex visual Gestalt processing impairments were shown in their sample at three months post injury. After excluding basic visual-perceptual problems, Shum, Harris, and O’Gorman (2000) obtained data that indicated poor visual memory in patients who had experienced a severe TBI, both in terms of their error rate, and rate of learning. In a sample of thirty-one patients who had sustained a severe TBI (PTA in days; \(M = 61.2, SD = 45.9\)), McKenna et al. (2006) also showed visual-perceptual impairments in the absence of primary sensory and motor impairments. These pertained to unilateral neglect (i.e., failure to orient to, respond to, or report, stimuli presented on the contralateral side to the lesion, 45.2\% of the sample); impairments of body schema (i.e., confusion of the positioning/spatial relationships between body parts, 25.8\%), and constructional skills (i.e., the integration of visual perception, motor planning and motor execution, 25.8\%). Based on a range of additional tests the authors were also able to rule out a common underlying cognitive and/or motor profile in patients showing impairment. That is, no significant differences were shown on measures of general cognition, behavioural memory, functional independence, or duration of post traumatic amnesia between the brain injured group that showed perceptual deficits and the thirty-five per cent that did not (McKenna et al., 2006). Taken together, the current literature indicates visual-perceptual impairments that may differ in origin (i.e., the nature of the lesion, its’ size, location and cortical consequence, these variables were not matched in the aforementioned studies), but share common functional expressions post traumatic brain injury.

4.2.3.1 Injury severity.

The effect of injury severity as a mediator in visual-perceptual processing has not been addressed specifically. Instead research has typically employed cohorts that fit either mild (e.g., Brosseau-Lachaine et al., 2008; Ponsford et al., 2011) or severe (e.g., Kersel et al.,
2001; Shum et al., 2000) classifications of severity. The work by McKenna et al. (2006) appears to provide no evidence concerning the effect of injury severity on visual processing. According to the PTA demographics reported, the patient sample utilised by McKenna et al. (2006) typically fall into the severe category of injury (PTA, \( M = 61.2, SD = 45.9 \), range 11-204 days) (McKenna et al., 2006; Williamson, Scott, & Adams, 1996). Group comparisons led the authors to conclude that visual processing deficits were not mediated by injury severity in their sample given that no differences in PTA were shown between the impaired and unimpaired groups (McKenna et al., 2006).

A closer look at their data, however, shows a pattern of reduced PTA in those without impairment across all three visual-perceptual categories: i) unilateral neglect; those without impairment showed a mean of 49.4 (SD = 37.3), with impairment, 75.8 (SD = 52.6), ii) body schema; a mean of 58.8 (SD = 50.9) and 68.9 (SD = 26.3) respectively, and iii) constructional skills; a mean of 54.9 (SD = 40.3) and 77.9 (SD = 58.0) respectively. It is likely that their null result reflects the variable spread of their sample (i.e., an overall PTA standard deviation of 45.9) and thus, the likelihood of a significant relationship between visual processing deficits and PTA would have been amplified by employing correlational analyses instead. Despite their discussion acknowledging the significant limitations of their small sample size (e.g., reduced and/or potentially insufficient power for group analyses, \( n = 14, 8, \) and 8 for the perceptual categories respectively), McKenna et al. (2006) make no mention of the variability of data. The authors may have missed an opportunity to identify aspects of the role of injury severity in visual-perceptual impairment.

Similarly, relatively little work has addressed visual processing following mTBI specifically (Brosseau-Lachaine et al., 2008). There is some evidence from neuropsychological assessments, however, to suggest visual memory (Ponsford et al., 2011; Rohling et al., 2011), visual organisation (Gestalt) (Brosseau-Lachaine et al., 2008), and visual motion deficits (Patel, Ciuffreda, Tannen, & Kapoor, 2011). A handful of studies have also assessed and reported disruptions to vision itself, particularly regarding vergence and accommodative deficits (e.g., blurred vision and diplopia) (Green et al., 2010a, 2010b; Thiagarajan, Ciuffreda, & Ludlam, 2011) (see Figure 4.5 for a breakdown of visual deficits in the current mTBI literature).

In a re-analysis of twenty-five studies used in a series of prior meta-analytic reviews, Rohling et al. (2011) showed that visual memory domains were among the most affected immediately post injury in mTBI. By three months post injury all neuropsychological domains had improved to within normative ranges, a commonly reported finding following
mTBI. More recently though, Ponsford, Cameron, Fitzgerald, Grant, and Mikocka-Walus (2011) presented data that showed visual memory deficits in patients with mTBI at both the one week and three month mark post injury. Similarly, while the data from Brosseau-Lachaine et al. (2008) showed impaired Gestalt processing, simple linear (first order) visual stimuli processing was intact. This may indicate that higher order visual processing may be more vulnerable to insult, and generally affected for more than three months post injury (the commonly hypothesised neuropsychological recovery period following mTBI).

![Figure 4.5](image)

**Figure 4.5.** Commonly reported clinical symptoms in non-strabismic (i.e., not a result of an imbalance of the eye muscles) vergence disorders in mTBI. The category ‘Others’ includes symptoms such as headache, dizziness, ocular pain, and poor visually-based concentration. Taken from Thiagarajan et al. (2011).

### 4.2.3.2 Hemispheric specificity.

Evidence for the specialisation of hemispheres during local/global processing has been shown in healthy control samples (Fink et al., 1996; Martinez et al., 1997), and in both adult (Fitz, Conrad, Hom, & Sarff, 1992; Robertson & Lamb, 1991) and child (Akshoomoff, Feroleto, Doyle, & Stiles, 2002) clinical (TBI) samples. Generally, the data identifies a bias of the left hemisphere for local and analytical processing, and a right hemispheric bias for global and holistic (Gestalt) processing (Akshoomoff et al., 2002; Fink et al., 1996; Fitz et al., 1992; Martinez et al., 1997; van Kleec, 1989). Patients with lesions isolated to either hemisphere typically illustrate deficits to the associated aspect of visual processing. Both Robertson and Lamb (1991), and Delis, Robertson, and Efron (1986), have shown pronounced and fascinating illustrations of this bias in patients with unilateral injury (see Figures 4.6 and 4.7). In both cases an intriguing distinction is shown between patients with
left versus right hemispheric lesions and the resultant supremacy of global or local aspects of visual memory, recall, and reproduction.

Figure 4.6. Data collected from two TBI patients by Robertson and Lamb (1991). a) The Rey Osterrieth figure. b) Replication of the figure from memory by a patient with left hemispheric injury illustrates dominance of the right hemisphere (i.e., a global processing bias). c) Replication of the figure from memory by a patient with right hemispheric injury illustrates dominance of the left hemisphere (i.e., a local processing bias).

Figure 4.7. Example illustrations from the Delis et al. (1986) pilot study (Navon figures). a) and b) show original stimuli in both linguistic and nonlinguistic formats. c) and d) show the replication of these stimuli from memory by a patient with right hemispheric damage, and thus the correct recall of local, but not global, information. e) and f) show the replication of these stimuli from memory by a patient with left hemispheric damage, and thus the correct recall of global, but not local, information.
Neuroimaging work using positron emission tomography (PET) has shown that temporal-parietal activation in the prestriate cortex (V2) distinguishes between global and local processing (Fink et al., 1996). Activation in the right lingual gyrus has been shown during global-level processing, while the left inferior occipital cortex is associated with local-level processing (see Figure 4.8). The functional magnetic resonance imaging (fMRI) work from Martinez et al. (1997), however, has suggested that left hemispheric activation may be shown for both global and local processing, with a trend for increased activation during local/detailed processing (see Figure 4.9). Localised lesion neuroimaging work is yet to be published, however resultant local/global impairments would be expected to reflect the patterns of activation mapped to date.

Spatial integration abilities are also lateralised. Injury to the right hemisphere is associated with the impaired organisation of spatial configurations while injury to the left fosters the oversimplification of spatial form (Akshoomoff et al., 2002). Data from Akshoomoff et al. (2002) further confirmed that hemispheric specialisation for these specific visuo-spatial skills are lateralised at birth. Children who had had prenatal/perinatal injury to either left or right hemispheres produced a poorer copy of the Rey-Osterrieth Complex Figure (Osterrieth, 1944; Rey, 1941) relative to controls (Akshoomoff et al., 2002). Over two experiments brain injured children continued to use immature strategies of reproduction and, even at ages eleven to fourteen, produced drawings that reflected a bias toward the global shape of the figure, or its internal details, according to the location of their injury. However, the children also showed improvement in their ability over time, indicating the advancement of spatial perception as the child develops and the enhanced neuroplasticity of the young brain.

4.2.3.3 Electrophysiological evidence.

Deficits in visual organisation have also been demonstrated electrophysiologically. Attenuated P300 amplitudes and reduced P300 latencies have been shown following severe TBI (Lew, Lee, Pan, & Date, 2004). The P300 event related potential (ERP) indicates the detection of novel stimuli among similar distracter stimuli. P300 amplitude is taken to reflect the activity during cerebral processing as visual input is assessed and updated in working memory, while latency reflects the speed of stimulus classification (Lew et al., 2004). Thus, the reduction of both of these ERP parameters in TBI patients, despite similar response accuracy, theoretically implicates impaired visual organisation and categorisation. These data have since been replicated using affective stimuli in an oddball paradigm (Doi, Morita,
Figure 4.8 (Left). Relative regional cerebral blood flow (rCBF) increases associated with globally and locally directed attention. Red arrows indicate the local maximum within the area of activation. Right hemispheric neuronal activation centred on the lingual gyrus during globally directed attention and left hemispheric neuronal activation centred on inferior occipital cortex during locally directed attention is shown. LG = Large stimulus with global attention. LL = Large with local attention. SG = Small with global. SL = Small with local. Taken from Fink et al. (1996).

Figure 4.9 (Above). (A) Activation profile of a single subject, seen in three planes. The green lines depict the position of the horizontal and lateral views. Significantly correlated voxels are shown on a red to yellow scale, voxels with highest correlation coefficient values are in yellow. The LH is on the right. (B) Activation profiles for three additional subjects in the acquired coronal plane (slice 2). Taken from Martinez et al. (1997).
Sarno et al. (2000) showed further that the synchronisation of information processed during visual perception in different brain regions (i.e., channel OZ, occipital, versus channel CZ, temporal) may be disrupted. That is, damage to the cortex following severe TBI results in disruptions to the timing of the processing of incoming visual stimuli in different regions of the brain, such that the information is slightly misaligned, and subsequently skew perception.

To summarise, visual perception appears to be damaged following traumatic brain injury irrespective of damage to vision and visual pathways (McKenna et al., 2006; Ponsford et al., 2011; Shum et al., 2000). According neuropsychological data, impairments in visual perception appear further to conform to the established lateralisation of visual processing, where local processing is impaired following unilateral damage to the left hemisphere, and global processing impaired by damage to the right (Delis et al., 1986; Robertson & Lamb, 1991). Visual memory, visual motion, visuo-spatial abilities, and visual organisation (Gestalt) deficits have all been shown post injury, and to various degrees of injury severity (Brosseau-Lachaine et al., 2008; McKenna et al., 2006; Patel et al., 2011; Ponsford et al., 2011; Rohling et al., 2011; Shum et al., 2000).

4.3 Language

4.3.1 Language and communication deficits.

Broca’s area in the inferior frontal gyrus and Wernicke’s area in the posterior temporal lobe have been recognised as the cortical epicentres of the brain’s ability for speech production and comprehension respectively since the late nineteenth century. Of course the anatomical foundations of human language are significantly more complex than the involvement of these two areas or the connections between them. As with the visual system, a number of cortical regions have emerged as fundamental to aspects of language, for example in word and sentence recognition (Dronkers, Wilkins, van Valin Jr., Redfern, & Jaeger, 2004). These have included the parietal cortex in Brodmann’s area (BA) 39 (J. R. Binder et al., 1997), a range of temporal areas including BA 20, 21, and 42 (J. R. Binder et al., 1997; Dronkers et al., 2004), mid-frontal cortex in BA 46 (Dronkers et al., 2004), and frontal BA 9, and 47 (Dronkers et al., 2004; Muller et al., 1997). Damage to any one of these areas may leave the language system vulnerable to impairment. Figure 4.10 provides an example case study of language-related activation in a healthy twenty-six year old male.
Language and communication impairments following TBI are well documented in the literature (Hinchliffe, Murdoch, & Chenery, 1998; J. LeBlanc et al., 2006). These generally conform to four broad areas; lexical comprehension and production, semantics, discourse processes, and reading/listening skills (Ewing-Cobbs & Barnes, 2002; Moran & Gillon, 2004). Numerous factors have been shown to mediate the type and extent of these deficits, including age at the time of the injury (i.e., pediatric, childhood, adolescence, and adulthood), premorbid language and education, injury demographics (i.e., type, location, and severity), and time since the trauma (i.e., acute versus recovery) (J. LeBlanc et al., 2006; Moran & Gillon, 2004; Sullivan & Riccio, 2010). Leblanc et al. (2006), for instance, showed that education and severity of TBI as classified by GCS score predicted language comprehension and expression in the early acute phase post injury.

![Image of brain activity from Binder et al. (1997)]

Figure 4.10. Language areas identified in a 26 year old healthy male. Activated areas in the left hemisphere include the superior temporal sulcus, middle temporal gyrus (L56), inferior temporal gyrus (L56-44), fusiform gyrus (L44), angular gyrus, (L56-32), inferior frontal gyrus (L20-8), anterior cingulated (L8), and perisplenial cortex/precuneus (L8). The right posterior cerebellum is activated, as are small foci in the right dorsal prefrontal cortex and right angular gyrus. Taken from Binder et al. (1997).

More specifically, deficits have been shown in primary language functions such as simple picture naming (Hinchliffe et al., 1998; Kerr, 1995), linguistics and metalinguistics, including ambiguous sentences, synonyms, and semantic absurdities (Hinchliffe et al., 1998), comprehension and expression of extended discourse (Hartley & Jensen, 1991; Snow, Douglas, & Ponsford, 1997), and phonemic (Baldo & Shimamura, 1998; Jurado, Junque, Pujol, Oliver, & Vendrell, 1997; Jurado, Mataro, Verger, Bartumeus, & Junque, 2000; Kave, Heled, Vakil, & Agranov, 2011) and semantic fluency (Grossman, 1981; Kave et al., 2011; R. C. Martin, Loring, Meador, & Lee, 1990). Using an extensive language battery designed to assess the language system across its hypothesised hierarchy of structure and complexity,
Hinchliffe et al. (1998) showed nicely that the linguistic system following closed head injury is significantly impaired. The deficit was most pronounced on measures tapping the lexical-semantic system.

### 4.3.2 Verbal fluency deficits.

As noted, a verbal fluency deficit in patients post traumatic brain injury has been established, both to phonological assessments of fluency (Baldo & Shimamura, 1998; Jurado et al., 1997; Jurado et al., 2000; Kave et al., 2011), and to semantic fluency tasks (Grossman, 1981; Kave et al., 2011; R. C. Martin et al., 1990), although, the latter has been relatively under-investigated. In a meta-analysis that incorporated six hundred and sixty seven TBI patients (over thirty studies published between 1986 and 2002), Henry and Crawford (2004) showed that deficits on phonemic and semantic fluency tasks seemed to be equivalent. Given the effortful response initiation, recall, retrieval, maintenance, and switching required for both tasks (Ojeda et al., 2010), comparable poor performance across phonological and semantic assessments are often taken as an indication of deficient executive abilities. Henry and Crawford (2004) interpreted their data in this way, and used further analyses to confirm that the TBI and healthy control groups were adequately matched on premorbid IQ (Nelson, 1982) and current verbal IQ (Wechsler, 1955) across the studies measuring phonological fluency. This provides an important indication that poor fluency identified in the brain injured group on phonemic tasks is not an artefact of reduced intelligence generally, or inferior verbal skills. The effect of slowed information processing speed on performance across the thirty studies could not be ruled out however; brain injury accounted for considerably more variance in fluency performance than processing speed measured by the Trail Making Test – Part A (TMT-A) (W. Reitan, 1990), but not significantly so. The same analyses could not be completed for the semantic data because too few studies have been published in the area.

According to our current maps of brain functionality, poor executive function following brain injury is considered reflective of frontal lobe damage (Baldo & Shimamura, 1998; Jurado et al., 1997; Jurado et al., 2000; Parks et al., 1988). Semantic fluency, while shown to be sensitive to frontal lobe functionality (Owen, Downes, Sahakian, Polkey, & Robbins, 1990; Pujol et al., 1996; Stuss et al., 1998) has generally been associated with left temporal lobe activation (Grossman, 1981; Henry & Crawford, 2004; A. Martin, Wiggs, Lalonde, & Mack, 1994). The clearest evidence has come from fMRI data obtained in healthy controls (Pujol et al., 1996), and temporal regions have already been established as vital for object perception, recognition, imagery and naming (Martin et al., 1994; Pujol et al., 1996; Stuss et
As such, the literature generally points to the involvement of two overlapping but dissociable systems during phonological and semantic based fluency tasks (Jurado et al., 2000; Zakzanis, McDonald, & Troyer, 2011). In addition to frontal executive function, the latter theoretically relies on the organisation of the semantic memory store (See Chapter 3: Section 3.3.2: Fluency, Memory Structure and Strategy).

To date, there is clear empirical support for theoretically overlapping but dissociable pathways. Work has shown that patients with frontal lobe lesions do produce fewer items than controls on both phonological and semantic tasks, implicating the frontal lobes more generally in the organisation, initiation, and retrieval of appropriate words needed for both task types (Baldo & Shimamura, 1998). Temporal lobe sensitivity during semantically driven fluency has been confirmed by a number of study designs including an imaging study using healthy controls (Pujol et al., 1996), research done in temporal lobe atrophy (intact frontal) in dementia (Mummery et al., 2000), and a lesion location-based analysis (Henry & Crawford, 2004). However, some exceptions have been noted. Jurado et al. (2000) identified frontal lobe lesions by MRI and showed reduced word size to the phonemic category only. Even more uniquely, not all patients illustrated a fluency deficit, even in the presence of large bilateral frontal lesions. Similarly, patients with damage to the left anterior temporal region were shown by Stuss et al. (1998) to have intact semantic fluency production relative to controls, although this result was borderline ($p < .07$). Despite these exceptions, in sum the literature advocates distinguishable frontal and temporal involvement in phonemic and semantic fluency respectively.

4.3.2.1 Left versus right hemispheric lesions.

The established relative laterality of hemispheres pertaining to verbal (left hemisphere) and visual-spatial (right hemisphere) processing also holds true in the TBI literature. Patients with left hemisphere lesions have been shown to perform worse on verbal tests (Miceli, Caltagirone, Gainotti, Masullo, & Silveri, 1981), and patients with left temporal lobe epilepsy (TLE) illustrate poorer performance on both phonemic and semantic tasks than those with right TLE (Martin et al., 1990). Left unilateral frontal lobe lesions have been associated with significant word fluency impairments relative to right hemisphere frontal lobe lesions (Benton, 1968; Janowsky, Shimamura, Kritchevsky, & Squire, 1989; Perret, 1974), or temporal and posterior lesions, which do not differ from each other (Perret, 1974). This has also been established in written verbal fluency (Thurston Word Fluency Test, TWFT) (Thurstone & Thurstone, 1949). Pendleton, Heaton, Lehman, and Hulihan (1982) showed that
the greatest impairment in written fluency was associated with frontal, relative to nonfrontal lesions, with left relative to right hemispheric lesions, and with left frontal, relative to right frontal lesions.

On the other hand, Joanette and Goulet first reported a right hemisphere semantic fluency-specific deficit in 1986 following the assessment of thirty-five vascular right brain-injured patients. These data led them to conclude that lexico-semantic processing is instead supported by processing in the right hemisphere (Joanette & Goulet, 1986), for which there has since been some additional supporting evidence, for example, in split-brain patients, and in a SPECT (Single Photon Emission Computer Tomography) study (see Goulet, Joanette, Sabourin, & Giroux [1997] for discussion). However, the authors challenged their previous conclusion in a 1997 study when they hypothesised that the fixed delivery order of the tasks (i.e., phonological followed by the semantic) may have caused higher rates of fatigue and reduced attention common in TBI patients, and that this may have been responsible for the poorer performance recorded for semantic fluency. Randomised delivery of semantic and phonological fluency tasks, among some other methodological changes, did in fact show that patients with right hemisphere injury were equally impaired across phonological and semantic categories (Goulet et al., 1997). At least one published study, however, remains inconsistent with these trends by showing equal impairment in patients with frontal lobe damage, independent of the side of the lesion (e.g., Miceli et al., 1981).

### 4.3.2.2 Precise lesion sites.

More recently, rather than the coarse comparison of left versus right and/or unilateral damage, Stuss et al. (1998) investigated fluency performance as a function of more precise frontal lobe lesion sites in seventy-four patients. The authors showed that patients with left dorsolateral and/or striatal lesions illustrated the poorest performance, and moderate impairment was associated with superior medial frontal damage to either left or right hemisphere, and to left parietal damage (but not left anterior temporal damage). This was true for both phonological and semantic fluency tasks; except that semantic fluency performance was also impaired by patients with right dorsolateral and inferior medial region lesions (see Figure 4.11). Moreover, phonological fluency was not significantly impaired in patients with damage to any of the following regions: the right dorsolateral cortical or connecting striatal regions; the right posterior area; or the medial inferior frontal lobe of either hemisphere (Stuss et al., 1998).
Figure 4.11. Letter-based (F-A-S total) and semantic (animals) average fluency scores by group; RDL = right frontal dorsolateral and/or lenticular striate; LDL = left frontal dorsolateral and/or lenticular striate, SM = superior medial frontal involvement from LF, RF or BF patients, either in isolation or in combination with inferior medial lesions; IM = inferior medial frontal lobe involvement from either RF, LF or BF lesions; RNF = right nonfrontal involvement; LP = left parietal damage; LT = left temporal damage. Taken from Stuss et al. (1998).

Functional imaging research provides even greater precision. Where positron emission tomography (PET) scans have supported both frontal and temporal lobe involvement in fluency performance (Frith, Friston, Liddle, & Frackowiak, 1991; Parks et al., 1988), functional magnetic resonance imaging (fMRI) studies point to the particular involvement of the left inferior frontal gyrus (Paulesu et al., 1997; Phelps, Hyder, Blamire, & Shulman, 1997) specific to the posterior opercular portion (Paulesu, et al., 1997), as well as the anterior cingulate (Phelps et al., 1997), left thalamus (Paulesu et al., 1997), and left middle frontal gyrus (Pujol et al., 1996) during phonemic fluency tasks. In contrast, the left retrosplenial region has been implicated during semantic fluency tasks (Paulesu et al., 1997) (See Figure 4.12).

4.3.2.3 Clustering and switching.

Irrespective of the fluency type, clustering and switching rely on processes that incorporate both the executive functions and the integrity and organisation of the semantic memory store (Kave et al., 2011; Troyer, Moscovitch, & Winocur, 1997). As described in Chapter 3: Section 3.3.2: Fluency, Memory Structure and Strategy clustering involves the retrieval of words that are associated by their meaning. While this is technically a semantically-driven strategy and typically prominent in the semantic fluency task, even
where the goal is phonemic, meaning-based clusters are often formed (for instance, words beginning with the letter 'S'; *slither, snake, sin*), and this reflects the lexical stores of the semantic memory system. Meanwhile, as illustrated in lesion and imaging research, both tasks rely on frontal lobe executive functioning for effortful strategic search, response, monitoring, flexibility, and set shifting, which together allows for *switching* to a new cluster once the present one is exhausted.

**Figure 4.12.** Top: on the left, a cortical rendering of the lateral surface of the left hemisphere illustrates the location of the area which was activated to a significantly greater extent during phonemic verbal fluency – the posterior opercular portion of the left IFG (BA 44/6). On the right, the graph illustrates the time course of the BOLD contrast for this area. Bottom: on the left, the retrosplenial posterior cingulate (BA 31), which was activated to a greater extent by semantic fluency, is illustrated on a medial view of the left hemisphere. On the right, the graph illustrates the time course of the BOLD contrast for the most significantly activated voxel in this area. Taken from Paulesu et al. (1997).

In theory, then, the *number* of clusters and switches can be considered reflective of executive functionality, whereas the *size* of the cluster may be indicative of the semantic memory store (Kave et al., 2011). With this in mind Kave et al. (2011) reported reductions in total output, number of switches, and number of clusters on both tasks by TBI patients, but no differences in mean cluster size. Although patients who had sustained a TBI demonstrated greater deficits to semantic relative to phonemic fluency, the data was considered indicative
of impaired executive functionality given that the deficit was shown to switching (i.e.,
theoretically executive) rather than clustering (i.e., theoretically semantic). The assessment of
lesion location in their patient group would have complemented this data well given the
established literature implicating frontal lobe functionality with executive systems (Baldo &
Shimamura, 1998; Jurado et al., 1997; Jurado et al., 2000; Parks et al., 1988) and temporal
lobe functionality with semantic memory (Grossman, 1981; Henry & Crawford, 2004; A.
Martin et al., 1994; Pujol et al., 1996). However, the authors failed to report injury
information for their sample (hemispheric, lobe, or otherwise).

Other interesting findings have come from the analysis of clustering and switching.
Grossman (1981) showed differences in the contents of clusters according to left versus right
hemispheric injury. Under fluency task conditions, patients with left hemisphere injury
produced words that rarely have common attributes, whereas patients with right hemisphere
injury produced many clusters of related items. Troyer et al. (1997) investigated cluster and
switching abilities according to injury location directly and showed that, in line with the
established literature, patients with frontal lobe lesions were unimpaired in clustering.
However they switched significantly less once a cluster was exhausted on both phonological
and semantic fluency\(^{26}\). The patients with temporal lobe lesions instead showed unimpaired
performance in terms of both clusters and switches to the phonological fluency task, however
their semantic fluency performance was characterised by fewer switches. Patients with injury
confined to the left temporal lobe also produced smaller clusters than patients with right
temporal lobe injury, consistent with Grossman’s (1981) work. Given that switching is
considered an executive function the authors speculated that impaired switching on semantic
fluency may result from damage to pathways connecting frontal and temporal regions (and
thus, represent additional frontal dysfunction by proxy). This also explains why switching
was normal for the phonological task because phonological fluency does not rely on anterior
temporal regions, and/or connecting pathways to the frontal lobe. Smaller clusters shown for
semantic fluency were explained by the dependence of this task on the integrity of the
semantic memory store (Troyer et al., 1997). Still, contrasting findings have been reported.
Stuss et al. (1998) showed no group effects on mean cluster size or on the proportion of
clusters to total output for either phonological or semantic fluency, irrespective of lesion

\(^{26}\) Although a frontal lobe group effect was found, it was patients with left dorsolateral frontal and superior medial frontal
injury that illustrated switching impairment, whereas injury in the right dorsolateral frontal and inferior medial frontal
regions was associated with unimpaired switching ability.
location. This was illustrated in both original patient groupings and following predictive (regression) re-categorisation of patients according to performance.

**4.3.2.4 Injury severity.**

Similar to visual-perceptual impairment, direct comparisons of fluency deficits according to the degree of injury post TBI have rarely been reported. Research has incorporated cohorts of mixed severity (mostly moderate to severe) (e.g., Troyer et al., 1997), or concentrated on either mild (e.g., Raskin & Rearick, 1996) or severe injury in isolation (e.g., Jurado et al., 2000). Work in mild TBI is most likely complicated by the variability in performance, where a number of individuals following mTBI perform at a level comparable to healthy controls, whereas others show deficits resembling those seen in moderate injury. As mentioned previously, the effects of mTBI are often quantitatively less, and faster to resolve (typically by three months), than those of moderate to severe injury (Binder, Rohling, & Larrabee, 1997; Schretlen & Shapiro, 2003). However, a portion of mTBI patients often complain of unremitting neuropsychological symptoms, despite a lack of evidence for these symptoms on standard neuropsychological examinations (Leininger, Gramling, Farrell, Kreutzer, & Peck, 1990; Raskin & Rearick, 1996; Zakzanis et al., 2011). These issues may explain some of the inconsistencies shown in the literature. For instance, Raskin and Rearick (1996) showed reduced performance on tasks of verbal fluency by patients following mTBI, but Leininger et al. (1990) reported no differences on phonological fluency.

Zakzanis et al. (2011) suggested that currently available neuropsychological batteries may be unable to accurately capture unremitting symptoms experienced by mTBI patients. The authors sought to capture some of this symptomatology via the assessment of clustering and switching in the hope that these fluency subcomponents may be more sensitive to subtle impairments post injury. For instance, larger effect sizes have been shown using these component measures in other cohorts with established verbal fluency deficits (i.e., Moore et al. [2006] in schizophrenia patients, discussed in Chapter Three). In a rare comparison, Zakzanis et al. (2011) measured clustering, switching, and fluency totals in mild, moderate, and severe injury, and in a healthy control group. The authors found no group differences in phonological fluency. For semantic fluency, the number of switches decreased as TBI severity increased, however, the mean cluster size actually increased according to injury severity. This latter result effectively indicates that their healthy control group was most
'impaired’ according to cluster size, however the authors did not comment on this finding. As suggested by Troyer et al. (1997; see Section 4.3.2.3 Clustering and Switching) these data may indicate a breakdown in communication between networks of semantic memory and executive function (i.e., as indicated by switching ability), the extent of which is exacerbated according to the severity of injury. As such semantic fluency switching ability may provide an indication of lasting injury effects, even between mild and moderate injury, with semantic switches differentiating 32% of scores between mild and moderate, and 45% of scores between mild and severe injury (Zakzanis et al., 2011).

In summary, the existing literature has demonstrated that traumatic brain injury is associated with impairments in language and communication (Ewing-Cobbs & Barnes, 2002; Hinchliffe et al., 1998; LeBlanc et al., 2006; Moran & Gillon, 2004). Semantic fluency impairments require further investigation, although current evidence has shown reduced performance on both phonological and semantic tasks (Baldo & Shimamura, 1998; Grossman, 1981; Jurado et al., 1997; Jurado et al., 2000; Kave et al., 2011; Martin et al., 1990). Furthermore, clustering and switching assessments appear to offer preliminary insight into the nature of these deficits, currently hypothesised to reflect a breakdown in connectivity between the semantic store and executive functionality (Troyer et al., 1997; Zakzanis et al., 2011).

4.4 Memory

4.4.1 General memory deficits.

Memory is extremely vulnerable to the effects of traumatic brain injury. Some work has claimed that it may be the most vulnerable of the cognitive functions (Tate et al., 1991), and the slowest to recover (Lezak, 1979), with deficits still apparent at ten years post-injury (Zec et al., 2001). Perhaps with the exception of already acquired procedural memory (Schmitter-Edgecombe & Nissley, 2000), virtually all aspects of memory have shown impairment as a result of head injury, including; encoding and consolidation (Wright & Schmitter-Edgecombe, 2011), visual and verbal memory (Ariza et al., 2006), spatial memory (Owen et al., 1990), working memory (McAllister et al., 1999; Owen et al., 1990), delayed memory (Schmitter-Edgecombe, Marks, & Fahy, 1993), prospective memory (i.e., memory for planned future actions) (Kinsella et al., 1996), episodic/autobiographical memory (or

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27 Elsewhere no differences in the amount of clusters have been shown between controls and patients for either types of fluency (Raskin & Rearick, 1996).
anterograde amnesia) (Carlesimo et al., 1998; Himanen et al., 2006), and semantic memory (McWilliams & Schmitter-Edgecombe, 2008; Perri, Carlesimo, Loasses, & Caltagirone, 2000) (See Vakil, 2005 for comprehensive review).

While memory deficits have been shown following mild, moderate, and severe traumatic brain injury (Lajiness-O'Neill, Erdodi, & Bigler, 2010), some nuances in the extent of impairment have been shown according to injury demographics. Several published reviews have indicated a relationship between injury severity and memory following traumatic brain injury (e.g., Vakil, 2005); with some evidence suggesting that permanent memory impairment may be associated with a PTA beyond three weeks (Bennett-Levy, 1984). Working memory impairment may be more pronounced following severe injury in children, and may actually decline overtime, whereas deficits following mild to moderate injury seem to remain relatively stable (Krawczyk et al., 2010). Functional MRI work has also shown quite distinct differences in regional activation, according to both the pattern of activation (McAllister et al., 1999), and relative strength of activation (i.e., over-activation) during working memory tasks (Newsome et al., 2008). This is evidence of compensatory and inefficient over-recruitment of cortical activity in compensation for the loss of white matter post injury. Further, right hemispheric focal lesions may be associated with a greater deficit in episodic memory, particularly in the retrieval of personal events occurring in the year prior to the injury (Carlesimo et al., 1998), and memory for living things seems to be more vulnerable to the injury than memory for nonliving objects (Carlesimo et al., 1998; King, Hough, Vos, Walker, & Givens, 2006). As mentioned in Chapter One, bilateral damage limited to the hippocampal formation was shown to precipitate both retrograde and anterograde memory impairment in three case studies assessed by Rempel-Clower, Zola, Squire, and Amaral (1996, see Figure 4.13). Finally, visual and verbal memory impairment has been shown to conform to lateralised functionality, where focal right temporal lesions are associated with visual memory deficits and focal left temporal lesions are associated with verbal memory deficits (Ariza et al., 2006). Patients with diffuse axonal injury (DAI) show impairments to both (Ariza et al., 2006).

4.4.2 Semantic memory abnormalities.

Relative to the work devoted to other aspects of memory, disruptions to semantic memory following TBI have not been widely investigated. Still, some consistencies have emerged from the available literature that point to a loss of efficient semantic processing
The Rey-Osterrieth figure. Patients were first asked to copy the figure (small box at top left), then asked to reproduce the figure from memory 10-15 minutes later. The copy (top) and the reproduction (bottom) are shown from left to right for three patients; GD, LM, and WH, and for a control subject (CON) matched to the three patients with respect to age, education, and WAIS-R Vocabulary and Information subscale scores. Taken from Rempel-Clower et al. (1996), p.5237.

ability post TBI. A number of methodologies have been employed including, subjective object description (McWilliams & Schmitter-Edgecombe, 2008), picture naming (Kerr, 1995; Perri et al., 2000), prose recall (Haut, Petros, & Frank, 1991a), list learning and recognition (Crosson, Novack, Rrenerry, & Craig, 1989; Crosson, Novack, Trenergy, & Craig, 1998; Levin & Goldstein, 1986), word finding (King et al., 2006), classic semantic priming (Perri et al., 2000; Schmitter-Edgecombe et al., 1993), and computational models of semantic structure (Devlin, Gonnerman, Andersen, & Seidenberg, 1998; Farah & McClelland, 1991).

Overwhelmingly the work suggests that the semantic store and its organisation remain intact following TBI (Hinchliffe et al., 1998; McWilliams & Schmitter-Edgecombe, 2008; Perri et al., 2000; Schmitter-Edgecombe et al., 1993), and that deficits shown by patients on various semantic tasks reflect instead disrupted access and inefficient execution of semantic information (Haut, Petros, Frank, & Haut, 1991b; McWilliams & Schmitter-Edgecombe, 2008; Perri et al., 2000). This is inferred from slower reaction times but comparable response patterns for TBI relative to neurophysiologically-intact individuals (McWilliams & Schmitter-Edgecombe, 2008; Perri et al., 2000), although alternate findings have also been published (e.g., Devlin et al., 1998; Hux, Beukelman, Dombrovskis, & Snyder, 1993). It is
also consistent with the trends established on tasks of verbal fluency (discussed in Section 4.3: Language).

In both prose recall (Haut et al., 1991a) and list learning research (Crosson et al., 1989; Crosson et al., 1998; Levin & Goldstein, 1986), patients with head injury perform worse overall (i.e., recall less information in total), yet their ability to recall salient semantic details and use semantic category chunking/clustering strategies to facilitate their recall is generally matched with control performance. Such abilities reflect the intact structure and integrity of the semantic store. The priming data suggests the same (Perri et al., 2000; Schmitter-Edgecombe et al., 1993). Perri et al. (2000) used the semantic priming paradigm to investigate the hypothesised breakdown in both access and storage of semantic information (akin to the longstanding debate in schizophrenia, see Chapter Three: Section 3.3.3: Research in Schizophrenia: Access versus Storage). Despite slower RT’s, the authors found comparable priming effects in severely injured TBI and control participants. That is, patient’s responses reflected utilisation of the preceding prime to the same degree as controls, consistent with prior priming work in severe TBI (Haut et al., 1991b). However, reduced performance was shown by patients on measures of object naming and semantic judgement, although this was interpreted as reflective of executive deficits (i.e., reduced efficiency in the effortful and intentional retrieval of information) (Perri et al, 2000).

Likewise King et al. (2006), in one of very few studies incorporating a mild TBI cohort, showed that mTBI patients were compromised in the retrieval of nouns and verbs using a word finding task (the Test of Adolescent Adult Word Finding; TAWF; German, 1990). While the TBI group were less accurate than controls at naming nouns in particular, they showed widespread deficits in reaction times which led to the authors’ conclusion that the impairment is executive (i.e., processing speed) rather than a reflection of poor lexical access/retrieval. However, neither study (i.e., King et al., 2006; Perri et al., 2000) included a standard executive function measure to confirm the existence and/or extent of executive impairment in their respective patient groups.

On the other hand, some authors have proposed that the integrity of the semantic store is in fact compromised following brain injury (Devlin et al., 1998; Hux et al., 1993). Hux et al. (1993) demonstrated that patients with severe TBI related superordinate-subordinate information in an idiosyncratic manner. Associations were more likely to be based on past experience and personal preference than according to the typical and anticipated
relationships, such as the superordinate category of ‘aquatic animals’ being related to the subordinate category of ‘fish’. (See Figure 3.7a, Section 3.3.3: Research in schizophrenia: Access versus storage).

McWilliams and Schmitter-Edgecombe (2008) found a similar absence in the reporting of superordinate category information by patients with various levels of injury severity. However, they concluded instead that this was reflective of reduced efficiency in the access of an intact semantic store. They asked participants to describe both living and non-living objects. TBI patients produced definitions that less often incorporated the core concept related to the object (i.e., could a blind rater identify the object?), its superordinate category (i.e., Toaster; “it’s an appliance”), and specific physical features (i.e., Camel; “they have a hump on the back”). Importantly, the authors reasoned that if the data were reflective of a breakdown in the semantic store then a differential pattern of responses would be shown from TBI and neurologically normal groups, particularly regarding feature-based information. Instead the patterns were comparable, with both groups producing more specific feature information about objects than general information, and similar amounts of information for living and non-living items (McWilliams & Schmitter-Edgecombe, 2008). Moreover, both groups produced more physical (or sensory) specific information for the living objects and more associative (or functional) information for the non-living objects, which is consistent with the hypothesis that functional information is more important in the description of non-living objects (i.e., toaster), whereas physical information is more important in the description of living objects (i.e., camel) (Devlin et al., 1998; Farah & McClelland, 1991; McWilliams & Schmitter-Edgecombe, 2008).

However, McWilliams and Schmitter-Edgecombe (2008) ran correlational analyses with the object descriptions and results obtained on a lengthy neuropsychological battery. While TBI patients showed significant correlations between object descriptions and other picture naming tasks, as well as semantic and phonological fluency, the control sample did not. This suggests that alternate cognitive deficits may influence performance on semantic tasks (such as the description of objects) post TBI. Given the established executive function and processing speed impairments in TBI, and the neuropsychological impairments demonstrated by their own patient’s assessments, the effect of these confounds should have

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28 Elsewhere mild traumatic brain injured patients have recorded increased accuracy in the naming of living versus non-living items (King et al., 2006).
been adequately investigated (e.g., covariates) (see following Sections: 4.6: Executive Function and 4.6.4: Processing Speed).

4.4.2.1 Injury demographics: Lesion location and injury severity.

Although the semantic memory literature generally indicates a similar pattern of findings in TBI, an obvious consideration is curiously missing from the majority of authors to date. As discussed at length in the previous Section 4.3.2 Verbal fluency deficits, research has associated semantic memory and semantic processing with the temporal lobe (Grossman, 1981; Henry & Crawford, 2004; Martin et al., 1994; Pujol et al., 1996). In fact, brain injury case studies who underwent a comprehensive semantic memory battery showed that the left temporal neocortex was fundamental in the proficient and accurate processing of semantic information (Wilson, 1997). Yet the majority of work has not considered the influence of lesion location when investigating semantic processing in patients who have experienced a head trauma. Some authors have either acknowledged and/or reported the potential influence of certain injury characteristics, such as duration of post-traumatic amnesia (PTA) and/or time since injury, yet have failed even to note lesion location when defining their sample, for example in Haut et al. (1991a), and McWilliams and Schmitter-Edgecombe (2008). Others may have provided sufficient injury information, indicating a mix of patients that incorporated both frontal and temporal injury, yet ran their analyses irrespective of lesion location (i.e., patients with TBI constituted one group), for example in Carlesimo et al. (1998), Perri et al. (2000), and Kerr (1995). Just as problematic, some work has included information regarding the cause of injury and then inferred the likely ensuing cortical damage. For instance, Schmitter-Edgecombe et al. (1993) stated that the majority of their patients had suffered their TBI as a result of a motor vehicle accident and thus made the assumption that their cohort had diffuse axonal injury (DAI); given the “high velocity” and “long-acceleration” of this kind of impact (p. 138). Of course, even if it is likely, this is not necessarily the case, and lesion location, especially where it presents a likely substantial mediator, should never be assumed in analyses.

There have been only a few exceptions where authors have controlled well for lesion location. An example of this is research by King et al. (2006) who ensured diffuse axonal injury in their mTBI sample from CT scans. Alternative work that has sought to assess the impact of diffuse injury versus specific lesions, for instance, in Devlin et al. (1998) who used participants with herpes encephalitis (specific sites of injury) and Alzheimer’s patients (diffuse injury) is valid, but should not be considered sufficient for the direct generalisation to
cohorts where brain injury is the result of a blunt trauma to the head, even where similarities have been shown (e.g., in Wilson, 1997).

Finally, as has been shown from the cognitive neuropsychological domains already reviewed, researchers typically recruit one severity cohort; for instance, mild (King et al., 2006), or severely injured patients (Haut et al., 1991b; Perri et al., 2000). Haut et al (1991a) published an isolated example of semantic recall investigated in both severe and moderately injured patients. Their data demonstrated that recall amount, but not semantic content, is mediated by injury severity. This example, along with investigations of other memory domains shown to be mediated by injury type and severity (see Section 4.4.1: General memory deficits), indicates that the systematic investigation of injury demographics and semantic memory is necessary.

To summarise, significant general memory impairments have been documented following mild to severe traumatic brain injury, with the extent of the memory deficit seemingly proportionate to the extent of damage to the brain (Ariza et al., 2006; Bennett-Levy, 1984; Lezak, 1979; Vakil, 2005). In spite of this, the organisation of the semantic memory network appears to remain intact post injury (Crosson et al., 1989; Haut et al., 1991a; Levin & Goldstein, 1986; Perri et al., 2000). Reduced performance in TBI on semantic priming paradigms is often interpreted as indicative of poor executive processes, although confirmation using standardised executive measures is required (McWilliams & Schmitter-Edgecombe, 2008; Perri et al., 2000).

4.5 Probabilistic Reasoning

4.5.1 Reasoning anomalies?

Probabilistic reasoning has not been investigated in traumatically brain injured cohorts to date. This is a substantial oversight given that reasoning abilities have been shown to rely on the executive functions including attention and inhibition, language, and memory, all of which are typically impaired following brain injury (see the following Section 4.6: Executive Function for discussion) (Krawczyk et al., 2010; Morrison et al., 2004). A number of other reasoning abilities have been investigated and generally appear reduced following TBI. These include deficits in theory of mind (ToM) abilities, which fall under inferential reasoning (i.e., literally inferring another’s state of mind for a given situation [Bibby & McDonald, 2005; Geraci & Cantagallo, 2011]), analogical reasoning (i.e., relational [semantic] reasoning requiring an individual to consider abstract relations among items when
solving problems, Krawczyk et al., [2010]), and deductive reasoning (i.e., where all information eventually points to the correct answer, Goverover, [2004]).

However, this work too is in its infancy, and vital considerations have again been overlooked. For instance, Hiscock, Inch and Gleason (2002) reported poorer performance in adult TBI on the Raven’s Progressive Matrices Task which measures relational/analogical reasoning (Krawczyk et al., 2010; Morsanyi & Holyoak, 2010). However, their sample included both open (i.e., skull fractures and penetrating head wounds) and closed head injury, and these were analysed as one cohort. Some injury demographics such as duration of coma, latency between injury and testing, and length of hospitalisation were reported, however, lesion location was not. Again, this is a significant oversight because the literature indicates that patients show differential deficits in analogical reasoning according to the location of cortical degeneration (Morrison et al., 2004). For instance, across picture and verbal analogies, patients with frontal lesions showed errors related to poor inhibition and working memory, whereas temporal lobe lesions were associated with meaning (semantic) based impairment (Morrison et al., 2004).

More generally, probabilistic and deductive reasoning have been shown to increase regional cerebral blood flow bilaterally in the mesial frontal region and in the cerebellum in healthy individuals. However, probabilistic reasoning was distinct in left dorsolateral frontal regions, whereas deductive reasoning was characterised by right hemispheric regional blood flow, as well as enhancements in associative occipital and parietal regions (Osherson et al., 1998). This work has clear implications for the assessment of reasoning abnormalities in TBI patients according to lesion location, and the likely effect of injury severity as well. Overall, there is a void in the literature in this area. Empirical research is warranted by deficits shown in other forms of reasoning (Bibby & McDonald, 2005; Geraci & Cantagallo, 2011; Goverover, 2004; Krawczyk et al., 2010), and by the lateralisation shown to probabilistic and deductive forms of reasoning (Osherson et al., 1998).

4.6 Executive Function

4.6.1 Executive dysfunction.

As described in Chapter Three (Section 3.6: Executive Function), executive functioning broadly involves effortful cognition, including control, flexibility, planning, and execution, all typically associated with frontal lobe functionality. As per Chapter Three, a discussion will follow on executive function generally, followed by the review of the
inhibition and switching, attention, and processing speed literature in TBI. Often these are inextricably linked, especially with regard to the measures from which aptitude in one or more of these areas is inferred. For example, the Stroop task can be used to measure all three; inhibition and switching, attention, and processing speed.

Unlike aspects of reasoning, extensive work has investigated executive dysfunction following traumatic brain injury, and while some of the nuances in the TBI population remain unclear, research has typically reported reduced cognitive function post injury (Ponsford, Draper, et al., 2008; Senathri-Raja, Ponsford, & Schonberger, 2010). Kersel et al. (2001) used the Similarities subtest from the WAIS-R and the Controlled Oral Word Association Test on adults with severe traumatic brain injury (N = 65). Forty five per cent and sixty nine per cent were shown to have mild to severe levels of impairment on these tests at six months post-injury, respectively. This had only dropped slightly at the one year mark; thirty eight and fifty five per cent, respectively. Elsewhere, meta-analytic research has sought to quantify executive deficits following TBI using estimates of effect size. These have, however, been inconsistent, with some work reporting small effect sizes (i.e., Belanger, Curtiss, Demery, Lebowitz, & Vanderploeg, 2005; Frenchmen, Fox, & Mayberry, 2005), and others finding the effect to be much larger (i.e., Mathias & Weaton, 2007).

4.6.1.1 Lesion location.

There is a high likelihood of damage to the frontal lobes following a traumatic brain injury, and thus it stands to reason that executive functions would be compromised (Krawczyk et al., 2010; Lipton et al., 2009). Prefrontal regions, especially the dorso-lateral prefrontal cortex (DLPFC), are particularly vulnerable to injury because of their proximity to the sphenoidal ridges and bony protrusions at the base of the skull (Krawczyk et al., 2010) (see Chapter One; 1.3.2: The neuroanatomical vulnerabilities of the brain to TBI). These same regions, including the DLPFC have been implicated in executive function (Lipton et al., 2009). Executive deficits can also occur due to lesions outside of frontal regions but part of integral neuronal pathways in frontal networks (Rieger & Gauggel, 2002). In fact, Anderson, Bigler, and Blatter (1995) showed that the presence and/or absence of frontal lobe lesions in sixty-eight TBI patients was unable to predict executive function performance using the Halstead Category Test and Wisconsin Card Sorting Test. No differences in performance were shown according to lesion location. They present MRI scans of an interesting case comparison where task performance was in the opposite direction than expected (i.e.,
executive impairment was shown by the patient without a frontal lobe lesion, see Figure 4.14).

Elsewhere both frontal and temporal regions have been implicated in cognitive control, and focal as well as diffuse injury has been linked with reductions in gray matter (Beauchamp et al., 2011b; Berryhill et al., 1995; Krawczyk et al., 2010), white matter (Beauchamp et al., 2011b; Wilde et al., 2005) and generally diffuse cortical thinning in these regions (Merkley et al., 2008). Lipton et al. (2009) showed that even in very mild TBI executive dysfunction was apparent and differentiated by lower DLPFC fractional anisotropy (FA), which indicates reduced white matter tracts (see Figure 4.15). The size of the frontal lobe lesion has also been shown to enhance the relationship between task performance and injury severity (Levin et al., 1993).

Figure 4.14. MRI scans of two TBI patients with very different performances on the WCST and Halstead Category Test. (Left) T2-weighted axial plane image demonstrating significant bifrontal lobe damage, with neuropsychological scores within normal limits. (Right) T2-weighted axial images from another TBI patient with no focal frontal lobe lesions, yet with significant impairment on neuropsychological tests. Taken from Anderson et al. (1995).
Figure 4.15. Frontal lobe white matter deficits in mTBI. Colour overlays on template brain images show region 1 where frontal white matter fractional anisotropy is lower in the patient group. Taken from Lipton et al. (2009).

4.6.1.2 Other mediators: Injury severity, age, and time since injury.

The relationship between injury severity and impairment in executive function is still poorly understood. One meta-analytic review reported that the effect of moderate to severe traumatic brain injury was more than three times the effect of mTBI on overall cognitive function (Schretlen & Shapiro, 2003). Schretlen and Shapiro (2003) also reported that overall cognitive function recovers most rapidly during the first few weeks following mild injury, and may recover fully within the first three months. This is not so following moderate to severe injury which generally shows improvement to cognitive function within the first two years but remains markedly impaired after this time (Schretlen & Shapiro, 2003), and may persist beyond ten years (Ponsford, Draper, et al., 2008).

At least some executive dysfunction is shown following mTBI (Erez, Rothschild, Katz, Tuchner, & Hartman-Maeir, 2009; Hartikainen et al., 2010; Lipton et al., 2009; Ponsford et al., 2011). Patients often report ongoing subjective memory and concentration problems, although some researchers have failed to find differences between mTBI and control groups (Anderson & Knight, 2010; Ord, Greve, Bianchini, & Aguerrevere, 2010; Ponsford et al., 2011). Furthermore, some impairments may be specific to isolated aspects of executive function such as goal setting (Beauchamp et al., 2011a) and multi-tasking (Anderson & Knight, 2010), rather than evident on executive function batteries. This may explain null results from some studies. In patients who have sustained a moderate to severe injury the literature typically agrees on pronounced executive dysfunction. In one study
patients with persistent symptoms following moderate injury demonstrated reduced executive function on a range on neuropsychological tests, along with indications of disrupted fronto-striatal networks on diffusion tensor images (Hartikainen et al., 2010). Patients post severe injury have demonstrated large and significant deficits across the gamut of executive neuropsychological constructs, including information processing speed and various aspects of attention (Mathias & Weaton, 2007).

Inconsistencies have also been shown in the literature with regard to the effect of age. While some data has indicated that individuals injured at younger ages perform better than those who sustain injury at an older age (Beauchamp et al., 2011a; Senathi-Raja et al., 2010), elsewhere work has suggested that children and adolescents may be more sensitive to long-term effects given that the injury complicates the maturational course of executive function development (MacNeill Horton Jr., Soper, & Reynolds, 2010). Moreover, it has been shown that adolescents with more severe TBI may underestimate their own degree of executive dysfunction (i.e., poor metacognition) (Wilson, Donders, & Nguyen, 2011); although, a similar relationship has also been shown in adults (Ciurli et al., 2010).

Finally, some work has shown that performance on executive measures may also be mediated by time since injury (Dimoska-Di Marco, McDonald, Kelly, Tate, & Johnstone, 2011; Senathi-Raja, et al., 2010). This finding, too, has not been consistent, with other meta-analyses reporting no such relationship (Frenchmen et al., 2005; Mathias & Weaton, 2007). It stands to reason that better executive abilities would be recorded for individuals with a better course of recovery over time, and that a greater time since injury is more likely to be associated with better recovery. However, inconsistencies from the meta-analytic literature are not explained by differences in injury severity, and severity is one of the variables most likely to mediate the recovery process (Ponsford, Draper, et al., 2008; Schretlen & Shapiro, 2003).

In short, while there have been some inconsistencies, it is clear that the executive functions are generally impaired following trauma to the brain, and it stands to reason that the extent and longevity of this impairment would be mediated by the severity and location of the injury, as well as the time since injury and age it was sustained. This has been shown by most research to date. Moreover, despite the goal of previous work to elucidate a post-injury prognosis generalisable to all patients, it seems that the resilience of the executive functions may be mediated by variables at both the individual and injury-based levels.
4.6.2 Mental inhibition and switching.

Over the last decade in particular, empirical investigations have begun to focus on damaged mechanisms of inhibition post traumatic brain injury (Duncan, Kosmidis, & Mirsky, 2005; Rao & Lyketsos, 2000). Behavioural inhibition has been shown in this cohort, where a failure to inhibit impulsive and/or socially inappropriate behaviour, both physical and verbal, is apparent (N. LeBlanc et al., 2005; Rao & Lyketsos, 2000). Rao and Lyketsos (2000) refer to these symptoms as part of a behaviour dyscontrol disorder, prevalent in five to seventy percent of patients following TBI, irrespective of injury severity. Empirical paradigms designed to assess effortful suppression of a motor response (i.e., inhibition) have all reported response inhibition failures post TBI. These include the go/no-go task (Levin et al., 1993; O’Keeffe, Dockree, Moloney, Carton, & Robertson, 2007; Roche et al., 2004), stop-signal task (Floden & Stuss, 2006; Logan, 1994), and the Continuous Performance Task (CPT; Conners, 1995, Duncan et al., 2005).

As discussed at length in Chapter Three (Section 3.6.3: The colour Stroop paradigm), the Stroop test is commonly used to assess cognitive inhibition. Similar to the data reported in schizophrenia, much of the work in TBI reports significantly larger Stroop effects for patients post injury. However, a closer look at the Stroop data from brain injured cohorts reveals that reported Stroop differences are most often shown to the control conditions (i.e., word reading and colour naming) or the incongruent condition in isolation (i.e., words of colours written in incongruent coloured ink), rather than an interference score (See Chapter Three, Figure 3.13 and Appendix C for Interference Score Calculation) (Larson, Kaufman, Schmalfuss, & Perlstein, 2007; Stuss et al., 1985). The Stroop task reflects a number of perceptual and cognitive processes, including attention and processing speed, thus it is imperative that the interference score is calculated and used in analysis where inhibition is the variable of interest (Dimoska-Di Marco et al., 2011). Although, in one study where the interference score was correctly calculated, Stroop inhibition differences were accounted for by slowed processing speed in analysis, suggesting that a true inhibition effect may not exist (Rios et al., 2004). However, this analysis may be suspect given that; (i) the derived score was calculated to already theoretically account for processing speed/attentional impairments, and (ii) there is no indication in this study as to whether the analysis of covariance applied was statistically appropriate (Miller & Chapman, 2001). Still, trends indicating that prominent deficits are specific to processing speed and attentional control, among other factors (i.e., fatigue), rather than inhibition on the Stoop task have been reported in two meta analytic reviews (Dimoska-
Di Marco et al., 2011; Mathias & Weaton, 2007). Further, where inhibition derived scores have not been calculated, some studies have reported no impairment to Stroop subtests, and this appears to be unrelated to injury severity; DAI (Schroeter et al., 2007), severe injury (Larson et al., 2007; Ponsford & Kinsella et al., 1992), mixed severity (Stuss et al., 1985).

An increased latency between word reading and colour naming on the Stroop task has also been shown by one meta-analysis incorporating ten studies (Ben-David, Nguyen, & van Lieshout, 2011). The authors suggested that this may be evidence of additional sensory-based impairments effecting colour naming ability (Ben-David et al., 2011). Sensory-related deficits are more likely to exist in patients with damage specific to the visual system/occipital lobe (reviewed in Section 4.2.2: Disruptions to Vision). However, the TBI patients used in analysis included both moderate and severely injured patients, and relevant injury demographics (i.e., focal lesion versus diffuse injury) were once again omitted from sample descriptions and analyses.

### 4.6.2.1 Stroop task neuroimaging.

Differential patterns of activation during Stroop performance have been reported in neuroimaging work. Healthy controls tend to show activity in regions associated with active cognitive control over behaviour (i.e., the dorsolateral prefrontal cortex) (Petrides, 2005), and interference and selective attention (i.e., the anterior cingulate cortex) (Bush, Luu, & Posner, 2000). Brain injured patients, however, show activation in these same regions, as well as in surrounding cortex, and often to a greater degree (Goethals et al., 2004; Mani, Miller, Yanasak, & Macciocchi, 2007; Soeda et al., 2005; Tlustos et al., 2011). Soeda et al (2005) hypothesised that these patterns of activation may reflect reduced interconnectivity between anatomical regions and associated networks as a result of the brain trauma. Given that these regions are established as integral to cognitive control (i.e., inhibition) and cognitive interference/selective attention, these patterns may provide evidence for differential mechanisms of inhibition and interference during the Stroop task in brain injured cohorts, not yet captured behaviourally.

Electrophysiologically, impaired cognitive control and cognitive evaluation following brain injury has been suggested from event-related potentials (ERPs). The N450, a marker of cognitive control, differentiates congruent and incongruent Stroop trials in healthy controls (West, 2003). In traumatic brain injury this ERP is attenuated, and no amplitude or latency differences are shown to congruent versus incongruent stimuli (Perlstein, Larson, Dotson, & Kelly, 2006). Attenuated error-negativity/error-related negativity (Ne/ERN) waveforms
during Stroop performance are shown, indicating poor evaluative control and performance monitoring (Larson et al., 2007). Patients also show delayed latencies to N200/P300 waveforms during go/no go tasks (i.e., behavioural inhibition), and this provides further indication of slowed stimulus processing post TBI (Campbell & de Lugt, 1995; Clark, O'Hanlon, Wright, & Geffen, 1992; Roche et al., 2004; Spikman, van der Naalt, van Weerden, & van Zomeren, 2004).

4.6.2.2 Mental switching.

Task switching measures cognitive flexibility and involves the change from one attentional focus to another according to task demands (see Chapter Three: Section 3.6.2: Mental Inhibition and Switching). The Stroop task has been considered the ‘Gold Standard’ assessment of attention, processing speed, and inhibition in TBI and has been used widely (Ben-David et al., 2011). However, it appears that the Stroop switching condition (see Chapter Three, Figure 3.13) has not been used in this cohort to date, with the exception of work from Perlstein’s group who have used a modified version (Perlstein et al., 2006; Seignourel et al., 2005). These authors have assessed mild, moderate, and severely injured patients on a novel, cued, single trial computerised version of the Stroop switching condition (see Cohen, Barch, Carter, & Servan-Schreiber, 1999). They reported that chronic moderate to severe TBI, but not mild TBI, was associated with deficits on this task (Perlstein et al., 2006; Seignourel et al., 2005). More severely injured cases, then, may suffer from reduced cognitive flexibility (i.e., switching) where the goal is to adhere to the changing of task rules.

Another method of assessing switching ability is by using the Trail Making Test (TMT; Reitan, 1958). The test comprises two forms. Form A, given first, displays numbers from 1-25 in a random arrangement and participants are required to draw a line between the numbers in ascending order as quickly as possible. Form B is identical except that both numbers and letters are presented and participants are required to draw in ascending order, alternating from number to letter (i.e., 1-A, 2-B, 3-C) (see Appendix D). The task is commonly used to measure processing speed, however, where a difference score is obtained between forms A and B, a measure of attentional switching while controlling for processing speed is computed (Reitan, 1955, 1958; Rios et al., 2004). Rios et al. (2004) gave both the Stroop and Trail Making Task to twenty-nine severely injured patients and, in keeping with the literature already reviewed, found that processing speed accounted for differences initially shown on the Stroop task, but not on the Trail Making Task. As such, their data indicate impairment in cognitive switching following TBI, over and above the effects of slowed
information processing. Note that while Rios et al. (2004) calculated the Stroop interference score, they did not employ the fourth Stroop switching condition, and thus, their Stroop and Trail Making tasks are in effect measuring different constructs; inhibition and switching respectively.

4.6.2.3 Injury severity and lesion location.

As already mentioned injury severity may mediate cognitive inhibition and switching abilities post brain injury, although more research comparing severity directly is needed. Like much of the TBI literature, some work using inhibition or switching tasks has made no mention of injury related information at all (e.g., Roche et al., 2004), while others have included the bare minimum (e.g., Duncan et al., 2005; Rios et al., 2004; Spikman et al., 2004; Stuss et al., 1985), or partial information (e.g., Perlstein et al., 2006; Soeda et al., 2005). Further, elsewhere, research that has provided a clear breakdown of injury related demographics fail to incorporate this information in their analyses (e.g., Clark et al., 1992; Larson et al., 2007; O’Keeffe et al., 2007; Ponsford & Kinsella, 1992).

The same is true in meta-analytic research. Ben-David et al. (2011) provided no injury information except to indicate that patients had sustained moderate to severe injuries across ten studies. Dimoska-Di Marco et al. (2011) obtained injury severity information for subjects in all thirty-nine studies included in review, and classified these into mild, moderate and severe groups accordingly, however no other injury demographics were reported. Similarly, Mathias and Weaton (2007) incorporated injury severity information and time since injury where it was available, but provided no lesion location data. The effect that this has on the reported trends is unclear. There is no way to determine whether severity or focal lesion location exists in excess within particular samples used in these reviews and skewed the data unrepresentatively. On the other hand, given that meta-analytic reviews have the advantage of large sample sizes, the likely mix of injury demographics may be akin to random, and thus representative, sampling.

Unfortunately, in the small number of studies where care has been taken with injury demographics, and included in analyses, the results have been inconsistent. For instance, Leblanc (2005) showed that neither injury severity nor lesion location predicted the ability of children to inhibit a motor response following their recovery. Whereas Levin et al. (1993) showed that the size of the frontal lobe lesion mediated (i.e., increased) the relationship between injury severity and response inhibition (see Section 4.6.1.1: Lesion location).
First, the existing literature highlights the necessity of using calculated derived scores for both the Stroop and TMT tasks, where the variables of interest are inhibition and switching respectively (Dimoska-Di Marco et al., 2011; Rios et al., 2004). As such, a measurement of inhibition and switching is obtained while accounting for the effects of other processes required by the task, such as attention and processing speed, which are likely to also be impaired, and to vary in degree of impairment across participants with injury/illness. This becomes more imperative given the likelihood of the statistical inappropriateness of attempting to account for these differences in covariate analyses (Green & Salkind, 2005; Field, 2005).

In summary, behavioural inhibition deficits are evident following a traumatic brain injury, although the extent of mental inhibition deficits in TBI remains somewhat unclear (Dimoska-Di Marco et al., 2011; LeBlanc et al., 2005; Ponsford & Kinsella, 1992; Stuss et al., 1985). This is typically due to the improper calculation of scores (i.e., using raw rather than derived scores) and the related issue of separating poor inhibition from other executive dysfunction (i.e., processing speed, attention) (Larson et al., 2007; Mathias & Weaton, 2007). By contrast, mental switching abilities appear consistently poor, especially following severe injury, although a relatively small amount of work has been completed to date (Perlstein et al., 2006; Rios et al., 2004).

4.6.3 Attention.

Attention-based deficits are widely shown following traumatic brain injury (Oddy et al., 1985; Ponsford, Draper, et al., 2008; Spikman, Deelman, & van Zomeren, 2000; Zino & Ponsford, 2006). In particular, impairment has been shown to selective/divided attention (Goethals et al., 2004; Stuss et al., 1989), and sustained/focused attention (Levin, High, Goldstein, & Williams, 1988; Stuss et al., 1989), and may persist to ten years post injury (Ponsford, Draper, et al., 2008). Given the frontal lobe involvement in attentional resources (Mateer & Mapou, 1996; Rios et al., 2004; van Zomeren & Brouwer, 1994), it is reasonable to assume that attention may be vulnerable to the effects of a brain injury in ways similar to broad executive functioning; that is, greater risk of attentional impairment may accompany focal injury to the frontal lobes and/or diffuse axonal injury.

However, there is ongoing debate in the literature as to whether poor performance on measures of attention reflects true deficits in attention (Madigan, DeLuca, Diamond, Tramontano, & Averill, 2000; Ponsford & Kinsella, 1992; Rios et al., 2004). Typical tasks
used to assess attention are performed under time pressure, and, even for tasks without a speeded component, evidence suggests that performance deficits may instead reflect processing speed impairments, rather than isolated attentional impairment; the slowed processing hypothesis (Madigan et al., 2000; Rios et al., 2004; Stuss et al., 1989). Discussed in more detail in the following Section 4.6.4: Processing Speed, where slowed information processing has been accounted for in analyses differences no longer exist on measures of focused/sustained attention (Ponsford & Kinsella, 1992; Spikman, van Zomeren, & Deelman, 1996), divided attention (Brouwer, Ponds, Van Wolffelaar, & van Zomeren, 1989; Spikman et al., 1996), selective attention (Ponsford & Kinsella, 1992), or supervisory attentional control (SAC; discussed below, Ponsford & Kinsella, [1992] but not in Spikman et al. [1996]). On the other hand, some authors hold that an attention-specific impairment does exist in TBI. Two proposals have been offered, the first suggesting that processing resources specific to attention are reduced (i.e., the attentional-resource hypothesis) (Schmitter-Edgecombe, 1996), and the second arguing that isolated or specific components of attention are damaged (i.e., component process hypothesis) (Park, Moscovitch, & Robertson, 1999; Rios et al., 2004; Whyte, Polansky, Fleming, Coslett, & Cavallucci, 1995).

First introduced by Shallice (1982), the supervisory attentional control (SAC) refers to the capacity to plan solutions to complex tasks, where goal-directed controlled attention is required. Inconsistent findings regarding SAC are difficult to interpret. First, because conceptualisation of the construct itself is not consistent across studies; some authors suggest that SAC is a unitary executive function, while elsewhere it is regarded the product of many interlinked elements of executive functioning (Rios et al., 2004; Spikman et al., 1996). Next, given likely reductions in processing speed, measures used to capture SAC should not involve time pressure. For instance, of the two studies reviewed here Ponsford and Kinsella (1992) used a time pressured task in their measurement of SAC and reported impairment (i.e., the Tower of London; 60 seconds provided to problem-solve), whereas Spikman (1996) did not, and found no impairment (i.e., a Lack of Consistency Score, derived from words reproduced in an initial but not subsequent trials). These inconsistent findings are equally as likely to be a product of either the SAC definition used or the use of time pressure, and essentially illustrate that the capacity for supervisory attentional control in TBI remains unclear. Further to this point, it is noteworthy that the tasks used may actually reflect predominantly dissimilar executive functions; that is, planning in the Tower of London, and
working memory in the Lack of Consistency Score. This highlights the importance of task selection when attempting to measure any one aspect of the executive functions.

In light of the debate, factor analyses have been used in attempts to determine the underlying mechanisms of attention deficits. Two dimensions have been shown; processing speed (low level process) and control (high level process) (Madigan et al., 2000; Spikman, Kiers, Deelman, & van Zomeren, 2001). More recently, however, Rios et al. (2004) identified four; processing speed, interference control, cognitive flexibility and working memory. The authors conceptualised the latter three as high level cognitive processes that are independent but interlinked aspects of cognitive control (see Figure 4.16). In this work, however, only the Trail Making difference score, which loaded on the ‘cognitive flexibility’ factor, maintained group differences once processing speed was considered in analyses. This is essentially further evidence of a switching deficit post TBI, discussed in Section 4.6.2.2: Mental switching, rather than an isolated deficit in attention, and thereby a further indication of the interlinked nature of the executive functions.

Figure 4.16. Four-factor solution regarding the underlying processes of attentional resources. These are clustered according to two dimensions; control (high level processes) and information processing speed (low level processes). The high level processes are considered to be relatively independent but interrelated subprocesses. Taken from Rios et al. (2004).
4.6.3.1 Injury related demographics.

Once again the work in this area has not adequately considered the potential impact of injury variables on reported outcomes. Studies have either incorporated patients with a mix of injury severity (e.g., Madigan et al., 2000; Spikman et al., 1996; Stuss et al., 1989; Zino & Ponsford, 2006), or concentrated on the effects of severe injury (e.g., Oddy et al., 1985; Ponsford & Kinsella, 1992). Moreover, as with the majority of TBI work, there are inconsistencies in the inclusion of injury demographics. For example, some authors report the duration of loss of consciousness (LOC) and/or Glasgow Coma Scale Score (e.g., Madigan et al., 2000), some report PTA (e.g., Spikman et al., 1996), and others report time since injury (e.g., Zino & Ponsford, 2006). None of the research reviewed here reported focal lesion location. As with studies of broad executive dysfunction, these variables need to be delineated and systematically assessed.

Taken together, the literature is currently unclear regarding the extent of attention deficits in TBI, should a true attention deficit exist. Patients certainly show reduced performance on measures designed to capture attention, however this performance may be explained by the combined effect of various components of executive dysfunction (Madigan et al., 2000; Ponsford & Kinsella, 1992, Rios et al., 2004). On the other hand, a selection of authors have argued for deficits specific to attention and hypothesised (i) reduced resources for controlling attention (e.g., Schitter-Edgecombe, 1996), and (ii) damage to certain components of attention post injury (e.g., Park et al., 1999; Rios et al., 2004; Whyte et al., 1995).

4.6.4 Processing speed.

As noted throughout this chapter, information processing speed is commonly impaired following traumatic brain injury and typically mediates the measurements of other interlinked and/or higher order cognitive constructs across visual and auditory modalities (Ben-David et al., 2011; Felmingham et al., 2004; Hillary et al., 2010; Ponsford, Draper, et al., 2008; Senathi-Raja et al., 2010; Spikman et al., 2004). In fact, slowed processing is one of the most consistent findings following brain injury (Rios et al., 2004). Clement and Kennedy (2003) presented data indicating that speed of information processing was the most vulnerable to the effects of brain injury, over and above deficits shown on the WAIS. As

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29 This rivals prior claims suggesting that memory is most vulnerable to the effects of brain injury (see Tate et al. [1991]).
such, arguments have been made supporting a slowed processing hypothesis that holds that
the primary deficit in TBI is a characteristically slower and less accurate processing ability
that, in turn, impacts on the neuropsychological domains (Rios et al., 2004). Accordingly, the
effect of slowed processing on outcome measures may be erroneously interpreted as
impairments specific to another domain (i.e., inhibition and attention, discussed previously).

Slower processing speeds have been shown in TBI across a range of domains,
including, audition (i.e., the Paced Auditory Serial Addition Test; PASAT) (Gronwall, 1977;
Ponsford & Kinsella, 1992), semantic memory (Haut et al., 1991b), visuomotor constructs
(i.e., Trail Making Test, Stroop, and Symbol Digit Modality) (Stuss et al., 1989; van Zomeren
& Deelman, 1976), and general executive function, including attention (Beauchamp et al.,
2011a). In the 1950’s Reitan (1955, 1958) identified that the Trail Making Test was able to
differentiate brain damaged and comparison healthy control subjects. Using total time as the
outcome measure, he showed that performance to Forms A and B separately, and the
cumulative total score, was indicative of brain damage, and established preliminary norms for
the cohort. More recently, Dimoska-Di Marco et al. (2011) reported that the control subtests
of the Stroop (i.e., word reading and colour naming that capture attention and processing
speed) are best at discriminating mild TBI and healthy subjects.

As suggested by the slowed processing hypothesis, where processing speed has been
controlled, differences are no longer shown on measures of attention (Brouwer et al., 1989;
Spikman et al., 1996), executive functions, including planning and inhibition (Brouwer et al.,
1989; Veltman, Brouwer, van Zomeren, & van Wolffelaar, 1996), cognitive flexibility
(Felmingham et al., 2004), and working memory (Hillary et al., 2010; Stuss et al., 1985). The
processing speed disadvantage has also been shown to be independent of; i) injury severity,
time since injury, and age-related variables following diffuse axonal injury (Felmingham et
al., 2004), and ii) performance accuracy following moderate to severe focal injury (Madigan
et al., 2000).

4.6.4.1 Anatomical explanations.

Speculations have been made about the underlying anatomical mechanisms of slowed
processing speed. The diffuse loss of cells likely results in the breakdown of networks,
indirect neural transmission (Felmingham et al., 2004; Rios et al., 2004), and/or reductions in
dendritic branching and myelination (Miller, 1994). Together this would culminate in slower
neural transmission. Correlations have also been shown between ventricular enlargement and
reduced psychomotor speed (e.g., Symbol Digit Modalities Test) (Johnson et al., 1994). Electrophysiological evidence supports these speculations with event-related potential work showing delayed latencies (Clark et al., 1992; Papanicolaou et al., 1984; Roche et al., 2004; Rugg et al., 1988), which are a classic indication of slowed stimulus processing (Pritchard, 1981). This is important given that the literature has shown cognitive ERP components to be most sensitive to the effects of trauma, especially compared with sensory components (Duncan et al., 2005).

To summarise, slowed processing speed appears to be an established deficit following traumatic brain injury (Beachamp et al., 2011a; Gronwall, 1977; Haut et al., 1991a; Ponsford & Kinsella, 1992; Stuss et al., 1989; vanZomeren & Deelman, 1976). Speed of information processing may actually be the most vulnerable of the neurocognitive domains to the effects of TBI, and may in fact explain deficient performance shown to other domains, for example, on measures of attention, although further research is required (e.g., Brouwer et al., 1989; Ponsford & Kinsella, 1992; Spikman et al., 1996). Processing speed also appears to be relatively independent of injury demographics, with comparable deficits recorded so far for individuals with varying degrees of injury severity and time since injury (Felmingham et al., 2004; Madigan et al., 2000).

4.7 Intelligence

As defined in Chapter 3: Section 3.7 Intelligence, according to the most prominently used intelligence scales (i.e., WAIS) (Curtis, Greve, & Bianchini, 2009; Lezak, Howieson, & Loring, 2004), intelligence has been conceptualised as incorporating both verbal and performance (i.e., visual-motor) components. Scores on these measures are also vulnerable to attention, processing speed, and memory. In the traumatic brain injury literature, data to date generally indicate that verbal skills remain most stable following injury, and recover more quickly, relative to performance IQ, including reasoning and visuo-spatial abilities.

Measurements of performance IQ have shown striking deficits in adult (Chadwick, Rutter, Brown, Shaffer, & Traub, 1981; Clement & Kennedy, 2003; Ferri et al., 2004), pediatric (Donders, 1997; Kay & Warschausky, 1999), and preperinatal TBI (Nass et al., 1989). For instance, Ferri et al. (2004) tested forty-six patients who had experienced a severe TBI on the WIAT-III and showed that only eleven of them obtained scores within the normal ranges of intellectual functioning. Seventy seven per cent had more pronounced performance than verbal IQ deficits. Importantly, and in keeping with the data reviewed so far, slowed processing speed was a clear, predominant symptom in their sample.
The beauty of the Wechsler tests is that they produce an isolated processing speed score, and most other subtests and related indices are therefore unaffected by processing speed impairments as they are not performed under time pressure. True to the prominence of slowed processing speed following TBI, information processing has illustrated the greatest deficits as captured by the WAIS subscale in severely injured individuals (Clement & Kennedy, 2003; Ferri et al., 2004), and on the Wechsler Intelligence Scale for Children—Fourth Edition, WISC–IV; (Wechsler, 2003) in child TBI (Donders & Janke, 2008).

To determine the extent of decline in intellectual ability following TBI it is imperative that premorbid functioning is obtained. Of course, it is unusual that an individual who sustains a brain injury has had an IQ assessment prior to their injury to make this comparison well. However, evidence has shown that reading tests (i.e., the National Adult Reading Test, NART; Nelson, [1982]) and the Wide Range Achievement Test-Revised (WRAT-R; Wilkinson & Robertson, [2006]) provide the most accurate estimates of premorbid intelligence to date (Crawford, Besson, & Parker, 1988; Johnstone et al., 1995; Moss & Dowd, 1991). In fact, Moss and Dowd (1991) presented a rare case study where measurement of IQ had been obtained for an individual in childhood who later had a traumatic brain injury. It showed that the NART produced a very accurate estimate of his premorbid IQ\textsuperscript{30}. In keeping with this idea, Johnstone, Hexum, and Ashkanazi (1995) showed that relative to other neuropsychological domains (i.e., attention, verbal and delayed memory, speed of processing, and cognitive flexibility), intelligence was the least affected by traumatic brain injury (using comparisons of premorbid WRAT-R and WAIS-III z-scores). Thus, while a decrease in IQ is certainly apparent relative to normative scores, it appears that relative to other neurocognitive domains intelligence remains relatively intact following traumatic brain injury.

4.7.1 Neuroimaging: White matter and intelligence.

Anatomically, connections have been made between white matter loss and intelligence. In 1994, Miller hypothesised that brain myelination was responsible for much of the variance in intelligence. Myelinated neurons facilitate the speeded transmission of information, and more intelligent brains have shown a range of differences that may be associated with increased myelination. These include greater variability in EEG measures, faster reaction times, and higher grey-white matter contrast on MRI scans. Miller (1994)

\textsuperscript{30}One study has shown more recently, however, that NART scores were correlated with injury severity, questioning the NART’s validity as a premorbid IQ measure (Morris, Wilson, Dunn, & Teasdale, 2005).
argued that the association of white matter and intelligence was evident in the natural increase of intelligence alongside the maturation of a child’s brain overtime (i.e., increased myelination during brain development), converse to the reductions in intelligence and response times shown in old age alongside brain atrophy and decreased myelination.

Ventricular expansion shown post-TBI is also considered to reflect the loss of white matter surrounding the ventricular system, and Johnson et al. (1994) showed that relative ventricular size (i.e., ventricle-to-brain ratio; proportion of brain volume occupied by the ventricles) predicted nonverbal performance IQ in men. On the other hand, the corpus collosum (i.e., large white matter mass connecting the cerebral hemispheres) is also considered vulnerable to TBI because of its midline location (Levin et al., 1990). However, structural changes to the corpus collosum post-TBI were unrelated to measures of intelligence (Johnson et al., 1994).

Hashimoto, Okumura, Shinoda, Abo, and Nakamura (2007) reported a case study more recently where, seven years following his mild TBI, a thirty-one year old man continued to illustrate reduced verbal IQ and attentional/switching frontal lobe dysfunction despite no evidence of abnormalities on MRI scans. Only when diffusion tensor imaging (DTI) was used were they able to explain the impairments. DTI is a method that illuminates white matter pathways responsible for connecting brain regions. The images showed that some fibres from the corpus callosum to the frontal cortex were missing in his left hemisphere when compared to the right, explaining his reduced verbal intelligence and focal left frontal impairment (see Figure 4.17) (Hashimoto et al., 2007).

**4.7.1.1 Injury severity and hemispheric specificity.**

Once again, the systematic comparison of important injury demographics has not been made within the traumatic brain injury and intelligence literature, including the time since the injury, its extent, type, and location. As mentioned, following mild trauma to the brain, a return to pre-injury cognitive functioning is generally anticipated within months (Carroll et al., 2004; Curtis et al., 2009; Rohling et al., 2011). Of course this is not true in all cases (Alexander, 1995; Binder et al., 1997), especially where the injury is one of multiple concussions and/or complicated mild injury (Rohling et al., 2011). At the more severe end of the injury scale, significant relationships have been found between IQ estimates and

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31 Persistent symptoms have actually been shown to reflect malingering in cases with financial incentives (Belanger et al., 2005; Curtis et al., 2009).
indices of injury severity in adults (i.e., duration of PTA and coma) (Ferri et al., 2004), and in children with complicated mild to severe TBI (i.e., duration of coma) (Donders & Janke, 2008). Large meta-analyses have also confirmed this relationship incorporating cases of mild to very severe injury, where duration of loss of consciousness has been shown to correlate with a variety of measurements of cognitive performance (Curtis et al., 2009; Dikmen, Machamer, Winn, & Temkin, 1995; Rohling et al., 2011; Schretlen & Shapiro, 2003).

**Figure 4.17.** Tractography from corpus callosum in a 31 year old case study with verbal IQ and frontal lobe impairments. (a) Lateral view on the right side. (b) Lateral view on the left side. (c) Anterior posterior view. (d) Top view. Arrow in (b) indicates the lack of fibres connecting the corpus callosum and frontal cortex in the left hemisphere relative to the right side. Taken from Hashimoto et al. (2004).

One rare unilateral comparison was published by Nass et al. (1989). Children who had sustained preperinatal injury to either their left or right hemisphere showed impairments that conformed to the established lateralisation of functionality. Left hemisphere lesions were associated with statistically superior full scale and verbal intelligence, whereas children with right hemispheric lesions had both reduced verbal and performance, and thus overall, intelligence. As well as supporting the lateralisation of intelligence, this pattern is further explained by the left-right maturational gradient hypothesis. Because it develops early, the left hemisphere is reduced in plasticity, and is thereby less likely to adopt novel functionality.
as readily as the right in compensation for the injury. Thus, as was demonstrated by Nass et al. (1989), intelligence is more vulnerable to early right hemisphere injury because of new (and relatively unwelcome) demands placed on the already established left hemisphere by default.

Overall, it appears that while verbal IQ remains relatively stable, performance IQ is generally reduced as a result of traumatic brain injury (Clement & Kennedy, 2003; Ferri et al., 2004). Performance IQ incorporates nonverbal abstract problem solving, reasoning, and visuo-spatial abilities, and these are typically shown to be deficit post-injury (Chadwick et al., 1981; Clement & Kennedy, 2003; Donders, 1997; Ferri et al., 2004, Kay & Warschausky, 1999; Nass et al., 1989). Such effects may be explained by damage to white matter tracts and the subsequent reduction in connectivity and flow of information processing as a result of the injury (Johnson et al., 1994; Miller, 1994). Further, while there is some indication that greater impairments on measures of IQ are shown by individuals with greater injury severity, and that aspects of intelligence are lateralised, additional systematic and standardised research is necessary (Donders & Janke, 2008, Ferri et al., 2004; Carroll et al., 2004; Nass et al., 1989).

### 4.8 Chapter Summary

The literature reviewed in this chapter has provided evidence of substantial impairment across each of the cognitive neuropsychological domains addressed. An exception may be with regard to probabilistic reasoning, although this reflects a gap in the literature specific to this variety of reasoning, and evidence points to the likelihood that this too would be affected by TBI; other aspects of reasoning have shown impairments including, inferential, analogical, and deductive reasoning (Bibby & McDonald, 2005; Geraci & Cantagallo, 2011; Goverover, 2004; Krawczyk et al., 2010), as have the executive functions that are utilised during reasoning (Krawczyk et al., 2010).

Fundamental oversights have been made in the majority of work to date specific to injury related demographics, and, it seems, the influence of these variables in cognitive neuropsychological outcome. Injury related information, for the most part, has been poorly and incompletely recorded and reported. Often, even where substantial information has been incorporated, this information has been ignored in analyses. As was discussed throughout, virtually all parameters of injury have the potential to mediate functional ability in each of the domains addressed. Research on cognitive neuropsychological functioning post TBI is insufficient where these obvious mediators have been ignored. Focal versus diffuse injury, lesion location, injury severity, and time since injury need to be systematically researched in
particular. Accordingly, so far the literature remains inconclusive on this point, especially given that the limited studies that have attempted to determine these influences report contrasting findings.

Some work has found no differences according to lesion location (e.g., comparable executive function in frontal versus nonfrontal lesions; Anderson et al. [1995]), and often this is in contrast with localised functionality established from replicated imaging data in healthy controls. However, a lack of differences according to lesion location may be evidence of brain changes occurring post TBI. For instance, the engagement of newly recruited networks in lieu of damaged ones, particularly given that differential patterns of cortical activation have been illustrated in this review more than once (Goethals et al., 2004; Mani et al., 2007; Soeda et al., 2005; Tlustos et al., 2011). In turn, this serves to highlight the importance of investigating other injury based variables that may mediate this hypothesised effect, such as the latency between injury and assessment.

More than one domain-based discussion indicated the tendency of mTBI patients to have recovered by three months post-injury. Yet contrasting data was available in each example (e.g., in visual-perceptual and fluency discussions). It may be that the classification of mTBI requires reconceptualisation. Perhaps an intermediate group exists between mild and moderate injury, where the trajectory of deficits more closely resemble those illustrated by patients suffering from moderate TBI. Again, however, this remains speculation until thorough injury severity investigations are undertaken.

Notably, the effect of gender on cognitive neuropsychological recovery has not been addressed in this review. Gender differences have not been widely investigated within each of the domains discussed here. In general, higher rates of men relative to women tend to sustain brain injury, and this is most likely reflective of lifestyle differences. However, there is some evidence to suggest that females may fare worse in recovery (Ponsford et al., 2008).

In summary then, while there is some inconsistent and incomplete work, the literature generally points to impairments following trauma to the brain across the cognitive neuropsychological domains reviewed here; visual-perceptual organisation, language, memory, executive function and intelligence. It stands to reason that the extent and longevity of this impairment would be mediated by the injury-related demographics discussed at length, although a considerable amount of research to support or refute this proposition is yet to be reported.
Chapter 5: Literature Review Summary and Research Aims

5.1 Summary of Literature

This chapter briefly summarises the previous literature review chapters and leads into the aims of this research study. Hypotheses are outlined in the following experimental chapter *(Chapter Seven: Cognitive neuropsychological profile in PFTBI)*.

5.1.1 Visual-perceptual organisation.

Impaired visual perception following a traumatic brain injury is demonstrated in the literature, even where damaged vision is excluded as an explanation (McKenna et al., 2006; Ponsford et al., 2011; Shum et al., 2000), and where the trauma is considered mild (Brosseau-Lachaine et al., 2008; Ponsford et al., 2011; Rohling et al., 2011). Visual memory, visual motion, visuo-spatial abilities, and visual organisation (Gestalt) deficits have all been shown post injury (McKenna et al., 2006; Patel et al., 2011; Shum et al., 2000). Poor Gestalt processing has been shown following even mild TBI at three months post injury (Brosseau-Lachaine et al., 2008), and patients with lesions in their right hemisphere (i.e., generally lateralised for global and holistic/Gestalt processing) show pronounced deficits in recalling and reproducing the global aspects of visual images (Delis et al., 1986; Robertson & Lamb, 1991).

Impaired visual processing is commonly reported in the schizophrenia literature (Joshua & Rossell, 2009; Parnas et al., 2001; Silverstein et al., 2000). In particular, visual organisation in perceptual processing has shown significant impairment. Global/Gestalt processing abilities are commonly reduced in patients (Buchanan et al., 1994; Joshua & Rossell, 2009; Rabinowicz et al., 1996; Silverstein et al., 2000), and more recently a preference for local information processing has been hypothesised as underlying poor visuo-spatial cognition in schizophrenia (Landraf et al., 2011). Nonetheless, some heterogeneity has been shown; work has suggested impairment may be mediated by illness chronicity (Parnas et al., 2001; Silverstein et al., 2000), and/or symptomatology (i.e., disorganised symptoms in particular; Knight & Silverstein, 1998; Silverstein et al., 2000; Uhlhaas et al., 2005; Uhlhaas et al., 2006). Moreover, it seems that where the Gestalt properties of an image are strong, patients may be able to perceive and utilise Gestalt principles successfully during visual processing (Chey & Holzman, 1997; Rief, 1991).
Two of the four reviewed studies measured visual perception in PFTBI. Forty one per cent \((n = 7)\) of Fujii & Ahmed’s (2002) case study review reported impaired visuo-spatial abilities relative to norms. However, later work from their retrospective chart review showed no deficits on the WAIS block design (i.e., spatial abilities) relative to healthy controls (Fujii et al., 2004).

5.1.2 Language.

Language and communication impairments following TBI are well documented in the literature, including, but not limited to, lexical comprehension and production, semantics, discourse processes, and reading/listening skills (Ewing-Cobbs & Barnes, 2002; Hinchliffe et al., 1998; LeBlanc et al., 2006; Moran & Gillon, 2004). Work has shown that the extent of damage to the language system post TBI is mediated by the relative stability of verbal skills prior to the injury, as indicated by estimates of premorbid language ability and education (LeBlanc et al., 2006). Injury demographics, especially injury severity, are also substantial mediators (LeBlanc et al., 2006; Moran & Gillon, 2004; Sullivan & Riccio, 2010). In schizophrenia, language and communication-based deficits are considered part of the core pathology. Unusual language deficits have been shown at most linguistic levels, including phonetics and phonology, prosody, morphology, syntax, semantics, pragmatics, and coherence (Covington et al., 2005; DeLisi, 2001; Levy et al., 2010; Rossell et al., 2010; Rossell & David, 2006). The available PFTBI research is not straight forward, however studies have generally reported some impairment to language in this cohort; impaired verbal learning (Bamrah & Johnson, 1991), language \((n = 2, 11.67\%);\) Fujii & Ahmed, 2002), WAIS vocabulary (Fujii et al., 2004), and verbal memory (Fujii et al., 2004; Sachdev et al., 2001).

5.1.2.1 Verbal fluency.

Based on the theoretical models of memory, semantic fluency tasks are considered less cognitively demanding than phonological fluency tasks because the closer storage of semantically related concepts facilitates faster retrieval from memory. This is typically illustrated by the greater number of semantic category words generated in a set time frame, relative to phonological (i.e., letter-based) word generation (Harrison et al., 2000; Landro & Ueland, 2008; Rossell et al., 1999). Impaired verbal fluency has been shown following traumatic brain injury to both phonemic and semantic fluency tasks, although there is a paucity of research in the latter (Baldo & Shimamura, 1998; Grossman, 1981; Jurado et al., 1997; Jurado et al., 2000; Kave et al., 2011; Martin et al., 1990). Furthermore, although the
data is not conclusive, there appears to be distinct involvement of frontal regions during phonological fluency and temporal regions during semantic fluency (Henry & Crawford, 2004; Mummery et al., 2000; Pujol et al., 1996). Such work suggests that TBI patients with lesions to one or both of these areas may show reduced fluency performance of the implicated type, although this has not always been illustrated to date (Jurado et al., 2000; Stuss et al., 1998).

Verbal fluency has been extensively researched in schizophrenia, and a deficit is well established to both fluency types (Bozikas et al., 2005; Elvevag et al., 2001; Kremen et al., 2003; Landro & Ueland, 2008), although semantic fluency has consistently shown a larger impairment (Henry & Crawford, 2005; Kremen et al., 2003; Landro & Ueland, 2008; Rossell et al., 1999). Fluency performance in schizophrenia is further reduced in patients with alogia (Sumiyoshi et al., 2005) and negative symptoms (Bowie et al., 2004). However, whether this reflects the intuitive relationship (i.e., poverty of speech in alogia and slowed processing speed in negative symptoms logically result in reduced fluency performance), or this symptomatology in schizophrenia effects semantic and/or lexical stores, pathways, or both, remains unclear, and may actually be impossible to elucidate.

In PFTBI, one study has reported verbal fluency outcomes to date, and indicated comparable performance between PFTBI and healthy controls (Fujii et al., 2004). This finding is counterintuitive given the prominent fluency impairments shown in both patients with traumatic brain injury and schizophrenia, and thus, may illustrate again the inadequacy of the available PFTBI research to date.

5.1.2.2 Clustering and switching.

The assessment of clustering and switching subcomponents in the verbal fluency literature has also been lucrative in uncovering subtle impairments in both TBI and schizophrenia (defined in Chapter 3.3.2 Fluency, Memory Structure, and Strategy). Post TBI, the ability to cognitively switch to a new cluster has shown impairment specific to semantic fluency, and this appears to be worse according to worse injury (Zakzanis et al., 2011). Clustering ability, however, may remain intact post injury for both fluency types (Raskin & Rearick, 1996; Zakzanis et al., 2011). Schizophrenia patients have shown reductions in the number of total words produced, clustered categories of words, and switches across categories (Henry & Crawford, 2005; Landro & Ueland, 2008; Troyer et al., 1997). Some authors have suggested, however, that patients may cluster and switch in the same way as
healthy controls, but that they utilise these strategies less effectively, and simply generate fewer words per cluster (Bozikas et al., 2005; Kosmidis et al., 2005; van Beilen et al., 2004). Cluster and switching analyses have not been reported in PFTBI to date.

5.1.3 Memory.

The literature has documented significant memory impairment following TBI, and this appears to apply to most, if not all, aspects of memory (Ariza et al., 2006; Carlesimo et al., 1998; Lezak, 1979; Owen et al., 1990; Perri et al., 2000; Tate et al., 1991). Impairment has been shown following mild to severe injury, with the extent of the memory deficit seemingly proportionate to the extent of damage to the brain (Bennett-Levy, 1984; Vakil, 2005). Memory is also impaired in schizophrenia and much of the work suggests that deficient memory is a persistent and heritable trait of schizophrenia, irrespective of symptom profile (Bartholomeusz et al., 2011; Broome et al., 2010; Cannon et al., 2005; Nieto & Castellanos, 2011; Pukrop et al., 2007). Recent work has shown, however, that an exception to this may be seen in late onset schizophrenia (Girard et al., 2011). Differential patterns of activation have been shown during memory tasks in imaging work (Broome et al., 2010; Ehrlich et al., 2011; Kumicki et al., 2009; Nestor et al., 2010; van Os et al., 2009), and recognition is considered less impaired than recall (Beatty et al., 1993; Kalkstein et al., 2010), albeit this is likely true for all individuals given that recognition, by nature, is an easier task because it involves memory cues.

The PFTBI literature is again somewhat inconsistent. Across the retrospective chart/case study publications reviewed impairments in memory have been shown relative to: i) norms (Fujii & Ahmed, 2002), ii) healthy controls (i.e., verbal memory, recall) (Fujii et al., 2004), and iii) TBIWP (i.e., verbal and nonverbal memory) (Sachdev et al., 2001). However, Bamrah and Johnson’s (1991) PFTBI case study showed normal memory and recall abilities.

5.1.3.1 Semantic memory.

Despite general memory impairment following TBI, the literature consistently suggests that semantic organisation is unaffected by the injury, with the majority of work emphasising that patient responses illustrate their ability to identify and utilise semantic information to the same degree as healthy controls (Crosson et al., 1989; Haut et al., 1991; Levin & Goldstein, 1986; Perri et al., 2000). This has been shown across various paradigms, including semantic priming where response patterns show that patients are able to take advantage of the preceding prime (Haut et al., 1991; Perri et al., 2000). Reduced overall
performance in TBI, illustrated by slower reaction times and reduced total output, may instead reflect a reduction in processing speed and/or access to existing information, as a result of white matter damage (McWilliams & Schmitter-Edgecombe, 2008; Perri et al., 2000).

Semantic memory and semantic priming have been heavily researched in schizophrenia, and impairments in semantic memory have consistently been illustrated across a number of study designs, including priming paradigms (Chen et al., 1994; Rossell & David, 2006; Rossell et al., 1998; Rossell et al., 1999; Rossell et al., 2000). Notably, a range of potential mediators have been identified in the priming literature, although the degree of influence of these variables on the priming data remains less clear. These include patient-related characteristics such as the effects of medication, other influences related to the disorder such as slowed processing, and symptomatology such as thought disorder, as well as parameters of methodology (i.e., SOA, relatedness proportion, prime-target relationship type, and degree of priming calculation) (Minzenberg et al., 2002; Morgan et al., 2006; Spitzer et al., 1993). Moreover, attempts to determine the underlying mechanism(s) of these deficits in patients, including, but not limited to, the debate regarding an access/retrieval and/or storage-specific impairment are ongoing (Allen & Frith, 1983; Aloia et al., 1996; Elgevag et al., 2001; Rossell et al., 2010; Rossell & David, 2006).

No data has been published pertaining to semantic memory specifically, or using a semantic priming paradigm in PFTBI to date.

5.1.4 Reasoning.

The assessment of probabilistic reasoning in TBI cohorts has not been reported in the literature. However, a number of other reasoning abilities have shown impairments, including inferential reasoning/theory of mind (ToM) deficits, analogical reasoning, and deductive reasoning (Bibby & McDonald, 2005; Geraci & Cantagallo, 2011; Goverover, 2004; Krawczyk et al., 2010). In general the literature suggests that this is likely to be a result of reduced executive function post injury, in particular, damage to focused attention, working, and short term memory (Krawczyk et al., 2010; Morrison et al., 2004). Reasoning biases in schizophrenia remain a contentious issue. On one hand, there is support for a general data gathering bias (i.e., jumping to conclusions), and/or perhaps a lowered threshold for decision making (Averbeck et al., 2010; Langdon et al., 2010; Moritz et al., 2007; 2009). On the other hand, some work has failed to find evidence of a reasoning impairment in schizophrenia at all.
(Colbert et al., 2010; Lincoln et al., 2010; Maher, 1992; Young & Bentall, 1997). Attempts to account for inconsistent findings have led to suggestions that lowered IQ (Lincoln et al., 2010), negative symptoms (Lincoln et al., 2010), and/or the presence/absence of delusions (Bentall & Swarbrick, 2003; Bentall & Taylor, 2006; Freeman, 2007; McKay et al., 2006; Woodward, Munz et al., 2009) may underlie poor reasoning. These too, however, have shown inconsistencies; IQ appears unrelated to the reasoning bias (Langdon et al., 2010), no bias has been shown in patients with delusions, current or remitted (Colbert et al., 2010; Young & Bentall, 1997), and no differences between deluded and nondeluded patients has been reported (Menon et al., 2011). Again, no PFTBI data has been published to date.

5.1.5 Executive function.

5.1.5.1 Mental inhibition and switching.

First, the existing literature highlights the necessity of using calculated derived scores for both the Stroop and TMT tasks, where the variables of interest are inhibition and switching respectively (Dimoska-Di Marco et al., 2011; Rios et al., 2004). As such, a measurement of inhibition and switching is obtained while accounting for the effects of other processes required by the task, such as attention and processing speed, which are likely to also be impaired, and to vary in degree of impairment across participants with injury/illness. This becomes more imperative given the likelihood of the statistical inappropriateness of attempting to account for these differences in covariate analyses (see Chapter Eight and Appendix T for discussion) (Green & Salkind, 2005; Field, 2005).

Patients post TBI have shown inhibition deficits behaviourally (LeBlanc et al., 2005; Rao & Lyketsos, 2000), and on a range of widely used tasks in empirical assessments of the effortful suppression of a motor response (Duncan et al., 2005; Levin et al., 1993; Logan, 1994; O’Keeffe et al., 2007; Roche et al., 2004). However, some work has reported proficient performance on the Stroop subtasks, although it is noteworthy that derived scores were not calculated here (Larson et al., 2007; Ponsford & Kinsella et al., 1992; Schroeter et al., 2007; Stuss et al., 1985). Further, two meta-analyses have suggested that alternative deficits prominent in TBI, including processing speed and attention, may underpin poor inhibition (Dimoska-Di Marco et al., 2011; Mathias & Weaton, 2007). However, these suggestions were made based on the degree of deficits shown to processing speed and attention across the studies included in meta-analysis, and no direct comparisons were actually made with measurements of inhibition. Impaired mental switching abilities have also been shown post
TBI (Perlstein et al., 2006; Rios et al., 2004), and to date it appears that poor cognitive flexibility (i.e. switching) may be mediated by injury severity; moderate to severe TBI patients demonstrated impaired switching using the fourth (switching) trial of the Stroop, but no impairment was evident in mild TBI patients (Perlstein et al., 2006; Seignourel et al., 2005), and severely injured TBI patients have shown impairments where the derived Trail Making difference score has been correctly calculated (Rios et al., 2004).

Patients with schizophrenia show both poor mental inhibition (Barch et al., 2004; Braff, 2010; Henik & Salo, 2004; Kang et al., 2011), and switching (Fisher et al., 2010; Ravizza et al., 2010; Smith et al., 1998; Wylie et al., 2010). There is a large amount of evidence for impairment in schizophrenia using the Stroop task (Barch et al., 2004; Brenton et al., 2011; Ferchiou et al., 2010; Orem & Bedwell, 2010), however, a number of versions of the task exist and may be responsible for some inconsistencies in the literature. For example, studies claiming increased facilitation and equivalent interference effects for patients relative to control participants have used single-trial versions of the task that may not be sensitive enough to capture true impairments (e.g., Barch et al., 2004). Provided correctly calculated derived scores are utilised, the four trial version appears to capture switching-inhibition effects well (Delis et al., 2001a; 2001b; Fine et al., 2008) (shown in Figure 3.13, Chapter 3.6.3: The colour Stroop paradigm).

Stroop task performance has not been reported in PFTBI. Pooling data from retrospective chart reviews, Fujii et al. (2004) reported no impairments on the TMT task (Parts A and B) for PFTBI patients following Bonferroni correction, although the authors did not report a derived switching score. Again, while this work is valuable, it appears inconsistent with the impairments recorded for both patients following traumatic brain injury, and those diagnosed with schizophrenia.

5.1.5.2 Attention.

While it is unclear whether TBI patients have a true attention deficit (rather than one influenced by time pressure and/or processing speed), it is clear that they show impairment on the current assessments of attention (Madigan et al., 2000; Ponsford & Kinsella, 1992, Rios et al., 2004). Attention-specific hypotheses have also been proposed: (i) the attentional-resource hypothesis, where processing resources specific to attention are reduced (Schmitter-Edgecombe, 1996), and (ii) the component process hypothesis, where only certain isolated components of attention are damaged (Park et al., 1999; Rios et al., 2004; Whyte et al.,
Selective, switching, and sustained attentional impairments have all been reported across a number of modalities and tasks, and independent of symptomatology (Benton et al., 2011; Chan et al., 2004; Egeland et al., 2003; Heinrichs & Zakzanis, 1998; Kumar et al., 2010; Perlstein et al., 1998). Impairments in attention are also considered a stable trait of the disorder having been demonstrated in healthy relatives (Birkett et al., 2007; Brenton et al., 2011), schizotypal personality (Gooding et al., 2006), first presentation (Wang et al., 2007), and chronic patients (Kurtz et al., 2001). Within the PFTBI literature reviewed, only one study reported on the outcome of measurements in attention, indicating that 11.76% (n = 2) of PFTBI patients demonstrated impairments (Fujii & Ahmed, 2002). This is once again somewhat inconsistent with the prominent deficits demonstrated in schizophrenia, and highlights again the need for more work in this area.

5.1.5.3 Processing speed.

Following TBI, slowed processing speed has been shown to a range of functional abilities, including audition (Gronwall, 1977; Ponsford & Kinsella, 1992), semantic memory (Haut et al., 1991), visuo-motor processing (Stuss et al., 1989; van Zomeren & Deelman, 1976), and attentional processes (Beauchamp et al., 2011). In fact, processing speed is arguably the most vulnerable to the effects of brain injury (Clement & Kennedy, 2003), and seems to be independent of injury severity, time since injury, and performance accuracy in TBI (Felmingham et al., 2004; Madigan et al., 2000). Moreover, the Stroop subtest and TMT scores are able to discriminate TBI from healthy control participants, even in cases of mild injury (Dimoska-Di Marco et al., 2011; Reitan, 1955; 1958). Likewise, marked reductions in processing speed have been shown consistently in schizophrenia (Brebion et al., 1998; Egeland et al., 2003; Ojeda et al., 2008; Savla et al., 2010). The Coding subtest of the RBANS has been used frequently in the literature as a measure of processing speed in schizophrenia, and is argued to be superior to other measurements (Brebion et al., 2007). For both of these patient groups there is ongoing speculation regarding the impact of processing speed on the measurement of other aspects of neurocognition, along with attempts to isolate other neurocognitive ability from the effect of slowed processing, either in task design or analysis (i.e., entering processing speed data as a covariate). This latter attempt has been highlighted numerous times as potentially erroneous; see for example Brebion et al., 1998; 2000; 2006; 2007; 2011 and Appendix T for discussion. Processing speed in PFTBI remains
relatively unclear due to important methodological concerns in the literature to date (e.g., Fujii et al., 2004 and Burg et al., 2000).

5.1.6 Premorbid and current IQ.

Substantial deficits in performance IQ (i.e., reasoning and visuo-spatial abilities) have been shown consistently in TBI (Chadwick et al., 1981; Clement & Kennedy, 2003; Donders, 1997; Ferri et al., 2004, Kay & Warschauisky, 1999; Nass et al., 1989). Reduced performance IQ is likely explained by damage to white matter and resultant disruptions to connectivity and information processing, and thereby likely to be more severe following worse injury. Conversely, verbal skills seem to remain relatively stable from prior to post injury. Of course there is no reason for premorbid IQ to differ from the normal, healthy distribution in TBI cohorts, and this has been confirmed in the literature (Crawford et al., 1988). By contrast, the majority of work in schizophrenia has shown reductions in both premorbid and post illness onset measurements of intelligence. A generalised intellectual impairment has been proposed as part of the disorder, and work has shown a relationship between lowered premorbid IQ and the development of illness (Cannon et al., 1999; Crawford et al., 1992; Henry & Crawford, 2005; Jespen et al., 2010). Premorbid estimates of IQ in PFTBI have not been reported, and the available literature reporting estimates of current IQ have been inconsistent. For instance, Bamrah and Johnson (1991) reported that their case study had IQ in the normal range, yet Fujii et al. (2004) and Sachdev et al. (2004) both identified reduced IQ in PFTBI from retrospective chart reviews.

5.1.7 General comments: TBI.

The TBI literature has consistently indicated that performance on the majority of cognitive neuropsychological domains discussed here are affected by a number of variables. Authors have acknowledged that the type and extent of deficits illustrated following TBI are mediated by injury-specific demographics, including: the age of injury acquisition, injury severity (i.e., LOC and PTA), injury type (i.e., closed-head versus penetrating), injury location (i.e., hemisphere and lobe), and the time since injury (Leblanc et al., 2006; Moran & Gillon, 2004; Sullivan & Riccio, 2010). In addition, common impairments in certain aspects of cognition post injury, such as poor processing speed and reduced attention, are implicated in many of the paradigms used to determine performance elsewhere (e.g., in measures of semantic priming), causing the extent of the deficit to be difficult to isolate. Premorbid language and education (IQ) has also been identified as a mediator.
The literature is often specific about certain injury details and resultant effects, for example, where visual Gestalt processing is reduced in patients with right hemispheric lesions relative to those with left sided lesions (Delis et al., 1986; Robertson & Lamb, 1991). This culminates in a large amount of work having reported and/or speculated about the various influential aspects of injury in their respective cohorts and the distinguishable patterns in their outcome of interest that follow. While specifics have been highlighted across most neuropsychological domains in the preceding review chapters, this does not necessarily provide a clear picture of these relationships. It is reasonable to assume that most injury-based variables probably affect most aspects of neurocognition, and that some further variation would be shown according to the particular sample used in a research study. As such, where study results show group differences on neuropsychological outcomes in TBI, correlational analyses should be explored with all relevant injury variables specific to the utilised sample.

5.1.8 General comments: Schizophrenia.

Similarly, the schizophrenia literature has long been complicated by various aspects related to the illness. Again authors have discussed their findings with an acknowledgement of the likely mediating role of the following: age of illness onset, illness duration, symptomatology (i.e., including positive, negative, and/or disorganised symptoms, and/or often the presence/absence of delusions), processing speed and attention (also implicating working memory depending on the task), intelligence, and the effects of medication (e.g., Henry & Crawford, 2005; Rossell, 2006; Rossell et al., 1999). Ultimately this illustrates the likelihood of substantial influences on the collection and interpretation of cognitive neuropsychological data, and yet, this too is not straightforward given that no one influential factor is consistently found for any particular outcome across studies. Thus, again, it is imperative that where group differences are shown, relationships with the illness-related factors identified here are examined particular to the study sample.

5.1.9 General comments: PFTBI.

The PFTBI data may therefore be complicated by both sets of mediators identified previously in TBI and schizophrenia separately, and as such, need to be submitted to identical explorations. In addition, this summary has compounded some general findings from the available PFTBI literature to give a condensed indication of current trends pertaining to each domain, and how these relate to the trends established in TBI and schizophrenia. However, as
highlighted in detail in *Chapter Two (Section 2.7)*, it is once again stressed that the PFTBI work to date contains significant limitations, and in some cases very questionable methodology. Accordingly, the summary presented here regarding PFTBI should be interpreted with this in mind. In particular, aspects of the work reported in PFTBI to date seem to suggest proficient neuropsychological abilities. Yet, with reference to the substantial deficits established in both TBI and schizophrenia this is unlikely to be accurate. At the very least, patients with PFTBI should illustrate deficits comparable to those in TBI and schizophrenia. In fact, it stands to reason that patients with PFTBI may even show further reductions in cognition, reflecting the additive effect of dual diagnosis.

### 5.2 Research Aims

The primary aim of this research project was to determine the cognitive neuropsychological profile in patients with psychosis following a traumatic brain injury (PFTBI). This work represents the first systematic assessment of this cohort using standardised neuropsychological measures, and a battery of this size. A secondary aim, also unique to this work, was to compare the PFTBI data with data obtained from three control groups: (i) patients with TBI without psychosis (TBIWP) who were matched as closely as possible on injury-related variables to the PFTBI group, (ii) patients with schizophrenia/schizoaffective disorder, (iii) and a healthy control sample, collected in identical and controlled test settings.

The following neuropsychological domains were assessed:

- Visuo-spatial and Gestalt processing
- Language and verbal fluency
  - phonological
  - semantic
- Memory
  - immediate
  - delayed
  - semantic (priming)
- Probabilistic reasoning
- Executive function
  - mental inhibition and switching
  - processing speed
- attention

- Premorbid and current IQ

It was not an aim of this research to determine the neuropsychological profile of the two patient control groups (i.e., TBIWP and schizophrenia) or of the healthy control group. Aims particular to each statistical analysis technique are discussed in turn.

5.2.1 Group wise comparisons.

As a first step, the objective of the group wise comparisons were to determine whether statistically significant differences existed between the four cohorts, according to the mean (standard deviation) scores obtained on each of the cognitive neuropsychological measures.

5.2.2 Correlational analyses.

Cognitive neuropsychological measures that showed statistically significant group differences were submitted to correlational analyses with the injury and illness-related factors identified in the literature (highlighted in the General Comments above, and discussed further in Chapter Seven).

5.2.3 Discriminant function analysis.

Discriminant function analysis (DFA) was conducted to determine whether cognitive neuropsychological scores could correctly classify individuals in the four participant groups. From there, DFA was used to investigate how well the classification procedure would correctly predict cognitive neuropsychological scores in a new sample.

5.3 Summarised Research Hypotheses

PFTBI patients were expected to illustrate inferior performance on all measures, with intermediate performance by the patient control cohorts, and superior performance by the healthy cohort. Domain specific hypotheses are contained in Section 7.2 Hypotheses. Correlational analyses were expected to provide evidence for the relationship between injury/illness-related factors and cognitive neuropsychology (see Chapter Eight). Last, DFA was expected to distinguish between the PFTBI and healthy cohorts at a minimum (see Chapter Nine).

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32 However, these were hypothesised where clear and relevant trends have been established in the literature.
Chapter 6: Empirical Study Design and Description of Samples

6.1 Introduction

This chapter provides details on ethical approval, empirical study design, recruitment, and classification procedures used to determine injury severity and clinical ratings, before presenting a thorough demographic description of the final four participant groups used in this research. Cohorts are first discussed according to general demographics (e.g., age, IQ), followed by a detailed breakdown and statistical comparison of traumatic brain injury-related variables (TBIWP and PFTBI groups). This is followed by a comprehensive itemisation and analysis of clinical characteristics, including a standardised comparison of antipsychotic medication for the schizophrenia and PFTBI groups. The chapter closes with a summary of the strengths and weaknesses of the final sample groups.

6.2 Ethical Approval

Full ethical approval for the research protocol was granted by the Alfred Hospital (#301/08), Austin Health (#H2008/03325), Epworth Healthcare (#49610), RMIT University, and Monash University (#CF09/0211-2009000081). These documents can be found in Appendix E.

6.3 Study Design and Power

As discussed in Chapter Two, the standardised and systematic assessment of psychosis following traumatic brain injury (PFTBI) is a novel research endeavour. This research was designed around the recruitment and assessment of PFTBI patients, who were considered a ‘convenience’ sample. That is, PFTBI recruitment was the primary objective of this research project with no upper limit set for the sample size. Patients with PFTBI may constitute up to ten per cent of individuals who sustain a traumatic brain injury (Davison & Bagley, 1969; Fujii & Ahmed, 2001; Fujii et al., 2004; Newburn, 1998). However, where recruitment is confined to a single city (i.e., Melbourne, Australia), with limited recruitment sites available for collaboration (i.e., the Alfred, Epworth and Royal Talbot Hospitals), over a short recruitment period (i.e., 18 months of a PhD candidature), the number of available cases is relatively reduced. With this, and the anticipated considerable morbidity of the PFTBI cohort, recruitment and testing were expected to be challenging. Recruitment procedure and outcome are discussed in the following Section 6.4: Recruitment.
An a priori power calculation was conducted to provide an estimation of the sample size required for adequate statistical power. This was a difficult task, due to the considerable limitations of the existing PFTBI research (discussed in Chapter Two), and is therefore considered a tentative assessment. The work from Fujii et al. (2004) was deemed most appropriate for this estimation. Using a logical memory task similar to the one to be used in this project, the authors established that PFTBI patients were significantly impaired relative to a normative sample, with a large effect size; Cohen’s $d = -1.42$ (Green & Salkind, 2005). Setting alpha at 0.05, excellent statistical power is obtained (i.e., 0.80) with a total of fourteen participants (i.e., seven per group; PFTBI and healthy controls). In light of this analysis an absolute minimum of seven PFTBI patients was set as a recruitment goal for this research project.

It was imperative that a traumatic brain injury without psychosis (TBIWP) cohort was matched demographically to the PFTBI group and, thus, the minimum recruitment goal for this group was identical to the PFTBI cohort. With regard to the schizophrenia and healthy control comparison groups, extensive research has illustrated significant impairment in schizophrenia on cognitive neuropsychological tasks (see Chapter Three), with generally large effect sizes. Across the domains of interest, for instance, relevant effect sizes are as follows; perceptual organisation ($d = 1.46$; Keri et al., 2005), phonological fluency ($d = 1.67$; Ojeda et al., 2010), semantic fluency ($d = 1.32$; Ojeda et al., 2010), memory (word recall) ($d = 0.99$; Brebion et al., 2011), reasoning (ToM) ($d = 0.84$; Corcoran et al., 1995), inhibition (antisaccades) ($d = 1.51$; Manoach et al., 2002), processing speed ($d = 1.14$; Brebion et al., 2011), and attention (digit symbol) ($d = 1.54$; Ojeda et al., 2010). As with the PFTBI calculation, setting alpha at 0.05 and power at 0.80, a total of between twelve and thirty-eight participants were required to detect statistically significant differences on neuropsychological tasks of this nature (that is, an absolute minimum of nineteen per group when comparing schizophrenia patients with healthy controls). Accordingly, a goal of twenty participants in each of the schizophrenia and healthy control cohorts was considered feasible for this research project. Recruitment outcomes for these groups are contained in the following section (6.4: Recruitment).
6.4 Recruitment

Four participant groups were recruited;

(i) a dually diagnosed psychosis following traumatic brain injury (PFTBI) group;

(ii) a control TBI without psychosis group (TBIWP);

(iii) control patients diagnosed with schizophrenia/schizoaffective disorder, and

(iv) a healthy control group.

The PFTBI group was recruited from private practice clientele of A/Prof Malcolm Hopwood \( (n=3) \), a participant database registry held at the Monash-Alfred Psychiatry research centre (MAPrc) \( (n=6) \), and the Royal Talbot Hospital via the Brain Disorders Program at Austin Health (Community Brain Disorders Assessment and Treatment Service, CBDATS) \( (n=1) \). CBDATS comprises medical, nursing, psychology, neuropsychology and social work team members who provide support and rehabilitation services for patients with brain impairment and psychiatric illness in Victoria. The TBIWP group was recruited from the Monash-Epworth Rehabilitation Research Centre (MERRC) database \( (n=1) \), the MAPrc database \( (n=7) \), and via affiliates of the researchers \( (n=2) \). Schizophrenia/schizoaffective \( (n=23) \) and healthy control \( (n=23) \) participants were recruited from a secondary registry held by Prof Susan Rossell at MAPrc. The registry was developed by Prof Rossell during various research appointments in Melbourne beginning in 2006. It contains contact and demographic information for approximately 300 individuals who have previously given their consent to be contacted about research participation. These are healthy individuals as well as patients with various diagnoses (e.g., schizophrenia, bipolar disorder, depression/anxiety, anorexia nervosa, Alzheimer's disease).

Following a presentation of the research project to the relevant CBDATS staff and the dissemination of general project information sheets (see Appendix F), patients that met criteria for the PFTBI group were identified and approached about the study by their treating clinician at CBDATS and/or by A/Prof Malcolm Hopwood. If they were interested in participation the student researcher then met with them to discuss the project goals and participation requirements at length. Participants contained on all databases utilised for the research had already given their voluntary consent to be contacted about participating in research projects. If individuals contained on a database appeared to meet the criteria for participation the student researcher made telephone contact with them, and explained the research project and requirements of participation in detail.
6.4.1 PFTBI and TBIWP recruitment and matching.

Table 6.1 details the recruitment success rates for the PFTBI group. During recruitment, a substantial number of patients were identified as having had been diagnosed with PFTBI (N = 43), however a proportion of these were considered unable to perform the battery of tasks due to the extent of their injury (n =18). Only one of twelve patients from the CBDATS program was recruited for participation for this reason, and this patient (#P05) demonstrated the greatest (or equal greatest) impairment across all tasks. He was also excluded from the semantic priming task because his capacity for sustained concentration and his motor speed was inadequate for task completion (see Chapter Seven for details of the assessment battery). Another patient (#P04) who was recruited from A/Prof Malcolm Hopwood’s private practice and who had formally been part of the CBDATS program following a severe injury, provided accuracy data on the priming task that was only just above chance level at the short SOA (related, 54.17%, unrelated 62.5%), and below chance level at the long SOA (related, 41.67%, unrelated, 45.83%)

Thus, based on the degree of impairment (and n =1 case complicated by cannabis use disorder) only 58.14 per cent of PFTBI patients screened for participation were approached. Of those, the recruitment success rate was 40 per cent.

Table 6.1
PFTBI Recruitment Sources and Success Rates

<table>
<thead>
<tr>
<th>Source</th>
<th>Identified</th>
<th>Approached</th>
<th>Successful</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBDATS</td>
<td>12</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Epworth Hospital</td>
<td>2</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>A/Prof Hopwood Private Clinic</td>
<td>6</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>MAPrc Database</td>
<td>23</td>
<td>17</td>
<td>6</td>
</tr>
<tr>
<td>Total</td>
<td>43</td>
<td>25</td>
<td>10</td>
</tr>
</tbody>
</table>

Recruitment of the PFTBI sample was additionally slowed by the necessary review of many case files, and in light of the time constraints on the project the matching of case by case across each brain injury variable with the TBIWP cohort was compromised. Moreover, 

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33 Performance at the long SOA was at least partially due to fatigue and loss of motivation. Despite adequate breaks and encouragement patient #P04 had significant morbidity that affected his ability to perform the task well. His data provided an important indication of PFTBI performance at the severe end of the spectrum.
despite extensive review of the MERRC database over an eighteen month recruitment period, only three close to exact TBIWP matches were identified on a case by case basis (i.e., < 5% difference either way on continuous variables, see Tables 6.6-6.8). The MERRC database established by Professor Jennie Ponsford in 1985 contains approximately 3,200 cases who have sustained a traumatic brain injury, with detailed records pertaining to their injury. Of the three identified, only one individual agreed to participate. Nonetheless, while cases were not matched one on one, they were well matched as a group. Two exceptions were, i) more time had lapsed between injury and research participation in the PFTBI cohort (\(M = 24.80\) years, \(SD = 10.89\)), relative to the TBIWP group (\(M = 9.80\) years, \(SD = 9.35\)) and, ii) a substantial number of TBIWP patients were in an induced coma following their injury (seventy per cent), compared with only ten per cent of those diagnosed with PFTBI (see Section 6.8: Traumatic Brain Injury Demographics for inferential statistics).

6.4.2 Inclusion criteria.

All participants were between eighteen and sixty-five years of age (\(M = 38.59\), \(SD = 12.05\)), and demonstrated acceptable English/communication skills necessary for task completion. Acceptable visual acuity (e.g., at least the equivalent of Snellen’s 20/30 vision) was met by all participants (corrective eyewear was permitted).\(^{34}\) Acceptable colour vision was met by all but one participant from the schizophrenia/schizoaffective group who had self-reported colour vision deficiency, and consequently did not complete the Stroop Task. Diagnosed stroke, Multiple Sclerosis (MS), Huntington’s disease, Parkinson’s disease, premorbid cognitive, learning, or memory difficulties, and/or a previous psychosis/mania warranted exclusion from the study. However, no participants met these criteria. Patients with substance abuse related TBI, and/or who had participated in drug/cannabis use in the three months prior to testing were also to be excluded. Again however, individuals who met these criteria were discarded as potential recruits during the thorough screening process. Finally, any patient with current delirium or severe current morbidity was to be excluded from the study. As mentioned, two patients from the PFTBI group had substantial morbidity as a result of their injuries (i.e., #P04 and #P05). Both were considered capable of completing the assessment battery, with the exception of #P05 on the computerised priming task only.

\(^{34}\) This process ensured that cognitive neuropsychological performance from either TBI group was not mediated by additional visual deficits as a result of their injury.
PFTBI patients were required to have developed psychosis following their traumatic brain injury (i.e., family history of psychosis was permitted but no indication of psychosis was allowed prior to the injury). Schizophrenia/schizoaffective patients were not permitted to have a history of head injury. It was considered impractical to exclude any participant on the basis of psychiatric co-morbidity (i.e., other Axis 1 conditions including depression, anxiety etc.), and as such these were allowable from all cohorts. Two participants from the healthy control group had previously been diagnosed with depression, and no co-morbid conditions were recorded for the TBIWP group. Given the higher prevalence of co-morbidities in psychosis, co-morbidities in the PFTBI and schizophrenia cohorts are detailed in Section 6.9: Clinical Demographics.

6.5 Procedure

Participants were initially given a copy of the plain language statement (PLS) and informed voluntary consent was taken when the researchers were satisfied that participants understood their involvement in the project fully (Appendix G). All participants were deemed capable of providing informed voluntary consent for themselves. A screening questionnaire to confirm inclusion criteria eligibility, and a participant demographic form, was then completed (see Appendices H and I). This process took approximately twenty minutes. Participants were then asked about their family history, and given three self-report measures, including, (i) the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) included as a simple screen for the presence of anxiety and depression, (ii) the LEEDS Dependence Questionnaire (Raistrick et al., 1994) used to rule out alcohol abuse and/or dependence (i.e., potential participants who met this criteria were to be excluded from the study), and (iii) the Edinburgh Handedness Inventory (Oldfield, 1971) included to allow for the examination of laterality effects, should the cohorts have unequal ratios of left and right dominant hands. Table 6.2 summarises these measures and provides their psychometric properties. The forms themselves are contained in Appendix J.

Patients who had had a traumatic brain injury were further asked about the details of their injury (this was incorporated in the participant demographic form contained in Appendix I). Permission for the release of injury and/or illness related information from relevant hospitals and/or clinicians was given via the consent form signed by patients. PFTBI injury related information was substantiated by extensive case history files from the CBDATS and A/Prof Hopwood’s private clinic (n =4), and the remainder from the combined information
Table 6.2
Description and Psychometric Properties of Self-Report Measures

<table>
<thead>
<tr>
<th>Measure</th>
<th>Author(s)</th>
<th>Structure</th>
<th>Reliability</th>
<th>Validity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital Anxiety and Depression Scale (HADS)</td>
<td>Zigmond &amp; Snaith, 1983</td>
<td>14-item (2 subscales; 7 depression/7 anxiety) self-administered scale. Items are rated on a 4-point Likert scale (0-3), with higher scores indicating the endorsement of features of depression/anxiety. On each subscale, scores of 8-10 are suggestive of ‘borderline abnormal’, and 11-21 of ‘abnormal’, indicating clinically significant levels at mild and severe intensity, respectively.</td>
<td>Cronbach’s α = 0.84 (anxiety subscale), and 0.83 (depression subscale) (Dagnan, Chadwick, &amp; Trower, 2000).</td>
<td>Concurrent validity, r = 0.66-0.70, p&lt;0.05 Clark &amp; Watson, 1991.</td>
</tr>
<tr>
<td>LEEDS Dependence Questionnaire</td>
<td>Raistrick et al., 1994</td>
<td>10-item self-administered scale rated on a 4-point Likert scale (0-3, 0=never, 1=sometimes, 2=often, 3=nearly always), designed to measure the severity of dependence on drugs and/or alcohol (irrespective of the substance). Items address the following: pre-occupation, salience of substance use, compulsion to start, planning around substance use, maximising effect, narrowing of using repertoire, compulsion to continue, primacy of effect, constant state, and cognitive set. 1-10 is suggestive of low to moderate dependence, 11-20 of moderate to high dependence, and 21-30 of high dependence.</td>
<td>Cronbach’s α = 0.94, Test-retest, r = 0.95 (Raistrick et al., 1994). In clinical populations; Cronbach’s α = 0.92 (Ford, 2002).</td>
<td>Acceptable content, concurrent, discriminant, and convergent validity (Raistrick et al., 1994). In clinical populations; concurrent validity, r = 0.32, p &lt;0.001, convergent validity ranged from 0.44 for somatic symptoms to 0.51 for global severity, p&lt;0.001 (Kelly, Magill, Slaymaker, &amp; Kahler, 2010).</td>
</tr>
<tr>
<td>Edinburgh Handedness Inventory (EHI)</td>
<td>Oldfield, 1971</td>
<td>10-item self-administered scale. Participants are asked to rate whether they perform each of the items with their left, right, or both, hand(s); effectively a 5-point Likert scale including ‘exclusively left’, ‘left’, ‘both’, ‘right’, and ‘exclusively right’. A laterality quotient is computed as 100 x (R-L)/(R+L). Scores below –40 indicate left handedness, between –40 and 40 indicate ambidexterity, and above 40 indicate right handedness.</td>
<td>Test-retest, r = 0.91 (McFarland &amp; Anderson, 1980).</td>
<td>Factor stability cosines all &gt; 0.98 (McFarland &amp; Anderson, 1980).</td>
</tr>
</tbody>
</table>
provided by relevant hospitals, and by the patient where access to the physical file was not possible. In one case (i.e., #P08) injury information was verified by a first degree relative because hospital files had been destroyed and confirmation from someone other than the patient was deemed necessary by the researchers. TBIWP injury information was gained from the combined information provided by hospitals and the patient.

Participants then took part in either one (i.e., healthy controls and TBIWP) or two (i.e., PFTBI and schizophrenia) testing sessions of approximately two hours duration each;
   i) clinical assessment for patients with psychosis (PFTBI and schizophrenia)
   ii) cognitive neuropsychological battery (all)
These were completed on different days at the patient’s convenience, and in accordance with their capabilities. Adequate breaks were provided between tasks to avoid fatigue. Following the testing sessions, participants were given a copy of the debriefing statement (contained in Appendix K) and asked if they had any questions or concerns regarding the research. A senior member of the research team was always available in the event that the participant felt they needed further support for any reason. The debriefing statement contained a list of relevant contact numbers, including those for the senior researchers, the ethics manager, and chairperson of the research committee, should the participant have queries and/or concerns at a later date.

One patient diagnosed with schizophrenia (i.e., #S12) became distressed at the end of his final session. The appropriate steps were taken according to the ethical protocol outlined in the National Health and Medical Research Council’s National Statement on Ethical Conduct in Human Research (2007). The patient, who suffered from paranoid delusions, was seen by Professor Susan Rossell and it was determined that his distress was a result of elevated paranoia on the day of testing. Following discussions with Professor Rossell he was calmer and able to leave the hospital on his own. He granted permission for his data to remain in the research project for analysis.

Finally, participants were financially reimbursed for their time and travel expenses incurred as a result of participation (i.e., $25 for one session, and $50 for two). Empirical procedures pertaining to the classification of TBI severity, clinical assessment, and cognitive neuropsychological assessment are explained in the following sections (6.5.1 and 6.5.2) and following chapter (Chapter Seven), respectively.
6.5.1 Injury severity (TBIWP and PFTBI).

Injury severity was defined according to the parameters identified by the Department of Defense and Department of Veterans Affairs (DoD/DVA; contained in Appendix A). These parameters incorporate the common definition and are consistent with both the American Congress of Rehabilitative Medicine (ACRM) definitions (Department of Defense and Department of Veterans Affairs, 2008), and peer-reviewed publication conventions (Mathias & Coats, 1999; McAllister et al., 1999; McWilliams & Schmitter-Edgecomb, 2008; Ponsford et al., 2008). The parameters consider information from structural imaging, loss of consciousness (LOC), alteration of consciousness, post-traumatic amnesia (PTA), and Glasgow Coma Scale (GCS) score. As discussed in Chapter Four, the convention for determining injury severity is typically the assessment of LOC, PTA, and GCS information, although LOC/PTA is often used alone where GCS information is not available. This was the case with the majority of the current sample. As such, assignment of injury severity adhered to the DoD/DVA definition for LOC, PTA, and GCS (where available) as closely as possible. Where information from one or more of the parameters indicated inconsistent levels of severity for a particular case, the most appropriate classification was given. For instance, the LOC and PTA data for patient #T02 indicated a severe injury, while his GCS score was within the mild range. In this case, a classification of severe injury was given due to quite extensive periods of LOC/PTA, and with reference to additional existing patient file notes suggesting the same.

6.5.2 Clinical assessment.

All PFTBI and schizophrenia patients underwent a clinical assessment conducted by a trained and qualified member of the research team for this project (Prof Rossell or Dr Thomas). The session included the research version of the Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID-I/P; First, Spitzer, Gibbon, & Williams, 2002), the Positive and Negative Syndrome Scale (PANSS; Kay, Fiszbein, & Opler, 1987), the Scale for the Assessment of Positive Symptoms (SAPS; Andreasen, 1984), and the Thought Language and Communication Index (TLC; Andreasen, 1986). The SCID-I modules for psychotic disorders (and associated symptoms) were used to confirm psychosis. No other modules from the SCID-I were administered; given the chronicity of patients it was determined that the administration of the lengthy SCID-I measuring all Axis I and II disorders was not possible. Current symptomatology was rated using the PANSS. The SAPS was included to provide additional detailed information on the nature of hallucinations and types of delusions present
in the cohorts, especially given that PFTBI (i.e., neurological) patients were likely to show a distinction in their profile of visual hallucinations (Cummings & Miller, 1987). By contrast, the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1982) was not included because it provides comparable information to the PANSS. The TLC acquired detailed information on the presence/absence of eighteen cognitive and behavioural traits of thought disorder (Andreason, 1986)\(^\text{35}\). A brief description of each measure and the relevant psychometrics are contained in Table 6.3. The session was audio recorded to ensure the clarity and completeness of the clinical information. Consent for audio recording was obtained during voluntary informed consent (see the consent form in Appendix H).

### 6.6 Statistical Analyses

The statistical analyses of demographic, injury-related, and clinical variables are described here. Analyses pertaining to cognitive neuropsychological variables are discussed in the following chapter (Chapter Seven). Statistical analyses were conducted using IBM® SPSS® software, Version 19 (IBM Corporation, 2011). Data integrity was initially determined by screening all variables for erroneous inliers, outliers, out-of-range variables, and plausible means and standard deviations (Green & Salkind, 2005; van den Broeck, Argeseanu Cunningham, Eeckels, & Herbst, 2005).

There were no missing data for general demographic or TBI injury variables. Missing Value Analysis (MVA) indicated that there were no patterns of concern for missing clinical data; Little’s MCAR Test, \(\chi^2 (47, N=33) = 0.00, p = 1.00\). Missing clinical data is explained by missing values for patient #S12 on the SAPS scale only\(^\text{36}\). Reduced sample sizes are highlighted where relevant in the tabulated results in Section 6.9: Clinical Demographics.

Categorical variables were analysed via two-way contingency table analysis (i.e., chi-square), with the Holms Bonferroni method of alpha correction for Type I error where post hoc tests were required. Continuous variables were assessed for violations of normality via histograms, box and whisker plots, skewness and kurtosis, and Kolmogorov-Smirnov and

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\(^{35}\) The more comprehensive TLC was employed because the profile of thought disorder in PFTBI is unknown (see Chapter Two). However, the analysis of this profile is not within the scope of this thesis. Thus, only the global and total scores obtained from the TLC are presented (Section 6.9 Clinical Demographics), along with statistical analyses illustrating that the presence of thought disorder was not significantly greater in either psychosis cohort, and thus, did not unduly mediate their neuropsychological profile.

\(^{36}\) Patient #S12 did not complete the full clinical interview due to his elevated paranoia on the day of testing.
**Table 6.3**  
*Description and Psychometric Properties of Clinical Measures*

<table>
<thead>
<tr>
<th>Measure</th>
<th>Author(s)</th>
<th>Structure</th>
<th>Reliability</th>
<th>Validity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structured Clinical Interview for DSM Disorders (SCID)</td>
<td>First et al., 2002</td>
<td>Diagnostic exam used to determine DSM Axis I (mental disorders). Including mood episodes, psychotic and associated symptoms, psychotic disorders, mood disorders, substance use disorders, anxiety disorders, somatoform disorders, eating disorders, and adjustment disorder. NB. Only the psychotic and associated symptoms and psychotic disorders modules were used in this research.</td>
<td>Inter-rater reliability, $\kappa = 0.60$-0.83 (Lobbestael, Leurgans, &amp; Arntz, 2011). In schizophrenia, $\kappa = 0.94$ (Skre, Onstad, Torgersen, &amp; Kringlen, 1991).</td>
<td>Considered the ‘gold standard’ in determining the accuracy of clinical diagnoses (Shear et al., 2000; Steiner, Tebes, Sledge, &amp; Walker, 1995).</td>
</tr>
<tr>
<td>Scale for the Assessment of Positive Symptoms (SAPS)</td>
<td>Andreasen, 1984</td>
<td>34-item instrument for rating positive symptoms of psychosis using a 6-point Likert scale; 0=nil, 1=questionable, 2=mild, 3=moderate, 4=marked, and 5=severe. The scale consists of 4 subscales (hallucinations, delusions, bizarre behaviour, and positive formal thought disorder).</td>
<td>Inter-rater reliability, $\kappa = 0.40$-0.97 (4 subscales), 0.89 (Global rating). Internal consistency, Cronbach’s $\alpha = 0.72$-0.86 (4 subscales), 0.58 (Global rating). Test-retest, $r = 0.02$-0.57 (4 subscales) 0.40 (Global rating) (all $p&lt;0.0005$ except bizarre behaviour) (Schulberg, Quinlan, Morgenstern, &amp; Glazer, 1990).</td>
<td>Concurrent validity, $r = 0.77$ ($p&lt;0.0001$) (Kay, Opler, &amp; Lindenmayer, 1988).</td>
</tr>
<tr>
<td>Thought, Language, and Communication Index (TLC)</td>
<td>Andreasen, 1986</td>
<td>Clinical rating scale for thought disorder. 18-item and Global Rating, scored on 4- to 5-point Likert scale; 0=absent, 1=mild, 2=moderate, 3 =severe, 4=extreme.</td>
<td>Inter-rater reliability, all 18-items $\kappa = 0.81$ (Harvey et al., 1992). Inter-rater reliability, $\kappa = -0.02$-0.89 (Andreasen, 1986).</td>
<td>Concurrent validity, $r = 0.71$ ($p&lt;0.001$) (Davis, Simpson, Foster, Arison, &amp; Post, 1986). See Andreasen and Grove (1986) for further discussion. (continued)</td>
</tr>
</tbody>
</table>
Table 6.3
Description and Psychometric Properties of Clinical Measures (continued)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Author(s)</th>
<th>Structure</th>
<th>Reliability</th>
<th>Validity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive and Negative Syndrome Scale (PANSS)</td>
<td>Kay et al., 1987</td>
<td>Rating scale for symptom severity. 30-item (7 constitute the Positive Scale, 7 the Negative Scale, and 16 the General Psychopathology Scale), 7-point rating instrument. Each item is accompanied by a complete definition as well as detailed anchoring criteria for all seven rating points, which represent increasing levels of psychopathology: 1=absent, 2=minimal, 3=mild, 4=moderate, 5=moderate/severe, 6=severe, and 7=extreme. Scoring is performed on a separate rating form in consultation with the Rating Manual. The highest applicable rating point is always assigned, even if the patient meets criteria for lower ratings as well. The PANSS is scored by summation of ratings across items; potential ranges are 7-49 for the Positive and Negative Scales, and 16-112 for the General Psychopathology Scale. The Composite Scale is arrived at by subtracting the negative from positive score, thus yielding a bipolar index that ranges from -42 to +42.</td>
<td>Internal consistency, Cronbach's $\alpha = 0.73$ (Positive Scale), 0.83 (Negative Scale), 0.79 (General Psychopathology Scale). Test-retest, $r = 0.80$ ($p&lt;0.001$) (Positive Scale), 0.68 ($p&lt;0.01$) (Negative Scale), 0.66 ($p&lt;0.01$) (Composite Scale), and 0.60 ($p&lt;0.02$) (General Psychopathology Scale) (Kay et al., 1987). Inter-rater reliability, $r = 0.83$-0.87 ($p &lt;0.0001$) (Kay et al., 1988).</td>
<td>Criterion-related validity, $r = 0.86$ (Positive Scale), 0.90 (Negative Scale), 0.84 (General Psychopathology Scale) (all $p&lt;0.001$) (Kay et al., 1987). Concurrent validity, $r = 0.77$ (Positive Scale), $r = 0.77$ (Negative Scale), $r = 0.52$ (General Psychopathology Scale) (all $p&lt;0.0001$) (Kay et al., 1988). Construct, pharmacological, and typological validity, see Kay et al. (1987) for discussion.</td>
</tr>
</tbody>
</table>
Shapiro-Wilk statistics (+/- 2 x the standard error convention; Groeneveld & Meeden, 1984). Continuous variables conforming to the normality assumption were analysed using one way analysis of variance (ANOVA) and Student-Newman-Keuls (SNK) post hoc tests. Where the assumption of homogeneity of variance was violated for these variables, the more conservative Welsh $F$ ratio is reported with Dunnett’s C post hoc tests to control for Type I error. The majority of continuous variables were not normally distributed, and were analysed using nonparametric tests given that statistical transformation s did not achieve normality. Mann-Whitney $U$ tests were performed where two groups were compared (i.e., injury demographics, clinical ratings of psychosis). Kruskal-Wallis $H$ tests were used in the comparisons of all four groups, with Mann-Whitney $U$ post hoc tests and the Holms sequential Bonferroni method performed to control for Type I error across all pairwise comparisons (Green & Salkind, 2005).

### 6.7 General Demographics

The descriptive and inferential statistics for demographic variables are contained in Table 6.4. The healthy control group were significantly younger than the schizophrenia group, although age was matched for all other group comparisons. The majority of participants from all groups were male (≥ 90 %, no significant group differences). Compared to the healthy control group, the PFTBI group had a significantly reduced number of total years of education, with no other group differences in education recorded. Cohorts were also statistically matched when these data were assessed according to the level of educational attainment (e.g., primary school versus tertiary degree); $\chi^2(24, N=66)= 34.60, p = .08$, Cramers’ $V = .42$ (Appendix L, Figure L1).

One hundred per cent of participants from the healthy control, schizophrenia, and PFTBI groups were residing in an urban location at the time of participation, whereas this was true for only seventy per cent of the TBIWP group. Differences in living location,

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37 Age at the time of participation was an exception to this rule. Age was normally distributed for all cohorts except the healthy control group, and distribution was not improved by data transformation. As such, ANOVA was deemed the most appropriate statistical test using the more conservative Welsh $F$ ratio, with Dunnett’s C post hoc tests to control for Type I error.

38 Reduced statistical power due to smaller group sizes for the PFTBI group (age participation) and the TBIWP and PFTBI groups (living location) meant that these comparisons did not reach statistical significance despite comparable mean scores with group comparisons that did, see Table 6.4.
### Table 6.4
**Group Comparisons on Demographic Variables**

<table>
<thead>
<tr>
<th>Variable</th>
<th>HC (n = 23)</th>
<th>TBIWP (n = 10)</th>
<th>SCZ (n = 23)</th>
<th>PFTBI (n = 10)</th>
<th>Statistic(^a)</th>
<th>p</th>
<th>Effect Size(^b)</th>
<th>Post hoc(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at Participation</td>
<td>32.78 (11.55)</td>
<td>35.90 (11.94)</td>
<td>43.61 (10.58)</td>
<td>43.10 (11.15)</td>
<td>(F(3, 24.87) = 4.13)</td>
<td>.02</td>
<td>.17</td>
<td>HC&lt;SCZ</td>
</tr>
<tr>
<td>Sex (% male)</td>
<td>95.65</td>
<td>90</td>
<td>91.30</td>
<td>90</td>
<td>(\chi^2(3, N=66) = .55)</td>
<td>.91</td>
<td>.09</td>
<td>NS</td>
</tr>
<tr>
<td>Education (years)</td>
<td>17.13 (2.64)</td>
<td>16.35 (2.19)</td>
<td>15.87 (3.58)</td>
<td>13.90 (2.81)</td>
<td>(F(3, 62) = 2.81)</td>
<td>.05</td>
<td>.12</td>
<td>PFTBI&lt;HC</td>
</tr>
<tr>
<td>Living Location (% urban)</td>
<td>100</td>
<td>70</td>
<td>100</td>
<td>100</td>
<td>(\chi^2(3, N=66) = 17.60)</td>
<td>.001</td>
<td>.52</td>
<td>HC&gt;TBIWP SCZ&gt;SCZ TBIWP&gt;HC</td>
</tr>
<tr>
<td>Currently Employed (%)</td>
<td>56.52</td>
<td>70</td>
<td>39.13</td>
<td>30</td>
<td>(\chi^2(9, N=66) = 29.41)</td>
<td>.001</td>
<td>.39</td>
<td>No Differences</td>
</tr>
<tr>
<td>Handedness (L/A/R)</td>
<td>2/3/18</td>
<td>0/4/6</td>
<td>0/1/22</td>
<td>2/1/7</td>
<td>(\chi^2(6, N=66) = 13.46)</td>
<td>.04</td>
<td>.32</td>
<td></td>
</tr>
<tr>
<td>LEEDS score</td>
<td>3.17 (3.26)</td>
<td>2.60 (3.47)</td>
<td>3.61 (4.20)</td>
<td>1.60 (2.99)</td>
<td>(\chi^2(3, N=66) = 3.61)</td>
<td>.31</td>
<td>.06</td>
<td>NS</td>
</tr>
<tr>
<td>Premorbid IQ (NART)</td>
<td>105.00 (7.04)</td>
<td>100.40 (9.07)</td>
<td>102.69 (6.48)</td>
<td>102.47 (4.74)</td>
<td>(F(3, 62) = 1.15)</td>
<td>.34</td>
<td>.05</td>
<td>NS</td>
</tr>
<tr>
<td>Current IQ (WASI)</td>
<td>98.18 (11.20)</td>
<td>87.00 (10.15)</td>
<td>84.78 (11.96)</td>
<td>72.20 (16.50)</td>
<td>(F(3, 61) = 11.15)</td>
<td>&lt;.001</td>
<td>.35</td>
<td>PFTBI&lt;SCZ=TBIWP&lt;HC</td>
</tr>
</tbody>
</table>

\(^{a}\) One way Analysis of Variance (ANOVA) (F), and chi-square (\(\chi^2\)).  
\(^{b}\) Partial \(\eta^2\) and Cramer’s V, respectively.  
\(^{c}\) Student-Newman-Keuls (SNK) (Education, Premorbid and Current IQ), and chi-square follow-up with Holms sequential bonferroni method to control for Type I error (Sex, Living Location, Currently Employed, Handedness).  
\(^*\) \(n = 22\) (HC WASI IQ only).  
\(^{†}\) Welsh’s F ratio, with Dunnetts C post hoc test to account for unequal error variance.  
\(^{††}\) Kruskal-Wallis H with effect size computed as chi-square statistic divided by \(N-1\).
however, were only significant between the TBIWP and healthy control, and TBIWP and schizophrenia groups.

Both the healthy control and TBIWP groups had a significantly greater percentage of current employment compared with the schizophrenia group, however, PFTBI cohort comparisons were no longer significant following Bonferroni correction. Significant differences were also demonstrated according to the type of employment, $\chi^2(15, N=66)=51.72, p < .001$, Cramers’ $V = .51$. While there was some variation between those in part time work, casual work, currently seeking work, or studying, the greatest differences were shown between those in full time work (i.e., healthy control and TBIWP) and those receiving a disability pension (i.e., schizophrenia and PFTBI) (Figure 6.1).

Differences in handedness (EHI) were no longer significant following post hoc analyses, $\chi^2(6, N=66)= 13.46, p = .04$, Cramers’ $V = .32$ (see Table 6.4). All groups had a majority of right handed participants. The TBIWP group contained a notable amount of participants who were ambidextrous, and twenty per cent of the PFTBI group were predominantly left handed ($n =2$), although this was also true for 8.70% of the healthy control group ($n =2$).

No differences in mean scores on the LEEDS dependence questionnaire were shown (Table 6.4), nor were the cohorts significantly different with regard to their LEEDS classification; $\chi^2(6, N=66)= 9.53, p = .15$, Cramers’ $V = .27$ (Appendix L, Figure L2). All four cohorts were also matched on premorbid (NART) IQ, and according to group means, all cohorts fell within the average range of premorbid intellectual function. However, for current IQ (WASI), only the healthy control group were considered within the average range, whereas the TBIWP and schizophrenia groups were classified as “low average” and the PFTBI group in the category below, as “borderline”. These differences were statistically different according to post hoc SNK analysis (see Table 6.4). The spread for current (WASI) IQ is detailed graphically in Figure 6.2. The plot illustrates a decline in current IQ following either traumatic brain injury or diagnosis of schizophrenia, which is exacerbated further in dually diagnosed (PFTBI) individuals. Chapter Seven discusses IQ further as part of the cognitive neuropsychological profile (Section 7.2.2.8: Intelligence Quotient).
Figure 6.1. Percentage participants within each employment category across the four participant groups.
Figure 6.2. Box-and-whisker-plot of WAIS IQ according to participant cohort. Sample minimums, lower quartile, median, upper quartile, and maximums are shown.

6.7.1 First degree relatives.

Table 6.5 presents the number of first and second degree relatives diagnosed with either a psychotic, psychiatric, and/or neurological disorder. No significant differences were shown across cohorts to the cumulative percentage of first degree relatives with a diagnosis, $\chi^2(9, N=39) = 14.66, p = .10$, Cramers’ $V = .35$. Where first degree relatives had received a diagnosis, the majority of these were for psychiatric conditions (e.g., depression, anxiety) (see Table 6.5). Similarly, no significant differences were shown across cohorts in the cumulative percentage of second degree relatives diagnosed with either a psychotic, psychiatric, and or neurological disorder, $\chi^2(6, N=25) = 6.54, p = .37$, Cramers’ $V = .36$. Significant cohort differences were found when the rates of diagnoses were collapsed across first and second degree relatives; $\chi^2 (9, N=68) = 20.18, p = .02$, Cramers’ $V = .31$. However, these were no longer significant following post hoc tests; psychotic, $p = .12$; psychiatric,
$p = .06$; and neurological, $p = .82$. Nonetheless, it is noted that a higher proportion of relatives of the schizophrenia and PFTBI patients had received diagnosis of a psychotic disorder compared to the healthy control and TBIWP relatives, and this finding is in accordance with the heritability literature (e.g., McGuffin et al., 1994; Must et al., 2011).

Table 6.5
First and Second Degree Relative Diagnoses

<table>
<thead>
<tr>
<th></th>
<th>Healthy Control</th>
<th>TBIWP</th>
<th>Schizophrenia</th>
<th>PFTBI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First Degree Relatives</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychotic</td>
<td>1</td>
<td>0</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>12</td>
<td>4</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>Neurological</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><strong>Second Degree Relatives</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychotic</td>
<td>2</td>
<td>0</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>3</td>
<td>1</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Neurological</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

*Note.* Cumulative total p/group is represented (i.e., cases with multiple relatives and diagnoses incorporated additively).

6.8 Traumatic Brain Injury Demographics

6.8.1 Individual TBIWP and PFTBI cases.

Injury demographics for the individual TBIWP and PFTBI participants are contained within Tables 6.6 and 6.7 respectively. Of the TBIWP cohort, six cases suffered their injury during their late teens to early twenties, two in their late twenties, one in his early forties, and one in his early fifties. The majority (i.e., seventy per cent) had had a motor vehicle accident (e.g., pedestrian or driver/passenger), one patient had a bicycle accident, and two had been physically assaulted. Lesion location was confined to the left hemisphere for two patients, the right hemisphere for five, and both hemispheres for three (see Table 6.6 and Figure 6.3). Lesion location according to lobe is detailed in Figure 6.3. The duration of loss of consciousness (LOC) was quite variable for the TBIWP group, spanning from twenty minutes to three months. The majority were in an induced coma (i.e., seventy per cent), and suffered post-traumatic amnesia (PTA) (i.e., eighty per cent), and this was again quite variable, spanning from thirty minutes to three and a half months. As such, four were considered to have sustained a mild TBI, two to have sustained a moderate TBI, and four to have sustained a severe TBI. Unrecovered memory loss was confined to the details of the trauma for fifty per cent of cases, with the remaining once again showing considerable variability spanning from no memory loss to six months. No obvious patterns are apparent.
from these variables, except to acknowledge that a frontal injury may attract a longer duration of LOC (see Table 6.6). The time since their injury at the time of participation was also variable; for three cases it had been approximately one year since injury, for three it was less than ten years, and for the remaining four it had been between eleven and thirty years. Finally, three of the cases had had more than one other mild injury prior to the one reported here.

The PFTBI group had all obtained their injury prior to the age of twenty five; with eighty per cent of these between the teenage years (i.e., twelve to nineteen years of age). Three had obtained their injury in a rural location. Again the cause of injury for the majority of cases (i.e., sixty per cent) was a motor vehicle accident, with falling from a height ($n=2$), assault ($n=2$), and an equestrian accident explaining the remaining cases. Sixty per cent had a lesion confined to the right hemisphere, and forty per cent had lesions in both hemispheres (see Table 6.7 and Figure 6.3, see Figure 6.4 for lesion location according to lobe). The duration of LOC was extremely variable (i.e., ranging from one minute to ten months), as was duration of PTA (i.e., ranging from none to seven months post injury). Three patients were classified as having sustained a mild injury, three as moderate, and four as severe. Interestingly, only one case was induced in a coma post injury. Unrecovered memory loss was confined to less than one hour in all but one case who lost memories pertaining to approximately one month following the injury. Again there are no obvious patterns to these variables except to acknowledge the same greater duration of LOC with a frontal injury (i.e., as in the TBIWP cohort), and perhaps increased PTA where injury is to the frontal lobe in this cohort as well. The shortest latency between injury and assessment for the current project was twelve years, with one case having sustained injury more than forty-four years prior to the date of testing. Three had had prior mild injuries.
<table>
<thead>
<tr>
<th>Code</th>
<th>Sex</th>
<th>Age TBI (years)</th>
<th>TBI Location</th>
<th>Aetiology</th>
<th>Hemisphere</th>
<th>Lobe</th>
<th>LOC(min)</th>
<th>Induced Coma</th>
<th>PTA(min)</th>
<th>Memory Loss</th>
<th>Injury Severity</th>
<th>Years Post Injury</th>
<th>TBI history</th>
</tr>
</thead>
<tbody>
<tr>
<td>T01</td>
<td>M</td>
<td>18</td>
<td>Urban</td>
<td>MVA (pedestrian)</td>
<td>Right</td>
<td>Temporal</td>
<td>10,080 (1 week)</td>
<td>1-2 weeks</td>
<td>Nil</td>
<td>5-10 min</td>
<td>Moderate</td>
<td>7</td>
<td>4 prior (mild)</td>
</tr>
<tr>
<td>T02</td>
<td>M</td>
<td>18</td>
<td>Rural</td>
<td>MVA</td>
<td>Left/Right</td>
<td>Occipital/Fronto-temporal</td>
<td>20,160 (2 weeks)</td>
<td>1-2 weeks</td>
<td>14,400 (10 days)</td>
<td>&gt;2 hours</td>
<td>Severe</td>
<td>20</td>
<td>Nil</td>
</tr>
<tr>
<td>T03</td>
<td>M</td>
<td>27</td>
<td>Urban</td>
<td>MVA</td>
<td>Left</td>
<td>Occipital</td>
<td>20</td>
<td>Nil</td>
<td>30</td>
<td>2 days</td>
<td>Mild</td>
<td>1</td>
<td>Nil</td>
</tr>
<tr>
<td>T04</td>
<td>M</td>
<td>19</td>
<td>Rural</td>
<td>MVA (pedestrian, flipped over car)</td>
<td>Right</td>
<td>Frontal/Occipital</td>
<td>17,280 (12 days)</td>
<td>1-2 weeks</td>
<td>50,400 (5 weeks)</td>
<td>Accident/Trauma only</td>
<td>Severe</td>
<td>5</td>
<td>Estimates ~10 prior (mild/sports)</td>
</tr>
<tr>
<td>T05</td>
<td>M</td>
<td>17</td>
<td>Urban</td>
<td>MVA (Motorbike hit by car)</td>
<td>Right</td>
<td>Frontal</td>
<td>120,960 (3 months)</td>
<td>3 months</td>
<td>Nil</td>
<td>Accident/Trauma only</td>
<td>Moderate</td>
<td>30</td>
<td>Nil</td>
</tr>
<tr>
<td>T06</td>
<td>M</td>
<td>51</td>
<td>Urban</td>
<td>Bicycle accident</td>
<td>Right</td>
<td>Temporal-parietal</td>
<td>120 (2 hrs)</td>
<td>Nil</td>
<td>180 (3 hours)</td>
<td>Nil</td>
<td>Mild</td>
<td>3</td>
<td>Nil</td>
</tr>
<tr>
<td>T07</td>
<td>M</td>
<td>17</td>
<td>Rural</td>
<td>MVA (dirt bike)</td>
<td>Left</td>
<td>Temporal-parietal</td>
<td>20</td>
<td>Nil</td>
<td>180 (3 hours)</td>
<td>Accident/Trauma only</td>
<td>Mild</td>
<td>1</td>
<td>3 prior (mild)</td>
</tr>
<tr>
<td>T08</td>
<td>F</td>
<td>28</td>
<td>Urban</td>
<td>MVA</td>
<td>Left/Right</td>
<td>Frontal</td>
<td>65,520 (6.5 weeks)</td>
<td>6.5 weeks</td>
<td>141,120 (3.5 months)</td>
<td>Accident/Trauma only</td>
<td>Severe</td>
<td>13</td>
<td>Nil</td>
</tr>
<tr>
<td>T09</td>
<td>M</td>
<td>20</td>
<td>Urban</td>
<td>Assault</td>
<td>Right</td>
<td>Temporal</td>
<td>30,240 (3 weeks)</td>
<td>2-4 weeks</td>
<td>20,160 (2 weeks)</td>
<td>6 months</td>
<td>Severe</td>
<td>11</td>
<td>Nil</td>
</tr>
<tr>
<td>T10</td>
<td>M</td>
<td>41</td>
<td>Urban</td>
<td>Assault</td>
<td>Left/Right</td>
<td>Occipital-DAI</td>
<td>240 (2-4 hrs)</td>
<td>&lt; 1 week</td>
<td>540 (9 hrs)</td>
<td>Accident/Trauma only</td>
<td>Mild</td>
<td>9</td>
<td>Nil</td>
</tr>
</tbody>
</table>

*Note.* PTA refers to the loss of established memories that are eventually recovered whereas memory loss refers to memory that was never recovered post injury. Glasgow Coma Scale Score obtained for three cases, T02, T04, and T07 = 15, 3, and 12 respectively.
### Table 6.7

**Traumatic Brain Injury Demographics for Psychosis Following Traumatic Brain Injury Patients (PFTBI)**

<table>
<thead>
<tr>
<th>Code</th>
<th>Sex</th>
<th>Age (years)</th>
<th>TBI Location</th>
<th>Aetiology</th>
<th>Hemisphere</th>
<th>Lobe</th>
<th>LOC(min)</th>
<th>Induced Coma</th>
<th>PTA(min)</th>
<th>Memory Loss</th>
<th>Injury Severity</th>
<th>Years Post Injury</th>
<th>TBI history</th>
</tr>
</thead>
<tbody>
<tr>
<td>P01</td>
<td>M</td>
<td>19</td>
<td>Urban</td>
<td>MVA</td>
<td>Right</td>
<td>Temporal</td>
<td>1,440 (1 day)</td>
<td>Nil</td>
<td>10,080 (1 week)</td>
<td>30min-1hr</td>
<td>Moderate</td>
<td>16</td>
<td>Nil</td>
</tr>
<tr>
<td>P02</td>
<td>M</td>
<td>18</td>
<td>Urban</td>
<td>Fall from height</td>
<td>Right</td>
<td>Temporal</td>
<td>30</td>
<td>Nil</td>
<td>300 (5 hours)</td>
<td>Nil</td>
<td>Mild</td>
<td>23</td>
<td>Nil</td>
</tr>
<tr>
<td>P03</td>
<td>M</td>
<td>24</td>
<td>Urban</td>
<td>MVA</td>
<td>Right</td>
<td>Fronto-temporal</td>
<td>7,200 (5 days)</td>
<td>Nil</td>
<td>35,280 (3 weeks)</td>
<td>1 month</td>
<td>Severe</td>
<td>20</td>
<td>Nil</td>
</tr>
<tr>
<td>P04</td>
<td>M</td>
<td>15</td>
<td>Rural</td>
<td>MVA (pedestrian)</td>
<td>Right</td>
<td>Frontal</td>
<td>10,080 (1 week)</td>
<td>Nil</td>
<td>120,960 (3 months)</td>
<td>10-30 min</td>
<td>Severe</td>
<td>12</td>
<td>3 prior (mild)</td>
</tr>
<tr>
<td>P05</td>
<td>M</td>
<td>19</td>
<td>Urban</td>
<td>MVA</td>
<td>Left/Right</td>
<td>Frontal</td>
<td>403,200 (10 months)</td>
<td>Nil</td>
<td>282,240 (7 months)</td>
<td>Accident/ Trauma only</td>
<td>Severe</td>
<td>44</td>
<td>Nil</td>
</tr>
<tr>
<td>P06</td>
<td>M</td>
<td>17</td>
<td>Urban</td>
<td>Assault/Fall from height</td>
<td>Right</td>
<td>Occipital</td>
<td>1</td>
<td>Nil</td>
<td>Nil</td>
<td>Nil</td>
<td>Mild</td>
<td>14</td>
<td>Estimates ~10 prior (mild/assault)</td>
</tr>
<tr>
<td>P07</td>
<td>M</td>
<td>17</td>
<td>Urban</td>
<td>MVA (“hit and run” on bicycle)</td>
<td>Left/Right</td>
<td>Occipital</td>
<td>1,080 (18 hrs)</td>
<td>Nil</td>
<td>1,800 (30 hrs)</td>
<td>2-3 hours</td>
<td>Moderate</td>
<td>17</td>
<td>Nil</td>
</tr>
<tr>
<td>P08</td>
<td>F</td>
<td>22</td>
<td>Rural</td>
<td>MVA Motorbike</td>
<td>Left/Right</td>
<td>Frontoparietal</td>
<td>2,880 (48 hrs)</td>
<td>&lt; 1 week</td>
<td>10,080 (1 week)</td>
<td>10-30 min</td>
<td>Mode rate</td>
<td>34</td>
<td>Nil</td>
</tr>
<tr>
<td>P09</td>
<td>M</td>
<td>18</td>
<td>Urban</td>
<td>Assault</td>
<td>Left/Right</td>
<td>Occipital</td>
<td>240 (4 hrs)</td>
<td>Nil</td>
<td>Nil</td>
<td>Accident/ Trauma only</td>
<td>Mild</td>
<td>34</td>
<td>1 prior (mild)</td>
</tr>
<tr>
<td>P10</td>
<td>M</td>
<td>12</td>
<td>Rural</td>
<td>Equestrian accident</td>
<td>Right</td>
<td>Temporal-parietal</td>
<td>2,880 (48 hrs)</td>
<td>Nil</td>
<td>30,240 (3 weeks)</td>
<td>Accident/ Trauma only</td>
<td>Severe</td>
<td>34</td>
<td>Nil</td>
</tr>
</tbody>
</table>

*Note. PTA refers to the loss of established memories that are eventually recovered whereas memory loss refers to memory that was never recovered post injury. All cases sustained a closed head injury. Glasgow Coma Scale Score obtained for P03 only = 13.*
6.8.2 Group-wise comparisons.

Table 6.8 presents inferential statistics for traumatic brain injury-related variables. Statistical comparisons indicated that the TBI cohorts were well matched on all injury-related variables except for; i) the time between their injury and participation in this research, and ii) the proportion of those who had been in an induced coma. On average, the PFTBI cohort had sustained their injury almost fifteen years earlier than the TBIWP cohort. While this difference is exacerbated by participant #P05 who sustained his injury in 1967, the groups remain significantly different on this variable with #P05 removed from analysis; \(t(17) = -3.04, p = .01\) (i.e., the PFTBI cohort still sustaining their injury approximately twelve years earlier, \(M = 22.67, SD = 9.07\)). This is accounted for by three PFTBI cases with a latency of thirty-four years between injury and assessment. The difference primarily reflects a recruitment issue. TBIWP cases available and willing to participate in research tended to have suffered a recent injury, whereas those injured some time ago were more likely to have recovered well and were thus less motivated to volunteer for research participation. Ideally, a longer recruitment period would allow for the focused recruitment of TBIWP cases with earlier injury dates.

On the other hand, the significant group difference in the incidence of induced coma is unexpected and noteworthy. Even in this small sample, there is a substantial increase in the amount of those induced in a coma post injury from the non-psychotic group (TBIWP; 70%), versus cases who went on to develop psychosis (PFTBI; 10%), and this may offer preliminary evidence for the protective effect of coma immediately post-injury.

Figures 6.3 to 6.7 depict the classification of both TBI groups across a number of injury parameters not depicted in Table 6.8. Chi-square analysis revealed that the TBIWP and PFTBI groups were not significantly different according to injury severity, \(\chi^2(2, N=20)= .34, p = .84\), Cramers’ V = .13 (Figure 6.3); hemispheric lesion location, \(\chi^2(2, N=20)= 2.23, p = .33\), Cramers’ V = .33 (Figure 6.4); lobe of lesion location, \(\chi^2(8, N=20)= 6.33, p = .61\), Cramers’ V = .56 (Figure 6.5); length of induced coma, \(\chi^2(5, N=20)= 9.00, p = .11\), Cramers’ V = .67 (Figure 6.6); or duration of memory loss, \(\chi^2(8, N=20)= 7.83, p = .45\), Cramers’ V = .63 (Figure 6.7).
Table 6.8
*TBIWP and PFTBI Group Comparisons on Brain Injury Variables*

<table>
<thead>
<tr>
<th>Variable</th>
<th>TBIWP (n = 10)</th>
<th>PFTBI (n = 10)</th>
<th>Statistic $^a$</th>
<th>$p$</th>
<th>Effect Size $^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (% male)</td>
<td>90</td>
<td>90</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Age Participation</td>
<td>35.90 (11.94)</td>
<td>43.10 (11.15)</td>
<td>$t$ (18) = -1.39</td>
<td>.18</td>
<td>-.66</td>
</tr>
<tr>
<td>Age Injury</td>
<td>25.60 (11.68)</td>
<td>18.14 (3.43)</td>
<td>$U = 29.00, Z = -1.60$</td>
<td>.11</td>
<td>-.36</td>
</tr>
<tr>
<td>Injury location (% urban)</td>
<td>70</td>
<td>70</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Time since injury (yrs)</td>
<td>9.80 (9.35)</td>
<td>24.80 (10.89)</td>
<td>$t$ (18) = -3.30</td>
<td>.004</td>
<td>-1.56</td>
</tr>
<tr>
<td>LOC (%)</td>
<td>100</td>
<td>100</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>LOC (min)</td>
<td>26,464.00 (38,932.88)</td>
<td>42,903.10 (126,638.95)</td>
<td>$U = 40.00, Z = - .76$</td>
<td>.45</td>
<td>-.17</td>
</tr>
<tr>
<td>PTA (%)</td>
<td>70</td>
<td>90</td>
<td>$\chi^2(1, N=20) = 1.25$</td>
<td>.26</td>
<td>.25</td>
</tr>
<tr>
<td>PTA (min)</td>
<td>22,701.00 (44,616.64)</td>
<td>49,098.00 (89,783.87)</td>
<td>$U = 40.00, Z = - .76$</td>
<td>.45</td>
<td>-.17</td>
</tr>
<tr>
<td>Coma Induced (%)$^c$</td>
<td>70</td>
<td>10</td>
<td>$\chi^2(1, N=20) = 7.50$</td>
<td>.006</td>
<td>.61</td>
</tr>
<tr>
<td>Memory Loss (%)$^c$</td>
<td>90</td>
<td>80</td>
<td>$\chi^2(1, N=20) = .39$</td>
<td>.53</td>
<td>.14</td>
</tr>
</tbody>
</table>

$^a$ Independent Samples $t$-test ($t$), chi-square ($\chi^2$), and Independent-Samples Mann-Whitney U Test ($U$).

$^b$ Cohen’s $d$, Cramer’s $V$, and the Z statistic divided by the square root of $N$, respectively.

$^c$ Categorical dispersion for these variables shown below.
Figure 6.3. Injury severity classifications for TBIWP and PFTBI cohorts.

Figure 6.4. Hemispheric lesion location for TBIWP and PFTBI cohorts.
Figure 6.5. Lesion location according to lobe for TBIWP and PFTBI cohorts.
Figure 6.6. Duration of induced coma for TBIWP and PFTBI cohorts.

Figure 6.7. Duration of memory loss for TBIWP and PFTBI cohorts.
6.9 Clinical Demographics

Descriptive and inferential statistics for all cohorts on the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983) are contained in Table 6.9. No significant differences were shown according to HADS anxiety or depression mean scores across cohorts. However, significant differences were shown according to HADS anxiety classifications, $\chi^2(6, N=66) = 13.24, p = .04$, Cramers’ $V = .32$ (Figure 6.8). These reflected that the majority of healthy control and TBIWP participants were classified within ‘normal’ ranges, with none of these participants identified as abnormal, whereas between twenty and thirty per cent of schizophrenia and PFTBI participants indicated abnormal levels of anxiety. The cohorts were not significantly different regarding their HADS depression classification; $\chi^2(6, N=66) = 5.75, p = .45$, Cramers’ $V = .21$ (Appendix L, Figure L3).

Descriptive and inferential statistics for schizophrenia and PFTBI group comparisons on general clinical information are contained in Table 6.10. Diagnoses confirmed by clinical assessment were: schizophrenia cohort; schizophrenia ($n = 14$), schizoaffective ($n = 9$); PFTBI cohort; schizophrenia ($n = 6$), schizoaffective ($n = 2$), schizophreniform ($n = 1$), and paranoid psychosis ($n = 1$). Data for the clinical measures (i.e., TLC, PANSS, and SAPS

![Figure 6.8](image.png) Percentage participants qualifying for HADS Anxiety Questionnaire categories across participant groups.
Table 6.9
*Group Comparisons on the Hospital Anxiety and Depression Scale (HADS)*

<table>
<thead>
<tr>
<th>Variable</th>
<th>HC (n = 23)</th>
<th>TBIWP (n = 10)</th>
<th>SCZ (n = 23)</th>
<th>PFTBI (n = 10)</th>
<th>Statistica</th>
<th>p</th>
<th>Effect Sizeb</th>
<th>Post hocc</th>
</tr>
</thead>
<tbody>
<tr>
<td>HADS Anxiety</td>
<td>5.57 (2.66)</td>
<td>4.80 (2.86)</td>
<td>8.00 (3.69)</td>
<td>9.30 (5.72)</td>
<td>F(3, 23.81)=3.82</td>
<td>.02</td>
<td>.17</td>
<td>No Differences</td>
</tr>
<tr>
<td>HADS Anxiety</td>
<td>[4.05, 7.08]</td>
<td>[2.50, 7.10]</td>
<td>[6.48, 9.52]</td>
<td>[6.99, 11.60]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HADS Depression</td>
<td>2.87 (2.63)</td>
<td>2.90 (3.31)</td>
<td>5.13 (3.75)</td>
<td>5.00 (2.26)</td>
<td>χ²(3, N=66)=9.39</td>
<td>.03</td>
<td>.14</td>
<td>No Differences</td>
</tr>
<tr>
<td></td>
<td>[Mdn=3.00, Rg=11]</td>
<td>[Mdn=2.50, Rg=11]</td>
<td>[Mdn=4.00, Rg=14]</td>
<td>[Mdn=5.00, Rg=8]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a One way Analysis of Variance (ANOVA) (F), and Kruskal-Wallis H (χ²).
b Partial η² and effect size computed as chi-square statistic divided by N-1, respectively.
c Student-Newman-Keuls (SNK) and Mann-Whitney U tests with Holms sequential Bonferroni method to control for Type I error, respectively.
scores) are presented in Tables 6.11 to 6.13. Given that the detailed symptom profile of PFTBI is novel, all PANSS items (individual, subscale, and totals) were reported and analysed. The SAPS individual and subscale items (current and lifetime) were administered to obtain a detailed account of hallucination and delusions along with a global rating of bizarre behaviour, and thus, are also reported and analysed in full with the exception of positive thought disorder. Positive formal thought disorder from the SAPS is not presented here given that the total and global scores from the TLC offer a more comprehensive assessment; the sum of the total scores provides a quantitative measure of the severity of TLC disorder, while the global rating provides interpretable cut-offs for TLC severity (Andreasen, 1986) (see Appendix M for cut-off scores).

No significant group differences were shown regarding general clinical demographics, including age of psychosis onset, illness duration, and the existence of co-morbid conditions (Table 6.10). This includes both the overall percentage of patients diagnosed with a co-morbid condition (Table 6.10), and the analysis of diagnoses according to type of co-morbid condition (illustrated in Figure 6.9); $\chi^2 (7, N=33) = 7.27, p = .40$, Cramer’s $V = .47$. No significant differences between schizophrenia and PFTBI clinical profiles were shown, with the exception of i) the PANSS negative total score, and ii) SAPS lifetime grandiose delusions. Schizophrenia patients scored significantly higher on both of these indices relative to the PFTBI group. In general these data indicate that, perhaps with the exception of negative symptoms and lifetime grandiose delusions, the clinical profile of PFTBI is not unique relative to schizophrenia/schizoaffective disorder. That is, a generic profile for psychosis appears to be experienced by both groups.

---

39 Note, however, that current grandiose delusions were comparable across groups from both the PANSS and SAPS measures.
Figure 6.9. Percentage participants with comorbid conditions from schizophrenia and PFTBI cohorts. Note. Cumulative total p/group is represented (i.e., cases with multiple diagnoses incorporated additively).
Table 6.10
Schizophrenia and PFTBI Group Comparisons on General Clinical Variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>SCZ (n = 23)</th>
<th>PFTBI (n = 10)</th>
<th>Statistic&lt;sup&gt;a&lt;/sup&gt;</th>
<th>p</th>
<th>Effect Size&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Psychosis (yrs)</td>
<td>24.35 (8.13)</td>
<td>23.08 (4.26)</td>
<td>U = 109.50, Z = -22</td>
<td>.83</td>
<td>-0.04</td>
</tr>
<tr>
<td>Illness Duration (yrs)</td>
<td>19.26 (10.53)</td>
<td>20.03 (8.47)</td>
<td>U = 103.00, Z = -47</td>
<td>.64</td>
<td>-0.08</td>
</tr>
<tr>
<td>Psychosis Onset Latency (months)</td>
<td></td>
<td>59.60 (52.32)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Comorbid Condition (%)*</td>
<td>34.8</td>
<td>30</td>
<td>χ²(1, N=33)=.07</td>
<td>.79</td>
<td>0.05</td>
</tr>
</tbody>
</table>

<sup>a</sup> Independent-Samples Mann-Whitney U Test (U), and Chi-square test.

<sup>b</sup> Z statistic divided by the square root of N (r), and Cramer’s V.

* Categorical dispersion of comorbid conditions by group presented in Figure 6.9.

Table 6.11
Schizophrenia and PFTBI Group Comparisons on Thought Disorder (Thought, Language and Communication Index [TLC], Andreasen, 1986)

<table>
<thead>
<tr>
<th>Variable</th>
<th>SCZ (n = 23)</th>
<th>PFTBI (n = 10)</th>
<th>Statistic&lt;sup&gt;a&lt;/sup&gt;</th>
<th>p</th>
<th>Effect Size&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>TLC Global</td>
<td>3.09 (8.56)</td>
<td>1.10 (0.88)</td>
<td>U = 100.50, Z = -.60</td>
<td>.58</td>
<td>-0.10</td>
</tr>
<tr>
<td>TLC Total</td>
<td>9.65 (9.10)</td>
<td>8.40 (7.17)</td>
<td>t (31) = .39</td>
<td>.70</td>
<td>0.15</td>
</tr>
</tbody>
</table>

<sup>a</sup> Independent-Samples Mann-Whitney U Test (U), and Independent Samples t-test (t).

<sup>b</sup> Z statistic divided by the square root of N (r), and Cohen’s d respectively.
Table 6.12
Schizophrenia and PFTBI Group Comparisons on Clinical Variables: Positive and Negative Syndrome Scale (PANSS)

<table>
<thead>
<tr>
<th>Variable</th>
<th>SCZ (n = 23)</th>
<th>PFTBI (n = 10)</th>
<th>Statistic</th>
<th>p</th>
<th>Effect Size</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>POSITIVE SCALE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P1 Delusions</td>
<td>3.70 (1.36)</td>
<td>3.80 (1.81)</td>
<td>U = 108.50, Z = -2.26</td>
<td>.79</td>
<td>-0.05</td>
</tr>
<tr>
<td>P2 Conceptual Disorganisation</td>
<td>2.87 (1.74)</td>
<td>2.40 (1.07)</td>
<td>U = 98.00, Z = -0.69</td>
<td>.49</td>
<td>-0.12</td>
</tr>
<tr>
<td>P3 Hallucinatory Behaviour</td>
<td>2.43 (1.88)</td>
<td>2.50 (1.90)</td>
<td>U = 122.00, Z = -0.73</td>
<td>.90</td>
<td>-0.02</td>
</tr>
<tr>
<td>P4 Excitement</td>
<td>1.48 (0.99)</td>
<td>1.40 (0.70)</td>
<td>U = 110.00, Z = -0.26</td>
<td>.79</td>
<td>-0.05</td>
</tr>
<tr>
<td>P5 Grandiosity</td>
<td>2.30 (1.49)</td>
<td>2.20 (1.14)</td>
<td>U = 114.00, Z = -0.04</td>
<td>.97</td>
<td>-0.01</td>
</tr>
<tr>
<td>P6 Suspiciousness/Persecution</td>
<td>3.13 (1.55)</td>
<td>3.40 (1.84)</td>
<td>t (31) = -.44</td>
<td>.67</td>
<td>-0.17</td>
</tr>
<tr>
<td>P7 Hostility</td>
<td>1.26 (0.62)</td>
<td>1.50 (0.85)</td>
<td>U = 99.50, Z = -0.85</td>
<td>.40</td>
<td>-0.15</td>
</tr>
<tr>
<td><strong>POSITIVE TOTAL</strong></td>
<td>17.09 (6.72)</td>
<td>16.70 (6.83)</td>
<td>t (31) = .15</td>
<td>.88</td>
<td>0.06</td>
</tr>
<tr>
<td><strong>NEGATIVE SCALE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N1 Blunted Affect</td>
<td>2.30 (1.29)</td>
<td>1.90 (1.10)</td>
<td>U = 95.50, Z = -1.80</td>
<td>.42</td>
<td>-0.14</td>
</tr>
<tr>
<td>N2 Emotional Withdrawal</td>
<td>2.17 (1.30)</td>
<td>1.40 (1.17)</td>
<td>U = 71.50, Z = -1.84</td>
<td>.07</td>
<td>-0.32</td>
</tr>
<tr>
<td>N3 Poor Rapport</td>
<td>1.39 (0.84)</td>
<td>1.00 (0.00)</td>
<td>U = 90.00, Z = -1.57</td>
<td>.12</td>
<td>-0.27</td>
</tr>
<tr>
<td>N4 Passive/Apathetic Withdrawal</td>
<td>2.74 (1.57)</td>
<td>2.10 (1.37)</td>
<td>U = 87.00, Z = -1.13</td>
<td>.26</td>
<td>-0.20</td>
</tr>
<tr>
<td>N5 Difficulty in Abstract Thinking</td>
<td>2.09 (1.38)</td>
<td>1.50 (0.97)</td>
<td>U = 89.00, Z = -1.14</td>
<td>.26</td>
<td>-0.20</td>
</tr>
<tr>
<td>N6 Lack of Spontaneity</td>
<td>1.70 (0.97)</td>
<td>1.30 (0.67)</td>
<td>U = 91.00, Z = -1.13</td>
<td>.26</td>
<td>-0.20</td>
</tr>
<tr>
<td>N7 Stereotyped Thinking</td>
<td>1.22 (0.67)</td>
<td>1.30 (0.48)</td>
<td>U = 97.00, Z = -1.05</td>
<td>.29</td>
<td>-0.18</td>
</tr>
<tr>
<td><strong>NEGATIVE TOTAL</strong></td>
<td>13.61 (5.35)</td>
<td>10.50 (2.37)</td>
<td>t (31) = 2.31</td>
<td>.03</td>
<td>0.88</td>
</tr>
</tbody>
</table>

(continued)
Table 6.12
Schizophrenia and PFTBI Group Comparisons on Clinical Variables: Positive and Negative Syndrome Scale (PANSS) (continued)

<table>
<thead>
<tr>
<th>Variable</th>
<th>SCZ</th>
<th>PFTBI</th>
<th>Statistic&lt;sup&gt;a&lt;/sup&gt;</th>
<th>p</th>
<th>Effect Size&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median (n = 23)</td>
<td>Median (n = 10)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>GENERAL PATHOLOGY SCALE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>G1 Somatic Concern</td>
<td>2.00 (1.48) [Mdn = 1.00, Rg = 4]</td>
<td>1.60 (0.97) [Mdn = 1.00, Rg = 3]</td>
<td>U = 106.50, Z = -.38</td>
<td>.71</td>
<td>-0.07</td>
</tr>
<tr>
<td>G2 Anxiety</td>
<td>2.39 (1.23) [Mdn = 3.00, Rg = 4]</td>
<td>2.10 (1.52) [Mdn = 1.00, Rg = 4]</td>
<td>U = 97.00, Z = -.75</td>
<td>.46</td>
<td>-0.13</td>
</tr>
<tr>
<td>G3 Guilt Feelings</td>
<td>1.96 (1.02) [Mdn = 2.00, Rg = 3]</td>
<td>1.50 (1.08) [Mdn = 1.00, Rg = 3]</td>
<td>U = 80.50, Z = -1.49</td>
<td>.14</td>
<td>-0.26</td>
</tr>
<tr>
<td>G4 Tension</td>
<td>1.87 (1.32) [Mdn = 1.00, Rg = 4]</td>
<td>1.70 (1.34) [Mdn = 1.00, Rg = 4]</td>
<td>U = 108.00, Z = -.33</td>
<td>.74</td>
<td>-0.06</td>
</tr>
<tr>
<td>G5 Mannerisms &amp; Posturing</td>
<td>1.39 (0.72) [Mdn = 1.00, Rg = 2]</td>
<td>1.40 (0.97) [Mdn = 1.00, Rg = 3]</td>
<td>U = 109.50, Z = -.29</td>
<td>.77</td>
<td>-0.05</td>
</tr>
<tr>
<td>G6 Depression</td>
<td>1.57 (0.99) [Mdn = 1.00, Rg = 3]</td>
<td>1.80 (1.14) [Mdn = 1.00, Rg = 3]</td>
<td>U = 102.50, Z = -.59</td>
<td>.56</td>
<td>-0.10</td>
</tr>
<tr>
<td>G7 Motor Retardation</td>
<td>1.65 (1.11) [Mdn = 1.00, Rg = 3]</td>
<td>1.60 (0.97) [Mdn = 1.00, Rg = 4]</td>
<td>U = 113.00, Z = -.10</td>
<td>.92</td>
<td>-0.02</td>
</tr>
<tr>
<td>G8 Uncooperativeness</td>
<td>1.09 (0.42) [Mdn = 1.00, Rg = 2]</td>
<td>1.00 (0.00) [Mdn = 1.00, Rg = 0]</td>
<td>U = 110.00, Z = -.66</td>
<td>.51</td>
<td>-0.11</td>
</tr>
<tr>
<td>G9 Unusual Thought Content</td>
<td>2.91 (1.73) [Mdn = 3.00, Rg = 6]</td>
<td>2.90 (1.79) [Mdn = 3.00, Rg = 6]</td>
<td>U = 113.50, Z = -.06</td>
<td>.95</td>
<td>-0.01</td>
</tr>
<tr>
<td>G10 Disorientation</td>
<td>1.17 (0.58) [Mdn = 1.00, Rg = 2]</td>
<td>1.50 (1.27) [Mdn = 1.00, Rg = 4]</td>
<td>U = 102.00, Z = -.90</td>
<td>.37</td>
<td>-0.16</td>
</tr>
<tr>
<td>G11 Poor Attention</td>
<td>1.57 (0.90) [Mdn = 1.00, Rg = 3]</td>
<td>1.60 (0.84) [Mdn = 1.00, Rg = 2]</td>
<td>U = 110.00, Z = -.23</td>
<td>.82</td>
<td>-0.04</td>
</tr>
<tr>
<td>G12 Lack of Judgement &amp; Insight</td>
<td>2.22 (1.41) [Mdn = 2.00, Rg = 5]</td>
<td>2.40 (1.78) [Mdn = 1.50, Rg = 5]</td>
<td>U = 113.50, Z = -.06</td>
<td>.95</td>
<td>-0.01</td>
</tr>
<tr>
<td>G13 Disturbance of Volition</td>
<td>1.43 (0.95) [Mdn = 1.00, Rg = 3]</td>
<td>1.20 (0.42) [Mdn = 1.00, Rg = 1]</td>
<td>U = 110.00, Z = -.27</td>
<td>.78</td>
<td>-0.05</td>
</tr>
<tr>
<td>G14 Poor Impulse Control</td>
<td>1.30 (0.70) [Mdn = 1.00, Rg = 2]</td>
<td>1.60 (1.07) [Mdn = 1.00, Rg = 3]</td>
<td>U = 99.50, Z = -.85</td>
<td>.40</td>
<td>-0.15</td>
</tr>
<tr>
<td>G15 Preoccupation</td>
<td>1.17 (0.65) [Mdn = 1.00, Rg = 3]</td>
<td>1.20 (0.63) [Mdn = 1.00, Rg = 2]</td>
<td>U = 113.50, Z = -.12</td>
<td>.91</td>
<td>-0.02</td>
</tr>
<tr>
<td>G16 Active Social Avoidance</td>
<td>2.35 (1.30) [Mdn = 2.00, Rg = 4]</td>
<td>2.00 (1.15) [Mdn = 1.50, Rg = 3]</td>
<td>U = 98.00, Z = -.70</td>
<td>.48</td>
<td>-0.12</td>
</tr>
<tr>
<td><strong>GENERAL TOTAL</strong></td>
<td>28.04 (6.70)</td>
<td>27.20 (6.89)</td>
<td>t (31) = .33</td>
<td>.75</td>
<td>0.13</td>
</tr>
<tr>
<td><strong>COMPOSITE SCORE</strong></td>
<td>-3.48 (7.65)</td>
<td>-6.20 (6.49)</td>
<td>t (31) = .98</td>
<td>.34</td>
<td>0.37</td>
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<tr>
<td><strong>PANSS TOTAL</strong></td>
<td>58.74 (14.84)</td>
<td>54.40 (13.87)</td>
<td>t (31) = .79</td>
<td>.44</td>
<td>0.30</td>
</tr>
</tbody>
</table>

<sup>a</sup> Independent-Samples Mann-Whitney U Test (U), and Independent Samples t-test (t)
<sup>b</sup> Z statistic divided by the square root of N (r), and Cohen’s d respectively
### Table 6.13

**Schizophrenia and PFTBI Group Comparisons on Clinical Variables: Scale for the Assessment of Positive Symptoms (SAPS)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (Standard Deviation) [Median and range where appropriate]</th>
<th>PFTBI (n = 10)</th>
<th>Statistic</th>
<th>p</th>
<th>Effect Size</th>
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<tbody>
<tr>
<td><strong>HALLUCINATIONS</strong></td>
<td></td>
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<tr>
<td>Auditory Hallucinations</td>
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</tr>
<tr>
<td>Current</td>
<td>1.23 (1.77) [Mdn = 0.00, Rg = 5]</td>
<td>1.50 (2.01) [Mdn = 0.00, Rg = 5]</td>
<td>U = 105.50, Z = -.21</td>
<td>.84</td>
<td>-0.04</td>
</tr>
<tr>
<td>Lifetime</td>
<td>2.18 (2.06)</td>
<td>2.60 (1.78)</td>
<td>t (30) = -.55</td>
<td>.58</td>
<td>-0.18</td>
</tr>
<tr>
<td>Voices Commenting</td>
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<td></td>
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</tr>
<tr>
<td>Current</td>
<td>1.14 (1.81) [Mdn = 0.00, Rg = 5]</td>
<td>1.40 (1.96) [Mdn = 0.00, Rg = 5]</td>
<td>U = 101.50, Z = -.41</td>
<td>.68</td>
<td>-0.07</td>
</tr>
<tr>
<td>Lifetime</td>
<td>1.90 (2.27) [Mdn = 0.00, Rg = 5]</td>
<td>2.40 (1.84) [Mdn = 3.00, Rg = 5]</td>
<td>U = 97.50, Z = -.54</td>
<td>.59</td>
<td>-0.10</td>
</tr>
<tr>
<td>Voices Conversing</td>
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</tr>
<tr>
<td>Current</td>
<td>0.91 (1.77) [Mdn = 0.00, Rg = 5]</td>
<td>0.80 (1.75) [Mdn = 0.00, Rg = 5]</td>
<td>U = 107.00, Z = -.17</td>
<td>.87</td>
<td>-0.03</td>
</tr>
<tr>
<td>Lifetime</td>
<td>1.32 (2.03) [Mdn = 0.00, Rg = 5]</td>
<td>0.90 (1.91) [Mdn = 0.00, Rg = 5]</td>
<td>U = 98.50, Z = -.59</td>
<td>.56</td>
<td>-0.10</td>
</tr>
<tr>
<td>Somatic/Tactile Hallucinations</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Current</td>
<td>0.59 (1.18) [Mdn = 0.00, Rg = 4]</td>
<td>0.40 (0.84) [Mdn = 0.00, Rg = 2]</td>
<td>U = 105.00, Z = -.28</td>
<td>.78</td>
<td>-0.05</td>
</tr>
<tr>
<td>Lifetime</td>
<td>0.82 (1.44) [Mdn = 0.00, Rg = 4]</td>
<td>1.20 (1.48) [Mdn = 0.50, Rg = 4]</td>
<td>U = 90.00, Z = -.96</td>
<td>.34</td>
<td>-0.17</td>
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<tr>
<td>Olfactory Hallucinations</td>
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<tr>
<td>Current</td>
<td>0.45 (1.10) [Mdn = 0.00, Rg = 4]</td>
<td>0.40 (0.84) [Mdn = 0.00, Rg = 2]</td>
<td>U = 109.00, Z = -.06</td>
<td>.95</td>
<td>-0.01</td>
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<tr>
<td>Lifetime</td>
<td>0.95 (1.50) [Mdn = 0.00, Rg = 4]</td>
<td>1.10 (1.29) [Mdn = 0.50, Rg = 3]</td>
<td>U = 98.50, Z = -.54</td>
<td>.59</td>
<td>-0.10</td>
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<tr>
<td>Visual Hallucinations</td>
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<tr>
<td>Current</td>
<td>0.55 (1.22) [Mdn = 0.00, Rg = 4]</td>
<td>0.40 (1.26) [Mdn = 0.00, Rg = 4]</td>
<td>U = 102.50, Z = -.48</td>
<td>.63</td>
<td>-0.08</td>
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<tr>
<td>Lifetime</td>
<td>1.36 (1.59) [Mdn = 0.50, Rg = 4]</td>
<td>1.80 (1.48) [Mdn = 2.00, Rg = 4]</td>
<td>U = 92.00, Z = -.77</td>
<td>.44</td>
<td>-0.14</td>
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<tr>
<td>Global Rating Hallucinations</td>
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<tr>
<td>Current</td>
<td>1.39 (1.80) [Mdn = 0.00, Rg = 5]</td>
<td>1.60 (1.96) [Mdn = 0.50, Rg = 5]</td>
<td>U = 106.50, Z = -.37</td>
<td>.71</td>
<td>-0.07</td>
</tr>
<tr>
<td>Lifetime</td>
<td>2.50 (1.97)</td>
<td>3.10 (1.45)</td>
<td>t (30) = -.86</td>
<td>.40</td>
<td>-0.28</td>
</tr>
</tbody>
</table>

(continued)
<table>
<thead>
<tr>
<th>Variable</th>
<th>SCZ (n = 22)*</th>
<th>PFTBI (n = 10)</th>
<th>Statistic(^a)</th>
<th>p</th>
<th>Effect Size(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Delusions</strong></td>
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<tr>
<td>Persecutory Delusions</td>
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<tr>
<td>Current</td>
<td>2.18 (1.50)</td>
<td>2.30 (1.77)</td>
<td>(t (30) = -0.20)</td>
<td>.85</td>
<td>-0.06</td>
</tr>
<tr>
<td>Lifetime</td>
<td>4.18 (1.53)   [(Mdn = 5.00, Rg = 5)]</td>
<td>4.00 (1.56)   [(Mdn = 4.50, Rg = 5)]</td>
<td>(U = 95.50, Z = -0.67)</td>
<td>.50</td>
<td>-0.12</td>
</tr>
<tr>
<td>Delusions of Jealousy</td>
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</tr>
<tr>
<td>Current</td>
<td>0.14 (0.47)   [(Mdn = 0.00, Rg = 2)]</td>
<td>0.10 (0.32)   [(Mdn = 0.00, Rg = 1)]</td>
<td>(U = 109.50, Z = -0.04)</td>
<td>.97</td>
<td>-0.01</td>
</tr>
<tr>
<td>Lifetime</td>
<td>0.36 (0.95)   [(Mdn = 0.00, Rg = 3)]</td>
<td>0.30 (0.95)   [(Mdn = 0.00, Rg = 3)]</td>
<td>(U = 106.50, Z = -0.25)</td>
<td>.80</td>
<td>-0.04</td>
</tr>
<tr>
<td>Delusions of Guilt or Sin</td>
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<tr>
<td>Current</td>
<td>0.73 (1.08)   [(Mdn = 0.00, Rg = 3)]</td>
<td>0.60 (1.07)   [(Mdn = 0.00, Rg = 3)]</td>
<td>(U = 103.00, Z = -0.34)</td>
<td>.74</td>
<td>-0.06</td>
</tr>
<tr>
<td>Lifetime</td>
<td>1.45 (1.74)   [(Mdn = 0.00, Rg = 5)]</td>
<td>0.80 (1.32)   [(Mdn = 0.00, Rg = 3)]</td>
<td>(U = 88.00, Z = -1.01)</td>
<td>.31</td>
<td>-0.18</td>
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<tr>
<td>Grandiose Delusions</td>
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<tr>
<td>Current</td>
<td>1.32 (1.39)   [(Mdn = 1.00, Rg = 5)]</td>
<td>1.10 (1.37)   [(Mdn = 0.50, Rg = 4)]</td>
<td>(U = 99.00, Z = -0.47)</td>
<td>.64</td>
<td>-0.08</td>
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<tr>
<td>Lifetime</td>
<td>3.41 (1.87)   [(Mdn = 4.00, Rg = 5)]</td>
<td>1.70 (1.95)   [(Mdn = 1.00, Rg = 5)]</td>
<td>(U = 57.00, Z = -2.23)</td>
<td>.03</td>
<td>-0.39</td>
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<td>Religious Delusions</td>
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<tr>
<td>Current</td>
<td>0.55 (0.96)   [(Mdn = 0.00, Rg = 3)]</td>
<td>0.40 (0.97)   [(Mdn = 0.00, Rg = 3)]</td>
<td>(U = 102.00, Z = -0.43)</td>
<td>.67</td>
<td>-0.08</td>
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<tr>
<td>Lifetime</td>
<td>1.36 (2.06)   [(Mdn = 0.00, Rg = 5)]</td>
<td>0.60 (1.58)   [(Mdn = 0.00, Rg = 5)]</td>
<td>(U = 90.50, Z = -0.97)</td>
<td>.33</td>
<td>-0.17</td>
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<tr>
<td>Somatic Delusions</td>
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<tr>
<td>Current</td>
<td>0.91 (1.44)   [(Mdn = 0.00, Rg = 4)]</td>
<td>0.50 (1.08)   [(Mdn = 0.00, Rg = 3)]</td>
<td>(U = 95.50, Z = -0.75)</td>
<td>.46</td>
<td>-0.13</td>
</tr>
<tr>
<td>Lifetime</td>
<td>1.64 (2.11)   [(Mdn = 0.00, Rg = 5)]</td>
<td>1.00 (1.89)   [(Mdn = 0.00, Rg = 5)]</td>
<td>(U = 96.00, Z = -0.66)</td>
<td>.51</td>
<td>-0.12</td>
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<tr>
<td>Delusions of References</td>
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</tr>
<tr>
<td>Current</td>
<td>1.91 (1.44)</td>
<td>1.70 (1.57)</td>
<td>(t (30) = 0.37)</td>
<td>.71</td>
<td>0.12</td>
</tr>
<tr>
<td>Lifetime</td>
<td>3.82 (1.68)   [(Mdn = 4.00, Rg = 5)]</td>
<td>3.20 (1.69)   [(Mdn = 3.50, Rg = 5)]</td>
<td>(U = 82.50, Z = -1.17)</td>
<td>.24</td>
<td>-0.21</td>
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<tr>
<td>Delusions of Being Controlled</td>
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<tr>
<td>Current</td>
<td>1.36 (1.65)   [(Mdn = 0.00, Rg = 5)]</td>
<td>0.70 (1.49)   [(Mdn = 0.00, Rg = 4)]</td>
<td>(U = 86.00, Z = -1.13)</td>
<td>.26</td>
<td>-0.20</td>
</tr>
<tr>
<td>Lifetime</td>
<td>2.45 (2.24)   [(Mdn = 3.00, Rg = 5)]</td>
<td>1.70 (1.83)   [(Mdn = 1.50, Rg = 5)]</td>
<td>(U = 90.00, Z = -0.85)</td>
<td>.40</td>
<td>-0.15</td>
</tr>
</tbody>
</table>
Table 6.13  
Schizophrenia and PFTBI Group Comparisons on Clinical Variables: Scale for the Assessment of Positive Symptoms (SAPS) (continued)

<table>
<thead>
<tr>
<th>Variable</th>
<th>SCZ (n = 22)*</th>
<th>PFTBI (n = 10)</th>
<th>Statistic&lt;sup&gt;a&lt;/sup&gt;</th>
<th>p</th>
<th>Effect Size&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
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<tbody>
<tr>
<td><strong>DELUSIONS CONT’D</strong></td>
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<tr>
<td>Delusions of Mind Reading</td>
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</tr>
<tr>
<td>Current</td>
<td>0.95 (1.53) [Mdn = 0.00, Rg = 5]</td>
<td>0.80 (1.48) [Mdn = 0.00, Rg = 4]</td>
<td>U = 107.50, Z = -1.12</td>
<td>.90</td>
<td>-0.20</td>
</tr>
<tr>
<td>Lifetime</td>
<td>2.14 (2.14) [Mdn = 2.50, Rg = 5]</td>
<td>1.30 (1.77) [Mdn = 0.00, Rg = 4]</td>
<td>U = 85.50, Z = -1.07</td>
<td>.28</td>
<td>-0.19</td>
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<tr>
<td>Thought Broadcasting</td>
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<tr>
<td>Current</td>
<td>0.86 (1.36) [Mdn = 0.00, Rg = 4]</td>
<td>0.30 (0.95) [Mdn = 0.00, Rg = 3]</td>
<td>U = 87.00, Z = -1.23</td>
<td>.22</td>
<td>-0.22</td>
</tr>
<tr>
<td>Lifetime</td>
<td>1.64 (2.13) [Mdn = 0.00, Rg = 5]</td>
<td>0.70 (1.49) [Mdn = 0.00, Rg = 4]</td>
<td>U = 84.00, Z = -1.25</td>
<td>.21</td>
<td>-0.22</td>
</tr>
<tr>
<td>Thought Insertion</td>
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<tr>
<td>Current</td>
<td>0.32 (0.84) [Mdn = 0.00, Rg = 3]</td>
<td>0.20 (0.63) [Mdn = 0.00, Rg = 2]</td>
<td>U = 105.50, Z = -1.32</td>
<td>.75</td>
<td>-0.06</td>
</tr>
<tr>
<td>Lifetime</td>
<td>0.77 (1.38) [Mdn = 0.00, Rg = 4]</td>
<td>0.20 (0.63) [Mdn = 0.00, Rg = 2]</td>
<td>U = 89.50, Z = -1.15</td>
<td>.25</td>
<td>-0.20</td>
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<tr>
<td>Thought Withdrawal</td>
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<tr>
<td>Current</td>
<td>0.18 (0.66) [Mdn = 0.00, Rg = 3]</td>
<td>0.20 (0.63) [Mdn = 0.00, Rg = 2]</td>
<td>U = 109.00, Z = -0.38</td>
<td>.94</td>
<td>-0.01</td>
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<tr>
<td>Lifetime</td>
<td>0.45 (1.22) [Mdn = 0.00, Rg = 4]</td>
<td>0.20 (0.63) [Mdn = 0.00, Rg = 2]</td>
<td>U = 105.00, Z = -0.35</td>
<td>.72</td>
<td>-0.06</td>
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<tr>
<td>Global Rating of Delusions</td>
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<tr>
<td>Current</td>
<td>2.65 (1.30)</td>
<td>2.80 (1.62)</td>
<td>t (31) = -.28</td>
<td>.78</td>
<td>-0.09</td>
</tr>
<tr>
<td>Lifetime</td>
<td>4.82 (0.39) [Mdn = 5.00, Rg = 1]</td>
<td>4.50 (0.71) [Mdn = 5.00, Rg = 2]</td>
<td>U = 84.00, Z = -1.40</td>
<td>.16</td>
<td>-0.25</td>
</tr>
<tr>
<td><strong>BEHAVIOUR</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Global Rating Bizarre Behaviour</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>0.78 (1.04) [Mdn = 0.00, Rg = 3]</td>
<td>0.60 (0.84) [Mdn = 0.00, Rg = 2]</td>
<td>U = 108.00, Z = -3.2</td>
<td>.75</td>
<td>-0.06</td>
</tr>
<tr>
<td>Lifetime</td>
<td>2.64 (1.81) [Mdn = 4.00, Rg = 5]</td>
<td>2.00 (1.83) [Mdn = 2.00, Rg = 5]</td>
<td>U = 86.50, Z = -1.00</td>
<td>.32</td>
<td>-0.18</td>
</tr>
</tbody>
</table>

<sup>a</sup>Independent-Samples Mann-Whitney U Test (U), and Independent Samples t-test (t)  
<sup>b</sup>Z statistic divided by the square root of N (r), and Cohen’s d respectively  
<sup>*</sup>*n = 22 for SAPS ratings (schizophrenia group only), except for Global Rating of Delusions (Current) and Global Rating of Bizarre Behaviour (Current) where n = 23
6.9.1 Medications.

Current medications from both the schizophrenia and PFTBI groups are detailed in Table 6.14 along with statistical group comparisons. It has recently been shown that the total antipsychotic dose expressed as a percentage of the maximum recommended dose may be a superior method for standardising and comparing antipsychotic medications across groups, given (i) ambiguity associated with high dosages using the chlorpromazine equivalent (CPZ-e) method, and (ii) apparent problems associated with computing CPZ-e for the second generation antipsychotics (Hung, 2007; Yorston & Pinney, 2000). Percentage of the maximum daily dose is used here and recommended daily dose is taken from the US Department of Health and Human Services (Centres for Medicare and Medicaid Services). Because Clozapine is associated with both enhanced (e.g., Pallanti, Quercioli, & Pazzagli, 1999), and reduced (e.g., Rajji et al., 2010) neurocognitive function, statistical differences in Clozapine treatment were also investigated.

The schizophrenia and PFTBI cohorts were matched on antipsychotic dosage (including Clozapine treatment), antidepressant and anxiolytic use, as well as medications for the treatment of bipolar disorder/mania, epilepsy, cardiovascular, and other general conditions.

Table 6.14
Current Medications: Schizophrenia and PFTBI Group Comparisons

<table>
<thead>
<tr>
<th>Variable</th>
<th>SCZ (n = 23)</th>
<th>PFTBI (n = 10)</th>
<th>Statistica</th>
<th>p</th>
<th>Effect Sizeb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antipsychotic (% max. daily dose)</td>
<td>81.95 (86.00) [Mdn = 50, Rg = 343.75]</td>
<td>72.45 (39.05) [Mdn = 56.25, Rg = 113.81]</td>
<td>U = 99.00, Z = -.63</td>
<td>.55</td>
<td>-.11</td>
</tr>
<tr>
<td>Clozapine (%)</td>
<td>26.09</td>
<td>10</td>
<td>χ²(1, N=33)= 1.08</td>
<td>.30</td>
<td>-.18</td>
</tr>
<tr>
<td>Antidepressant (%)</td>
<td>56.52</td>
<td>50</td>
<td>χ²(1, N=33)= .12</td>
<td>.73</td>
<td>.06</td>
</tr>
<tr>
<td>Anxiolytic (%)</td>
<td>8.70</td>
<td>10</td>
<td>χ²(1, N=33)= .01</td>
<td>.91</td>
<td>.02</td>
</tr>
<tr>
<td>Bipolar/Mania (%)</td>
<td>13.04</td>
<td>-</td>
<td>χ²(1, N=33)= 1.44</td>
<td>.23</td>
<td>.21</td>
</tr>
<tr>
<td>Epilepsy (%)</td>
<td>8.70</td>
<td>10</td>
<td>χ²(1, N=33)= .01</td>
<td>.91</td>
<td>.02</td>
</tr>
<tr>
<td>Cardiovascular (%)*</td>
<td>21.74</td>
<td>30</td>
<td>χ²(1, N=33)= .26</td>
<td>.61</td>
<td>.09</td>
</tr>
<tr>
<td>Other (%)f</td>
<td>21.74</td>
<td>40</td>
<td>χ²(1, N=33)= 1.17</td>
<td>.28</td>
<td>.19</td>
</tr>
</tbody>
</table>

a Independent Samples Mann-Whitney U Test (U), and chi-square (χ²)
b Z statistic divided by the square root of N, and Cramer’s V
* includes anti-cholesterol and antihypertensive medications
#includes insomnia, stomach acid, muscle spasm, alcohol/opioid dependence, and arthritis medications, as well as vitamin supplements, fish oil, and contraceptives.
6.10 Strengths and Weaknesses of Samples

The recruitment and assessment of a PFTBI cohort where dual diagnosis is reliably confirmed is novel. The injury variables of this sample were mostly verified by hospital documentation and the presence of psychosis was determined by the standardised clinical assessment of all patients. As such, this is a major strength of both this research project generally, and of the recruited PFTBI sample specifically. Relative weaknesses inherent in smaller sample sizes are acknowledged, albeit power calculations discussed previously indicated that there was no cause for concern regarding a PFTBI sample size of ten in detecting reliable and valid neuropsychological differences.

The injury matched TBIWP cohort is a further significant strength, especially with regard to injury severity and broad (i.e., hemisphere and lobe) locus of patient lesions given that both of these variables have previously indicated the potential mediation of performance on neuropsychological tasks (see Chapter Four). This is despite the weakness introduced by i) unmatched latency between injury and assessment and, ii) induced coma, for which effects on neuropsychological performance are not well known. The average latency between injury and psychosis onset for the PFTBI sample was 59.60 months (4.97 years, Table 6.10). While this onset latency is extremely variable within the PFTBI cohort (SD = 52.32), it provides some indication that prior to five years post injury there may be some risk associated with the development of psychosis. This is also in keeping with onset latency figures provided by existing literature (i.e., approximately forty-seven per cent developed psychosis within the one to five year post injury latency band, see Chapter Two: 2.3.1: Onset Latency).

Accordingly, the fact that four of the TBIWP control cases sustained their injury five years or less prior to this assessment suggests that these individuals may still be at some risk for the development of psychosis. Although this is speculative based on prior literature and the demographics of the PFTBI sample, it should not be disregarded. Similarly, the large divide as to the inducement of coma following traumatic injury may in fact provide evidence of a protective effect of coma. On the other hand, this difference may reflect the development of TBI treatments overtime. Although the injury cohorts were statistically age-matched, time since injury was greater for the PFTBI cohort. Thus, earlier treatments simply may not have included induced coma as often. Nonetheless, this was an unexpected distinction and, as such, the influence of coma on the later development of psychosis is a proposition for future research. Of course, given that they are unmatched, both onset latency and coma represent
some limitation to this research project overall. As such, these variables should ideally be matched in future work of this nature to ensure against the potential for outcome mediation.

The healthy control and schizophrenia groups represent suitable comparison cohorts, and conform in size to power calculations indicated earlier in this chapter (Section 6.3: Study Design and Power). Statistical differences found across the groups to current employment type are unlikely to impact the results of this research given that the cohorts were matched on their level of educational attainment (albeit a significant difference according to the total number of years studied was noted between the healthy control and PFTBI cohorts only, see Table 6.4 and Appendix L). However, the relatively elevated levels of anxiety indicated by both schizophrenia and PFTBI participant self-report may potentially exert some effect, and thus, introduces another limitation to this work. The likelihood of this variable as a mediator of neurocognition is explored further in Chapter Eight.

A further limitation of this work relates to the Structured Clinical Interview for DSM-IV-TR (SCID-I/P; First et al. [2002]) administered to patients. Administration of the SCID-I was confined to modules for psychotic disorders due to the chronicity of patients and the lengthy size of the clinical battery in its entirety. Accordingly, this work cannot provide comment on all Axis I or Axis II conditions experienced by any of the participants. While the clinical profile of patients with PFTBI was not a major focus of this thesis the presence of Axis I and II conditions are likely to influence neuropsychological performance. The inclusion of the HADS (Zigmond & Snaith, 1983) along with access to patient files and existing patient clinicians helped to protect against this influence, however the full administration of the SCID-I/P will be a superior technique in future research where the life of the project is less constrained by time.

In addition, it is noted that the schizophrenia cohort included patients diagnosed with both schizophrenia and schizoaffective disorder. This was considered appropriate for the current research because the vital comparison was intended between patients with psychosis with and without a prior head injury, especially given the novel nature of the work and unclear clinical profile of patients with PFTBI to date. Nonetheless, work focused on the comprehensive classification of PFTBI clinically should distinguish between these diagnoses in statistical comparisons.
Chapter 7: Cognitive Neuropsychological Profile in PFTBI: Similarities and Differences with TBIWP, Schizophrenia, and Healthy Cohorts according to Group-Wise Comparisons

7.1 Introduction

In Chapter Five the existing relevant cognitive neuropsychological literature in PFTBI, TBIWP, and schizophrenia was summarised and the aims of this research project were outlined in detail. To reiterate, the principal aims of this work were to; (i) determine the cognitive neuropsychological profile of patients with PFTBI using a systematic and standardised neuropsychological battery, and (ii) compare the PFTBI profile with that obtained from a matched TBIWP sample, schizophrenia patients, and healthy participants, using identical measures and procedure. This chapter presents hypotheses, methods, results, and discussion for group-wise comparisons made across each cognitive neuropsychological domain. Chapters Eight and Nine present the data analysed using alternate techniques.

7.2 Hypotheses

As an imperative first step, group-wise comparisons were conducted to determine whether statistically significant differences on each neuropsychological measure existed between the four participant groups. In general, the PFTBI cohort was expected to illustrate inferior performance on all measures, reflecting the additive effect of dual diagnosis. This hypothesis was drawn from the existing PFTBI literature where impairments have been shown in visual perception (Fujii & Ahmed, 2002), verbal learning and verbal memory (Bamrah & Johnson, 1991; Fujii et al., 2004; Sachdev et al., 2001), memory relative to various comparison groups (Fujii & Ahmed, 2002; Fujii et al., 2004; Sachdev et al., 2001), attention (Fujii & Ahmed, 2002), and IQ (Fujii et al. 2001; Sachdev et al. 2004). Alternate reports of proficient performance (i.e., verbal fluency, cognitive switching obtained from TMT performance; Fujii et al., 2004) are counterintuitive given the substantial impairment established in patients who have experienced a traumatic brain injury, and in patients diagnosed with schizophrenia. Accordingly, results of this nature, as well as inconsistent findings on a number of other neuropsychological domains (see Chapter Five), may be a consequence of the poor and incompatible methodologies utilised in this literature to date, and thus did not inform the hypotheses in this thesis (methodological issues were discussed in Chapter Two). The healthy cohort was expected to illustrate superior performance in line with existing patient and control comparisons in the TBI and schizophrenia literature. No other hypotheses were made regarding the healthy cohort, with the exception of verbal
fluency and immediate versus delayed memory performance, according to the established trends in the healthy literature. Specific hypotheses for each of the domains are provided below.

7.2.1 Visual-perceptual organisation.

All three patient groups were expected to illustrate reduced visual-perceptual abilities, including both visuo-spatial and Gestalt abilities, relative to the healthy group. Because the existing literature is unclear, no specific hypotheses were made regarding the performance of the patient groups relative to each other, except that the poorest performance was predicted from the PFTBI group; TBIWP and schizophrenia groups have not been compared on these abilities to date, and visuo-spatial findings in PFTBI have been inconsistent, with no Gestalt processing findings having been reported.

7.2.2 Language.

It was hypothesised that all three patient groups would show impairments in language on the RBANS Language index and on verbal fluency. Subtle impairments were expected to emerge from the analysis of fluency from the number of words produced, phonological versus semantic fluency dominance, and clustering and switching proficiency. Participants in both the healthy and TBIWP cohorts were expected to produce a greater mean number of semantic category words relative to phonological category words in line with hypothesised models of memory (see Chapter Three: 3.3.3: Research in Schizophrenia). Patients with TBIWP were further expected to show general verbal fluency impairment, and thus generate fewer words for both types of fluency relative to healthy controls. The psychotic cohorts were also expected to produce a reduced number of total words to both fluency tasks. However, these groups were expected to show greater impairment to semantic, compared with phonemic, fluency. It was predicted that PFTBI patients would show the poorest performance of the four cohorts for both fluency types. With regard to clustering and switching performance, TBIWP patients were hypothesised to demonstrate reductions in the number of clusters and switches produced, but comparable mean cluster size. Based on the two major findings in the literature, patients with psychosis were expected to demonstrate one of two behaviours; (i) a reduced number of clusters and switches across categories, or (ii) comparable clusters and switches with reduced mean words per cluster.
7.2.3 Memory.

All four cohorts were expected to demonstrate poorer performance to delayed versus immediate memory assessments. The three patient groups were further expected to illustrate greater impairment generally, relative to the healthy group.

It was hypothesised that TBIWP patients would show reduced priming at the short SOA, but that long SOA priming would be comparable to healthy performance. This is because the speeded aspect of the short SOA priming task was expected to introduce additional cognitive load (i.e., speeded processing) that TBIWP patients would find difficult to integrate given their executive dysfunction (discussed in Section 7.2.5 Executive Function). Patients with schizophrenia were expected to show impaired priming at both the short and long SOAs, either in the form of reduced priming (i.e., reduced facilitation of speed and accuracy from the semantic relationship of word pairs) or as hypopriming (i.e., increased speed and accuracy to semantically un-related, relative to related word pairs). PFTBI patients were predicted to illustrate a priming pattern similar to schizophrenia patients, albeit PFTBI impairment was expected to be exacerbated in degree.

7.2.4 Reasoning.

Given the deficits established in other reasoning abilities, and the potential for executive dysfunction post injury, it was hypothesised that TBIWP patients would show reduced performance on the probabilistic reasoning task, compared to healthy controls. There was no reason to anticipate a “jumping to conclusions” style bias in this group, and thus, reduced performance was expected in their initial predictions of the likelihood that a certain coloured bead would be selected at random (i.e., either an over- or under-estimation). Because the findings in schizophrenia have been especially inconsistent to date, an expected response pattern for patients with schizophrenia was not hypothesised. The PFTBI cohort was expected to show the largest degree of impairment, however, no prediction was made as to whether their response pattern would most closely reflect TBIWP or schizophrenia.

In the original development of the task Huq et al. (1988) showed that the JTC bias was specific to patients with delusions. In fact, psychiatric control patients without delusions were even more conservative in their decision making than the control group. It was therefore hypothesised that patients with delusions would demonstrate the JTC bias when compared to patients without delusions, at least on their “draws-to-decision” and self-rated level of confidence, as was originally shown by Huq et al. (1988).
7.2.5 Executive function (mental inhibition and switching, processing speed, and attention).

Executive dysfunction has been established in all three patient cohorts; TBIWP (Ponsford, Draper, et al., 2008; Senathi-Raja et al., 2010), schizophrenia (Evans et al., 1997; Morice & Delahunty, 1996), and indications by chart review in PFTBI (Fujii & Ahmed, 2002; Fujii et al., 2004; Sachdev et al., 2001). Thus, all three patient groups were expected to illustrate executive dysfunction in the form of poor mental inhibition and switching, processing speed, and attention deficits, relative to healthy performance. Because no prior work has compared these three patient cohorts on mental inhibition, switching, or attention measures, no hypotheses were made specific to the nature of differences between patient cohorts, except to once again anticipate the greatest impairments in PFTBI. Although processing speed impairments have been reported in the PFTBI literature, no specific hypotheses were made given that these studies have shown important methodological concerns (e.g., Fujii et al., 2004 and Burg et al., 2000).

7.2.6 Intelligence Quotient: Premorbid and current IQ.

Intelligence Quotient (IQ) data has been presented in the previous chapter as a necessary aspect of the sample descriptions (Chapter Six: 6.7: General Demographics). However, the existing literature has demonstrated variations in both premorbid and current IQ assessments of TBIWP and schizophrenia. It was therefore imperative to determine premorbid and current IQ in PFTBI, and compare this with the patient and healthy comparison groups. An effort has been made to ensure that the repetition of information, where necessary, is minimal.

It was hypothesised that the TBIWP cohort would show premorbid IQ within normal ranges, but reduced current IQ. It was also predicted that the verbal aspects of IQ would be intact in this cohort. Patients with schizophrenia, by contrast, were expected to show reductions in both premorbid and current IQ, including verbal IQ. The PFTBI group were expected to demonstrate the poorest scores on current IQ measures. Given the likelihood that PFTBI patients are at an elevated risk for psychosis prior to their TBI, it was further hypothesised that they would show reductions in premorbid IQ comparable to schizophrenia.
7.3 Methods

7.3.1 Participants.

The PFTBI, schizophrenia, TBIWP, and healthy control groups who participated in this research project were detailed in Chapter Six. It is noted here, however, that group sizes were reduced for the following tasks; (i) the Stroop task (schizophrenia group, \( n = 22 \)), (ii) semantic priming (healthy and schizophrenia groups, outliers removed, \( n = 20 \) for both, PFTBI, \( n = 9 \)), and (iii) current IQ (healthy cohort, \( n = 22 \)) (see Chapter Six for details).

7.3.2 Experimental measures and procedure.

Participants completed an extensive cognitive neuropsychological battery designed to assess performance across each of the core domains identified in the preceding review chapters. The battery took approximately two hours to complete. Table 7.1 presents the assessments used to capture performance for each domain. Each measure will be discussed in turn. The psychometric properties for these assessments are contained in Table 7.4.

7.3.2.1 The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS).

The RBANS (Randolph, 1998) is a brief “paper-and-pencil” battery for the detection of neurocognitive deficits in a variety of disorders. The battery comprises twelve subtests, and produces five index scores as well as a total summary score (see Table 7.2). The battery has established internal consistency, test-retest reliability, inter-rater reliability, and concurrent validity (Randolph, 1998; Randolph, Tierney, Mohr, & Chase, 1998, Table 7.4). It also has clinical validity, including illustrated sensitivity in the detection of neurocognitive impairments in both schizophrenia and traumatic brain injury cohorts (McKay, Wertheimer, Fichtenberg, & Casey, 2008; Wilk et al., 2004). All participants were tested using Form A in accordance with the manual guidelines. Index scores were age adjusted and standardised such that the normal mean was equal to 100 with a standard deviation of 15, based on a normative sample (Randolph, 1998).
### Table 7.1
*Cognitive Neuropsychological Battery by Functional Domain*

<table>
<thead>
<tr>
<th>Domain</th>
<th>Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual-perceptual Organisation</td>
<td>Gabor Elements</td>
</tr>
<tr>
<td></td>
<td>RBANS Visuospatial/Constructional Index Score</td>
</tr>
<tr>
<td></td>
<td>- Figure Copy</td>
</tr>
<tr>
<td></td>
<td>- Line Orientation</td>
</tr>
<tr>
<td>Language</td>
<td>Phonological Fluency</td>
</tr>
<tr>
<td></td>
<td>Semantic Fluency</td>
</tr>
<tr>
<td></td>
<td>RBANS Language Index Score</td>
</tr>
<tr>
<td></td>
<td>- Picture Naming</td>
</tr>
<tr>
<td></td>
<td>- Semantic Fluency</td>
</tr>
<tr>
<td>Memory</td>
<td>RBANS Immediate Memory Index Score</td>
</tr>
<tr>
<td></td>
<td>- List Learning</td>
</tr>
<tr>
<td></td>
<td>- Story Memory</td>
</tr>
<tr>
<td></td>
<td>RBANS Delayed Memory Index Score</td>
</tr>
<tr>
<td></td>
<td>- List Learning Free Recall</td>
</tr>
<tr>
<td></td>
<td>- List Learning Recognition</td>
</tr>
<tr>
<td></td>
<td>- Story Memory Free Recall</td>
</tr>
<tr>
<td></td>
<td>- Figure Free Recall</td>
</tr>
<tr>
<td>Semantic Priming</td>
<td></td>
</tr>
<tr>
<td>Reasoning</td>
<td>Probabilistic Reasoning Task</td>
</tr>
<tr>
<td>Executive Function</td>
<td></td>
</tr>
<tr>
<td></td>
<td>- Mental Inhibition and Switching</td>
</tr>
<tr>
<td></td>
<td>Stroop (Derived Scores)</td>
</tr>
<tr>
<td></td>
<td>Trail Making Task (Difference Score)</td>
</tr>
<tr>
<td></td>
<td>- Processing Speed</td>
</tr>
<tr>
<td></td>
<td>Trail Making Task (A)</td>
</tr>
<tr>
<td></td>
<td>Stroop (Colour and Word Reading)</td>
</tr>
<tr>
<td></td>
<td>- Coding (RBANS subtest)</td>
</tr>
<tr>
<td></td>
<td>- Attention</td>
</tr>
<tr>
<td></td>
<td>RBANS Attention Index Score</td>
</tr>
<tr>
<td></td>
<td>- Digit Span</td>
</tr>
<tr>
<td></td>
<td>- Coding</td>
</tr>
<tr>
<td>Intelligence Quotient (IQ)</td>
<td>NART (Premorbid) IQ</td>
</tr>
<tr>
<td></td>
<td>WASI (Current) Full Scale IQ</td>
</tr>
<tr>
<td></td>
<td>- Vocabulary (Verbal IQ)</td>
</tr>
<tr>
<td></td>
<td>- Matrix Reasoning (Visuo-Spatial/Performance IQ)</td>
</tr>
</tbody>
</table>
### RBANS Subtest Description for the Five Index Scores

<table>
<thead>
<tr>
<th>Index</th>
<th>Subtests</th>
<th>Description</th>
<th>Maximum Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immediate Memory</td>
<td>List Learning</td>
<td>Immediate recall of a list of 10 items over four trials. One point awarded for each item recalled.</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>Story Memory</td>
<td>Immediate recall of a 12-item story, focusing on key aspects of the story over two trials. One point awarded for each item recalled.</td>
<td>24</td>
</tr>
<tr>
<td>Visuospatial/Constructional</td>
<td>Figure Copy</td>
<td>Direct copy of a complex geometrical figure containing 10 component parts. Two points for each component part (accurate drawing = one point, accurate positioning = one point).</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Line Orientation</td>
<td>Correct identification of two target lines from an array of 13 lines fanning out from a common centre point at sequential angles spanning 180 degrees. 10 trials; each line correctly matched awarded one point.</td>
<td>20</td>
</tr>
<tr>
<td>Language</td>
<td>Picture Naming</td>
<td>Name 10 basic line drawings of relatively common objects (e.g., a chair, well, trumpet). One point for each correctly named item.</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Semantic Fluency</td>
<td>Verbal generation of as many fruits and vegetables as possible in 60 seconds; one point for each exemplar provided.</td>
<td></td>
</tr>
<tr>
<td>Attention</td>
<td>Digit Span</td>
<td>Repeat strings of numbers that progressively increase from two to nine digits in length. A total of eight trials, two attempts (using new digits) provided for each digit length. Two points for correct repetition on first attempt, one point on second attempt.</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>Coding</td>
<td>Participants given a coding key where numbers 1-9 are matched with various symbols, and a separate sheet of symbols with an empty box beneath each one. They are required to insert the corresponding digit in as many boxes as possible within a 90 second time limit. One point per correct entry.</td>
<td>89</td>
</tr>
<tr>
<td>Delayed Memory</td>
<td>List Learning Free Recall</td>
<td>Recall as many words as possible from the initial List Learning subtest (10 items).</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>List Learning Recognition</td>
<td>20 words (10 foils) provided and participants give yes/no recognition of words from the original List Learning items.</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>Story Memory Free Recall</td>
<td>Recall as many aspects of the story from the Story Memory subtest (12 items).</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>Figure Copy Free Recall</td>
<td>Re-draw from memory the figure from the Figure Copy subtest.</td>
<td>20</td>
</tr>
</tbody>
</table>
7.3.2.2 **Gabor Elements Contour Integration Task (GECIT).**

Visual organisation (Gestalt processing) was assessed using the Gabor Elements Contour Integration Task (GECIT) created by Kovacs et al. (2000). The task consists of a series of fifteen cards containing a closed circular path of Gabor elements; Gaussian-modulated sinusoidal luminance distributions that closely model the known spatial frequency processing properties of cells in area V1. These are embedded in a random array of Gabor elements of the same spatial frequency and contrast, set against a uniform grey background (see Silverstein et al., 2000 for detailed discussion and Figure 3.5, Chapter Three, for an example stimulus). The cards are graded in difficulty by a reduction in the average spacing between elements for each consecutive card. Cards were presented on a flat table top and participants were instructed to identify the circular contour within 30 seconds by tracing it with their finger. Participants were given two attempts for each card. Following the first failed attempt they were shown the previous card for a second time and asked to re-identify the contour, although this time it was presented to them in an inverted orientation to remove location memory. Where this was successfully completed they were shown the more difficult card for a second time. At the failure of both attempts the task was concluded and the card number recorded.

7.3.2.3 **Verbal fluency.**

7.3.2.3.1 **Phonological fluency.**

Phonological fluency was assessed using the classic phonetic variants; ‘F’ ‘A’ and ‘S’ (The Controlled Oral Word Association Test [COWAT]; Spreen & Strauss, 1998). Participants were required to verbally produce words beginning with each letter in turn, excluding proper nouns (e.g., Australia, Bill), and the same word with a different suffix (e.g., jump, jumps, jumping). A 60 second time limit was set for each letter trial. The words generated were recorded, along with errors and perseverations, which were excluded from the totals.

7.3.2.3.2 **Semantic fluency.**

The Semantic Fluency subtest (fruits and vegetables) score from the RBANS was extracted to allow for the isolated analyses of semantically-driven fluency and comparison to the phonological data (see Table 7.2).
7.3.2.3 Clustering and switching.

Clustering and switching for both phonological and semantic fluency was analysed using the procedure developed by (Troyer et al., 1997, see Appendix N). In brief, clusters for phonological fluency consisted of successively generated words that began with the same first two letters (e.g., snake and snail), differed only by a vowel sound (e.g., foot and fat), rhymed (e.g., sour and scour), or were homonyms (e.g., flour and flower). Semantic fluency clusters were identified where words belonged to the same semantic subcategory; fruits, vegetables, salad items, and/or tropical fruits. Cluster size was counted beginning with the second word in each cluster. Switches were identified as the number of transitions between clusters, including single words. The raw number of switches was recorded and analysed, instead of a derived proportion score, as per Troyer et al. (1997). Two independent raters scored the data, with acceptable intraclass correlation: phonological fluency clustering, \( r_{ic} \) 0.90; phonological fluency switching, \( r_{ic} \) 0.93; semantic fluency clustering, \( r_{ic} \) 0.85; semantic fluency switching, \( r_{ic} \) 0.67.

7.3.2.4 Semantic priming.

7.3.2.4.1 Stimulus creation.

Ninety-six word pairs were created from nouns, verbs, and adjectives, listed in the MRC psycholinguistic database (Coltheart, 1981; Wilson, 1988). The pairs were semantically related, that is, they shared categorical and/or functional features such as oil-GAS and pause-HESITATE (see Appendix O for the full list of semantic pairs). The first word in each pair constituted the prime and its match constituted the TARGET. To meet the condition of a semantic relationship a pair had to be assigned an association score < 10 and a semantic score of ≥ 0.25 according to the ILCC Semantic Space Model Database (Institute for Language, Cognition and Computation [ILCC], 2010)\(^40\). The final list of matched semantic pairs had a

\(^{40}\) At least three types of word relationships exist (semantic, associative, and semantic-associative). Associative relationships refer to words related by a common association rather than semantic meaning per se; i.e., meek-MILD. Words can also share both types of relationships such as tongue-CHEEK (i.e., semantically related as parts of the body, and mouth specifically, and associatively related according to the colloquial phrase “tongue in cheek”). Semantic-only relationships were isolated and controlled to obtain a pure measure of semantically organised networks. Only one study has compared priming in schizophrenia using all three types of word relationships and findings suggested that patients show facilitation in the priming of associative-only word pairs, not shown by healthy controls (Nestor et al., 2006). While this may be further evidence of an idiosyncratic semantic memory store in schizophrenia this priming literature is in its infancy and, as such, semantic-only word pairs were chosen to avoid the ambiguous mediation of priming effects in both patient groups with psychosis.
mean association score of 3.20 (SD = 2.53) and a semantic score of 0.54 (SD = 0.09). The words were three to 10 letters in length and matched as closely as possible on a number of parameters, including: number of phonemes, number of syllables, number of lexical categories (as defined by Kucera and Francis, 1967), word frequency (Kucera & Francis, 1967), familiarity, concreteness, age of acquisition, and number of phonological neighbours. All parameter statistics were obtained from the English Lexicon Project Database (Balota et al., 2007). These statistics, along with tests of significance between prime and TARGET parameter values, are presented in Appendix O, Table O5.

Half of the word pairs (n = 48) were assigned to a short stimulus onset asynchrony (SOA) and the remaining half were assigned to a long SOA condition. For each SOA, 24 pairs remained semantically related, and 24 were pseudo-randomly shuffled to create prime-TARGET pairs that do not share a semantic relationship (i.e., unrelated pairs). Related and unrelated pairs were counterbalanced across four sets of lists so all targets were seen as a related and unrelated pair at each SOA (see Appendix P).

Relatedness proportion (RP) was manipulated using 96 filler word pairs also created from nouns, verbs, and adjectives, three to 10 letters in length, from the MRC psycholinguistic database (Coldheart, 1981; Wilson, 1988). These word pairs were not used in analysis but allowed for the necessary manipulation of RP in the following way; half of the filler pairs (n = 48) were assigned to the short SOA unrelated condition so that 25% of the total word pairs for the short SOA were related, and the remaining half were assigned to the long SOA related condition so that 75% of the total word pairs for the long SOA were related. This captures automatic and controlled processing at the short and long SOA respectively. Similar counterbalancing procedures were then employed by reversing the allocation across the four sets of lists so that each filler word pair was seen in both its related and unrelated form for each of the four sets; creating a total of eight sets of pairs (see Appendix P and Table P1).

Finally, 192 pseudo (i.e., nonword) pairs were generated to create a lexical decision task. The pseudo words (i.e., meaningless strings of letters, pronounceable because they conform to legal bigrams, e.g., ceeks) were taken from the ARC Nonword Database (Rastle, Harrington, & Coltheart, 2002). These nonword TARGETS were matched with an additional 192 primes (i.e., words that conformed to comparable lexical properties) taken from the MRC psycholinguistic database (Coldheart, 1981; Wilson, 1988). Half of these pairs (n = 96) were
assigned to the short SOA with the remaining half assigned to the long SOA condition, and these were similarly counterbalanced (reverse allocated) across the existing eight sets of pairs (see Appendix P).

7.3.2.4.2 Lexical decision semantic priming task.

Participants were seated at a viewing distance of 80cm from the monitor in a dimly lit room. Word stimuli were displayed in white 40-point Times New Roman centred vertically and horizontally on a 521 × 293mm 16:9 aspect ratio widescreen monitor with black background using Presentation® (Version 0.55, Build 03.10.03) experimental software. All participants completed a short and long SOA experimental block of approximately eight and ten minutes duration respectively. The short SOA block was always completed first. The lexical decision task is represented schematically in Chapter Three, Figure 3.8. A fixation cross (+) was shown on screen for 500ms at the beginning of each trial. The prime was then presented in lower-case letters for 200ms, followed by another fixation cross for an inter-stimulus interval (ISI) of either 50 or 550ms depending on the required SOA (i.e., either 250 or 750ms). The target was then presented in upper-case letters for 200ms, followed by a black screen for 1000ms during which time the participant could respond (i.e., response window). An inter-trial interval (ITI) of 1500ms was triggered by the expiration of the response window. Participants were instructed to respond as quickly and as accurately as possible with a button marked YES if the stimulus presented in upper-case letters (i.e., the target) was a word, or a button marked NO if it was not a word (i.e., pseudo- or non-word). Before beginning the experimental blocks, participants performed 24 practice trials at the short SOA to confirm their understanding of the task instructions. A short break was given between experimental blocks. Reaction time (RT; i.e., the time elapsed between onset of the target and the participant’s response) and accuracy for each trial were recorded by the software.

To account for the general slowing of response times often observed in patients, reaction time (RT) semantic priming effects were calculated as the percentage difference between RTs to semantically unrelated word pairs and RTs to semantically related word pairs. In line with Spitzer et al. (1993) the following calculation was used: ([unrelated – related] / unrelated) × 100 (See Chapter Three: 3.4.5 Methodological Concerns for discussion). Only correct responses were used in RT analyses. Accuracy priming was calculated as the percentage of correct responses to semantically related word pairs less the percentage of correct responses to semantically unrelated word pairs.
7.3.2.5 Probabilistic reasoning.

Probabilistic reasoning (i.e., the Jumping to Conclusions [JTC] bias) was investigated using an adaptation of Huq et al.’s (1988) original design. During the task explanation participants were initially shown two jars, each containing 100 beads with complementary colour ratios. Two trials were conducted: Trial 1 consisted of Jars A and B, where Jar A contained 85 pink and 15 blue beads and Jar B contained the opposite (85 blue/15 pink); Trial 2 consisted of Jars C and D, where Jar C contained 60 yellow and 40 red beads and Jar D contained the opposite (60 red/40 yellow, see Chapter Three, Figure 3.10 for actual task stimuli). Unlike the majority of work (see Garety and Freeman, 1999) participants were first asked to indicate the percentage likelihood that a certain colour bead would be drawn at random (Table 7.3). The task was then delivered on computer using the Microsoft Powerpoint® program. Beads were presented on screen one at a time representing a random draw from one of the jars\(^{41}\). Participants were required to make a decision as to which jar the beads were being drawn from, based on the colour of the beads drawn, and the colour ratio of the jars (theoretically) containing them. Preceding draws were left on screen for participants to see. Participants could request up to 20 draws before making a decision. In this way the “draws-to-decision” measurement was used that assesses the propensity for data gathering before making a decision (Colbert et al., 2010). Because the ratio is closer in the second trial it is expected that more draws are required to make a decision. Participants were also asked to estimate their level of certainty (%) once they had made a decision. They were requested to continue with the trial until they were >85% sure, or had reached the final (20\(^{th}\)) trial.

<table>
<thead>
<tr>
<th>Trial</th>
<th>Question</th>
<th>Correct Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>The likelihood of a pink bead from Jar A</td>
<td>85%</td>
</tr>
<tr>
<td>2</td>
<td>The likelihood of a yellow bead from Jar C</td>
<td>60%</td>
</tr>
</tbody>
</table>

\(^{41}\) The predetermined order of beads was taken from Colbert and Peters (2002) for the first trial (85:15 ratio), and from Dudley et al. (1997) for the second trial (60:40). Two versions of randomisation were used per trial (the second was the inverse order of the first) and these were counterbalanced across participants. See Appendix Q for the sequence of beads per trial.
7.3.2.6 Stroop task.

To obtain a measurement of both mental interference (i.e., inhibitory control) and switching (i.e., cognitive flexibility) the four-trial Stroop test was used; the Color-Word Interference Test (CWIT; Delis et al., 2001a; 2001b; Fine et al., 2008). Trial One contained 50 square patches of colour (red, blue, and green), and Trial Two contained the names of these colours written in English in an alternate order, and presented in black ink. These serve as base assessments for the participant’s ability to identify the colours and read the words respectively. Relative processing speed and attention can be calculated from Trials One and Two, and this formed two thirds of the measurement of processing speed. The number of errors on these trials was also recorded to determine the potential for a speed-accuracy trade-off in processing speed group-wise differences.

Trial Three, the incongruent trial, presented 50 of the same words printed in conflicting ink colour, where participants have to inhibit the habitual pre-potent response to read the word, and instead name the ink colour. Trial Four also presented these incongruent stimuli, however 50% were randomly boxed, and participants were required to make a rule change when they came to the boxed stimuli, from naming the ink colour to reading the word (see Chapter Three, Figure 3.13 for example stimuli). For each trial participants were instructed to read/identify stimuli aloud as quickly as possible, according to the trial rules, from left to right without skipping any (i.e., “as though reading a book”). They were instructed to correct themselves if they made a conscious error. Participants were initially given ten practice stimuli for each trial, and then the total time taken to complete the page was recorded, along with the number of errors.

Stroop inhibition and switching were assessed using derived scores as per Ben-David et al. (2011) and Rios et al. (2004, see Appendix C for calculation). As such, the measurement of these constructs taken from the third and fourth trial on the Stroop is isolated from the effect of processing speed and attention (i.e., using the measurements obtained in the first and second trials).

7.3.2.7 The Trail Making Test (TMT).

The Trail Making Test (TMT; Reitan, 1958) was used as a measure of processing speed and attentional switching. The test consists of Forms A and B. Form A, always given first, displays numbers from 1-25 in a random arrangement and participants are required to draw a line between the numbers in ascending order as quickly as possible. Form B is
identical except that both numbers and letters are presented and participants are required to draw in ascending order by alternating from number to letter (i.e., 1-A, 2-B, 3-C, see Appendix E). If they made a mistake they were required to go back to the last correct number/letter before proceeding. Before completing each form participants were given a smaller practice set of stimuli (shown in Appendix E) and then the time taken to reach the final number/letter was recorded.

Along with the individual analysis of Forms A and B two derived scores were also computed and analysed. First, the derived difference score (Total Time Form B – Total Time Form A). Here the executive component of attentional switching is isolated from processing speed effects. In line with Arbuthnott and Frank (2000) the ratio score was also computed (Total Time Form B/Total Time Form A). These authors have suggested that ratios > 3 offer evidence of executive dysfunction particular to set-switching.

7.3.2.8 Intelligence quotient.

7.3.2.8.1 Premorbid IQ.

The National Adult Reading Test (NART; Nelson, 1981) was used to determine premorbid IQ\(^42\). The NART is a 50-item single word reading test, and is graded in difficulty. The words violate grapheme-phoneme correspondence rules (e.g., ache, beatify), and therefore rely on prior (i.e., premorbid) knowledge of the correct pronunciation of the word, rather than current cognitive ability because the application of language rules does not result in the correct pronunciation. Each item is scored as correct/incorrect according to pronunciation and the total score is converted to an estimate of premorbid IQ. The estimate is equivalent to the Wechsler Adult Intelligence Scale-Revised (WAIS-R) scores and classifications, discussed in following section (7.3.2.8.2 Current IQ). The test and conversion formula is contained in Appendix R.

7.3.2.8.2 Current IQ.

The Wechsler Abbreviated Scale of Intelligence (WAIS; The Psychological Corporation; 1999) was used to determine current IQ. Given the size and demands of the neuropsychological battery as a whole, and the considerable impairment of participants, the

\(^{42}\) This is in accordance with literature that has established the validity of the NART post brain injury (Johnstone et al. [1995], Kersel et al. [2001], Moss & Dowd [1991]), and similar indications in schizophrenia (Szoke et al. [2008]).
two subtest short form (i.e., Vocabulary and Matrix Reasoning) was administered to reduce cognitive demands (Hersen, 2003). The Vocabulary subtest presents the participant with up to 33 word items both visually and orally, and requires that they provide an oral definition for the word. The task is graded in difficulty and each item is scored from 0-2 points according to the definition content (i.e., maximum score of 66). The Matrix Reasoning subtest presents up to 26 matrices/puzzle items that are graded in difficulty and are composed of four types of nonverbal reasoning; pattern completion, classification, analogy, and serial reasoning. The participant is required to complete the matrix by identifying the missing section from one of five response options. One point is awarded for each matrix correctly completed (i.e., maximum score of 26). Scores were age adjusted and standardised into a scaled score. These scaled scores were converted using existing norms into estimates of Wechsler Adult Intelligence Scale (WAIS; Wechsler, 1955) Full Scale IQ, with a mean of 100 and SD of 15.

7.4 Statistical Analyses

All statistical analyses were conducted using IBM® SPSS® software, Version 19 (IBM Corporation, 2011). Cognitive neuropsychological variables were screened according to cohort for erroneous inliers, outliers, out-of-range variables, and plausible means and standard deviations to ensure data integrity (Green & Salkind, 2005; van den Broeck et al., 2005). Missing Variable Analysis (MVA) indicated that there were no patterns of concern for missing data; there was no missing data except for the semantic priming task where <5% data was missing, Little’s MCAR Test, $\chi^2 (455, N=66) = 0, p = 1.00^{43}$.

7.4.1 Normality.

Continuous variables were assessed for violations of normality via (i) skewness and kurtosis statistics (i.e., according to the convention of +/- 2 x standard error, Groeneveld & Meeden, 1984), (ii) Kolmogorov-Smirnov and Shapiro-Wilk significance tests, (iii) the visual inspection of histograms, and (iv) box and whisker plots. Four of the 12 RBANS subtests were non-normal in distribution due to ceiling performance on the easier tasks (i.e., healthy controls and TBIWP on Picture Naming), and ≥ 70% by the majority elsewhere (i.e., all groups on Figure Copy and List Recognition, all three comparison groups on Line Orientation). The following were also non-normal in distribution; ‘f’ and ‘s’ phonological

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43 Reflects reduced cohort size for PFTBI (n = 9) due to the substantial morbidity, and therefore exclusion, of participant #P05 from the speeded semantic priming task.
<table>
<thead>
<tr>
<th>Measure</th>
<th>Author(s)</th>
<th>Structure</th>
<th>Reliability</th>
<th>Validity</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)</td>
<td>Randolph (1998)</td>
<td>A brief, individually administered test measuring attention, language, visuospatial/constructional abilities, and immediate and delayed memory. The test comprises 12 subtests and is suitable for administration of adults between the ages 18-89yrs. It takes 30min to complete in healthy individuals, and up to 2 hours in patient cohorts depending on the severity of their illness. Total scaled scores suggest the following neuropsychological status; 69 &amp; below=extremely low, 70-79=borderline, 80-89=low average, 90-109= average, 110-119=high average, 120-129=superior, 130 &amp; above=very superior.</td>
<td>Split-half reliability, average across all age groups, Fisher’s z = 0.80-0.88 (Subscales), and 0.94 (Total Scale Score). Test-retest (Form A to Form A), r = 0.55-0.78 (Subscales), and 0.88 (Total Scale Score) (all p&lt;0.05). Interrater reliability for the Figure Copy Subtest (only subjectively rated subtest), κ = 0.85 (Randolph, 1998). Reliable in schizophrenia (Randolph et al., 1998) and TBI (McKay et al., 2008) clinical populations. Construct validity, subscale correlations show expected relationships depending on the distinctness/crossover with the cognitive construct, r =0.28-0.63, and subscales with total scale scores, r = 0.68-0.77 (all p &lt;0.05). Concurrent validity, r = 0.38-0.82 (all p &lt; 0.05). The author also reports adequate content validity, and validity in both schizophrenia and TBI clinical populations (Randolph, 1998).</td>
<td>Demonstrated sensitivity to visual integration deficits in anisometropic/strabismic amblyopia, and in schizophrenia (see Green et al., 2009 for discussion).</td>
</tr>
<tr>
<td>Contour Integration Task</td>
<td>Kovacs et al. (2000)</td>
<td>15-card design. A closed circular path of Gabor elements are embedded in a random array of Gabor elements of the same spatial frequency and contrast to be identified by the participant. Each card becomes more difficult as the signal to noise ratio decreases (Δ; ratio of the average spacing between adjacent background elements to the average spacing between adjacent contour elements). Perception of gestalt considered better according to the number of cards accurately detected.</td>
<td>Inter-rater reliability, r_{icc} = 0.77 (p&lt;0.001) (healthy controls), r_{icc} = 0.66 (p&lt;0.005) (full sample; psychotic/schizophrenia and controls) (Green et al., 2009).</td>
<td>Construct validity (with WAIS vocabulary), r = 0.41 (p &lt; 0.05) (Lezak, Howieson, &amp; Loring, 2004).</td>
</tr>
<tr>
<td>The Controlled Oral Word Association Test (COWAT)</td>
<td>Spreen &amp; Strauss (1998)</td>
<td>Speeded verbal production of words (within 60 second time limit) beginning with a specified letter. Words must not be proper nouns or variants of the same word with a different suffix. Total words, clusters, switches, and errors generated (including perseverations) can be analysed.</td>
<td>Inter-rater reliability, r_{icc} = 0.96 (clusters), ICC = 0.99 (switches), r_{icc} = 0.99 (total) (all p&lt;0.05). Test-retest, r = 0.47 (clusters), r = 0.58 (switches), r = 0.70 (total) (all p&lt;0.05) (Ross, 2003).</td>
<td>Good concurrent validity for the RBANS Language Index (includes semantic fluency), Fisher’s z = 0.82. Test-retest (Form A to Form A), r = 0.75 (all p&lt;0.05) (Randolph, 1998).</td>
</tr>
<tr>
<td>Semantic Fluency (RBANS Subtest)</td>
<td>Randolph (1998)</td>
<td>Speeded verbal production of words (within 60 second time limit) that conform to a specific category (i.e., fruits and vegetables, animals). Words must not be the same word with a different suffix. Total words, clusters, switches, and errors generated (including perseverations) can be analysed.</td>
<td>Split-half reliability for the RBANS Language Index (includes semantic fluency), Fisher’s z = 0.82. Test-retest (Form A to Form A), r = 0.75 (all p&lt;0.05) (Randolph, 1998).</td>
<td></td>
</tr>
</tbody>
</table>
### Table 7.4
**Description and Psychometric Properties of Cognitive Neuropsychological Measures (continued)**

<table>
<thead>
<tr>
<th>Measure</th>
<th>Author(s)</th>
<th>Structure</th>
<th>Reliability</th>
<th>Validity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Probabilistic Reasoning (Beads) Task</td>
<td>Huq et al. (1988) Dudley et al. (1997) (60:40 ratio version)</td>
<td>Computerised task where participants are shown coloured beads on screen (one at a time) in one of two colours. They are told that the beads are being drawn randomly from one of two jars, each containing beads of the two colours (e.g., red and yellow) in complementary ratios (e.g., 85:15 and 15:85). Participants are to make a decision as to which jar the beads are coming from using their reasoning about the beads ratio. The speed at which they do this (“draws-to-decision”) is analysed, along with the certainty attached to their decision (0-100%). A one-question assessment of reasoning ability before the task can also be incorporated; “what is the likelihood (percentage chance) that a red bead will be drawn from the jar containing 85 red and 15 yellow beads?” The correct response being 85%.</td>
<td>No available psychometric properties; variations of the task have been used in research (esp. regarding delusions) since Huq et al. (1988) (see Dudley &amp; Over, 2003 for discussion).</td>
<td>No available psychometric properties; variations of the task have been used in research (esp. regarding delusions) since Huq et al. (1988) (see Dudley &amp; Over, 2003 for discussion).</td>
</tr>
<tr>
<td>The Stroop Task* (CWIT version)†</td>
<td>*Stroop (1935)  †Delis et al., (2001a; 2001b)</td>
<td>Four trial (card) version (50 stimuli p/card); colour patches (Card 1), names of colours in black ink (Card 2), names of colours in incongruent-coloured ink (Card 3), names of colours in incongruent-coloured ink, with randomly boxed stimuli requiring a rule change (read the word rather than name the ink colour; Card 4). Speeded task, Cards 1 and 2 provide control measurements. Card 3 indicates inhibition of the prepotent word-reading response (over ink colour identification). Card 4 indicates the same, plus cognitive flexibility (switching). Total time for each card, as well as derived scores accounting for control measurements, can be analysed.</td>
<td>Test-retest reliability, $r = 0.80$ (p&lt;0.05) (Houx et al., 2002).</td>
<td>Established validity in healthy and clinical populations (MacLeod, 1991; Sisk, 2002; Smith &amp; Nyman, 1974, see MacLeod, 1991 for detailed discussion).</td>
</tr>
<tr>
<td>The Trail Making Test (TMT)</td>
<td>Reitan (1958)</td>
<td>Two part paper-and-pen speeded test measuring visuomotor scanning, divided attention, cognitive flexibility, and processing speed. Participants must connect dots according to consecutive numbers (Part A), and alternating numbers/letters (Part B). Part B gives a measure of cognitive flexibility while accounting for processing speed (i.e., time difference between Parts A and B).</td>
<td>Test-retest reliability, $r = 0.60 – 0.90$ (Lezak et al., 2004). High inter-rater reliability (Fals-Stewart, 1992).</td>
<td>Concurrent validity with alternate tests of processing speed/cognitive flexibility, $r = -0.65$ (Digit Symbol and Part B) (p&lt;.01) (Corrigan &amp; Hinkeldey, 1987), and Full Scale WAIS IQ -0.44 -0.70 (p&lt;.01) (Goul &amp; Brown, 1970; Reitan, 1958). Demonstrated sensitivity in the detection of organic brain injury (Reitan, 1955; 1958).</td>
</tr>
</tbody>
</table>

(continued)
Table 7.4
Description and Psychometric Properties of Cognitive Neuropsychological Measures (continued)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Author (s)</th>
<th>Structure</th>
<th>Reliability</th>
<th>Validity</th>
</tr>
</thead>
<tbody>
<tr>
<td>The National Adult Reading Test (NART)</td>
<td>Nelson (1981)</td>
<td>A 50-item single word reading test graded in difficulty. The words violate grapheme-phoneme correspondence rules (e.g., ache, beatify) and therefore rely on prior (premorbid) knowledge of the correct pronunciation of the word. Total correctly/incorrectly pronounced words are summed (i.e., maximum of 50) and converted to premorbid IQ estimate.</td>
<td>Established internal consistency (Crawford et al. 1988; Nelson &amp; Willison, 1991), test retest reliability (Crawford et al. 1989) and inter-rater reliability (O'Carroll, 1987; Crawford et al. 1989).</td>
<td>Concurrent validity (with the WAIS), $r = 0.72$-$0.81$ (Lezak et al., 2004), and Moray House Test (current IQ), $r = 0.73$ ($p&lt;.001$) (Crawford et al., 2001). Case study evidence (Moss &amp; Dowd, 1991).</td>
</tr>
<tr>
<td>Wechsler Abbreviated Scale of Intelligence (WASI)</td>
<td>Wechsler/The Psychological Corporation, 1999</td>
<td>Two subtest short form (Vocabulary and Matrix Reasoning). The Vocabulary subtest is a 33 word item test that requires participants to provide an oral definition. Each item is scored from 0-2 points (maximum 66 points). The Matrix Reasoning subtest is a 26-item test that requires nonverbal reasoning. Participants identify the missing section of each matrix from five response options. Each matrix is worth 1 point (maximum 26 points). Scores are converted to estimates of WAIS full scale IQ.</td>
<td>Internal consistency/split half reliability, $r = 0.90$-$0.98$ (Vocabulary), $r = 0.88$-$0.96$ (Matrix Reasoning). Test re-test reliability, $r = 0.87$-$0.92$. Inter-rater reliability for subjectively scored Vocabulary subtest, $r = 0.99$ (Garland, 2005).</td>
<td>Content validity maintained from WAIS-III. Concurrent validity, two subtest full scale IQ with WAIS-III, $r = 0.87$ (Garland, 2005).</td>
</tr>
</tbody>
</table>

Note. No data is available for the Semantic Priming Lexical Decision Task given that this task has no standard administration.

4 Phonological Fluency (F-A-S).
fluency trials for the TBIWP group only, chunking and switching ratings on the verbal fluency data, all Stroop variables, all TMT variables, the initial prediction trials on the probabilistic reasoning task (i.e., C1 and C2, see Table 7.19 in 7.5: Results), and selected priming distributions from the healthy control, schizophrenia, and PFTBI cohorts. Although ANOVA techniques may remain robust even where normality is violated, alternative analyses were sought given that group sizes were < n = 30 (Green & Salkind, 2004). Data transformations were initially applied to all non-normal distributions but did not improve normality for a number of variables. Table 7.5 indicates all non-normal distributions and their applied solutions.

Table 7.5
**Non-normal Variables and Statistical Solutions**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBANS subtests (n = 4).</td>
<td>t-tests / Bonferroni correction for multiple comparisons.</td>
</tr>
<tr>
<td>Phonological fluency (f and s trials TBIWP cohort only).</td>
<td>Raw scores for these distributions considered most appropriate / conservative p value (i.e., p &lt; .01, interpreted with some caution).</td>
</tr>
<tr>
<td>Probabilistic reasoning (initial prediction data only).</td>
<td>t-tests / Bonferroni correction for multiple comparisons.</td>
</tr>
<tr>
<td>Selected priming distributions (healthy control, schizophrenia, and PFTBI cohorts).</td>
<td>Removal of outliers (healthy control; H05, H06, H10, H16, and H18; schizophrenia; S09, S13, S14, S17, and S21). Majority resolved, interpreted following with some caution; (i) healthy control group percentage correct related and unrelated conditions, short SOA, and (ii) PFTBI group percentage correct data all conditions.</td>
</tr>
<tr>
<td>Fluency (all clustering and switching variables only, n = 4).</td>
<td>Square root transformation.</td>
</tr>
<tr>
<td>All Stroop.</td>
<td>Log transformation. Trial One and Two errors were not improved by transformation; nonparametric statistics (Kruskal-Wallis H) used.</td>
</tr>
<tr>
<td>All TMT.</td>
<td>Inverse square root transformation.</td>
</tr>
</tbody>
</table>

### 7.4.2 Group-wise comparisons.

The following section details the statistical analyses specific to group-wise comparisons for each task. With the exception of the semantic priming task, probabilistic reasoning task, and the abovementioned t-tests indicated in Table 7.5, all analyses were performed using univariate Analysis of Variance (ANOVA), with participant group as the between subjects factor. Some additional paired t-test analyses were performed to address
specific hypotheses (i.e., phonological versus semantic comparisons in verbal fluency, and immediate versus delayed memory on the RBANS, discussed in the following section 7.4.3: Additional Analyses). Post hoc tests were performed using Student-Newman-Keuls (SNK) tests, except where the assumption of homogeneity of variance was violated (Table 7.6). In such cases the more conservative Welsh F ratio was reported, and Dunnett’s C post hoc was used to control for Type I error across pairwise comparisons. Partial Eta squared was used to determine effect sizes (Tabachnick & Fidell, 1996), except where data were submitted to independent sample t-tests, for which Cohen’s d was used instead (Green & Salkind, 2005). Partial Eta squared effect sizes were considered small at 0.01, medium at 0.09, and large at 0.25 (Levine & Hullett, 2002). Cohen’s d effect sizes of 0.2, 0.5, and 0.8 were interpreted as small, medium, and large respectively (Green & Salkind, 2005).

Table 7.6
Variables Violating the Assumption of Homogeneity of Variance

<table>
<thead>
<tr>
<th>RBANS Indices</th>
<th>Visuospatial Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBANS Subtests</td>
<td>List Learning, Figure Copy, Line Orientation, Picture Naming, Coding, List Recognition, Story Recall</td>
</tr>
<tr>
<td>Fluency</td>
<td>Phonological Fluency Switching, Semantic Fluency Mean Cluster Size and Switching.</td>
</tr>
<tr>
<td>Stroop</td>
<td>Colour Trial, Inhibition Trial, Derived Interference Score</td>
</tr>
</tbody>
</table>

7.4.3 Additional analyses.

7.4.3.1 Immediate versus delayed memory.

Paired t-tests were performed for each cohort using data from the RBANS Immediate Memory, and RBANS Delayed Memory indices. This analysis addressed the question of expected superior abilities to immediate memory recall relative to delayed memory recall.

7.4.3.2 Fluency-type.

Total words produced for phonologically-driven fluency (i.e., the sum of trials ‘f’, ‘a’, and ‘s’) were first divided by three to be comparable with semantically-driven fluency (one trial). Paired-sample t-tests were then run for each cohort separately to determine the relative within-group performance according to fluency type.

7.4.3.3 Semantic priming.

Semantic priming reaction time (RT) and accuracy raw scores were submitted to separate repeated measures ANOVA with SOA (two levels: short and long) and relatedness
(two levels: related and unrelated) as within subjects’ factors. Participant group was the between subjects’ factor. For both the RT and accuracy analyses, data met the assumption of sphericity, however the assumption of homogeneity of the variance-covariance matrices was violated: RT, Box’s $M = 62.13, F (30, 3,427.40) = 1.73, p = .008$; Accuracy, Box’s $M = 96.53, F (30, 3,487.33) = 2.69, p < .001$. This is likely a reflection of the aforementioned violations to normality, and of unequal group sizes. Again, while the ANOVA may remain robust under these conditions, an alpha level of $p < .01$ was applied to reduce the likelihood of a type I error. Equality of error variance was confirmed for two of the four conditions for RTs and for all but one condition for accuracy: RTs; unequal error variance to the unrelated conditions for both the short and long SOAs, and accuracy; unequal error variance to the related condition at the long SOA. To account for unequal error variance, post hoc analyses, where appropriate, were run using the Dunnett’s C test. Results for these variables should be viewed with some caution.

Multivariate analyses of variance (MANOVA) compared the four participant groups on RT and accuracy derived priming scores at both the short and long SOAs. The assumption of homogeneity of the variance-covariance matrices was met for the derived priming data; Box’s $M = 46.99, F (30, 3,517.03) = 1.31, p = .12$. Error variance across the groups was shown to be equal except for the accuracy priming at the short SOA. Accordingly, post hoc analysis, where appropriate, used the Dunnett’s C test.

7.4.3.4 Probabilistic reasoning.

The probabilistic reasoning task produces three indices per trial; (i) initial prediction, (ii) draws-to-decision, and (iii) confidence. A fourth index, jumping to conclusions (JTC) behaviour, is determined from the draws-to-decision data and defined as requesting ≤ two beads before making a decision. As mentioned in discussions on normality, the initial prediction data was submitted to $t$–tests with a Bonferroni correction to account for multiple comparisons ($p= .05 / 6$ comparisons = $p < .008$). The remaining probabilistic reasoning data was submitted to a repeated measures analysis of variance (ANOVA) with ratio (two levels: 85:15 and 60:40) and index (two levels: draws-to-decision and confidence) as within subjects’ factors. Participant group was the between subjects’ factor. Assumptions of homogeneity of variance and homogeneity of inter-correlations were met; Box’s $M = 50.06, F (30, 3797.08) = 1.42, p = .065$. Greenhouse-Geisser corrected $F$ values are reported because sphericity was violated, and error variance across groups was unequal. JTC
behaviour (the fourth index) was investigated using a two-way contingency table analysis (chi-square).

The same repeated measures and t-test analyses were then re-run on the data from the schizophrenia and PFTBI groups, with the presence of delusions as the grouping factor (according to scores on the Positive and Negative Syndrome Scale [PANSS; Kay et al., 1987]). To eliminate as many other influential variables as possible the TBIWP group were not included in this analysis. However, the healthy control group were incorporated in the group without delusions to ensure adequate statistical power; without the healthy control group the number of patients without delusions was \( n = 2 \). Assumptions of sphericity, homogeneity of variance and homogeneity of intercorrelations were violated; Box’s \( M = 28.43, F (10, 12,514.89) = 2.61, p = .004 \). The alpha level was thereby reduced to \( p < .01 \) to account for potential inequality of variance-covariance matrices. Greenhouse-Geisser corrected \( F \) values are reported given that sphericity was violated and the error variance across groups was unequal. Again, JTC behaviour was investigated using a two-way contingency table analysis (chi-square).

7.5 Results

7.5.1 Descriptive statistics and z-score illustrations.

Descriptive statistics for each cognitive neuropsychological measure are contained in Tables 7.7 to 7.25. In general, the PFTBI group illustrated the lowest mean performance across all tasks relative to the other three cohorts. For the sake of clarity, descriptive and inferential statistics, tables, figures, and discussion pertaining to each task are addressed in turn. Results are presented in the order introduced in Section 7.3.2: Experimental Measures and Procedure (i.e., according to measure rather than neuropsychological domain).

Scores derived from the cognitive neuropsychological measures were standardised (i.e., \( z \)-scores) using the following equation:

\[
z = \frac{\text{raw score} - \text{healthy control mean}}{\text{healthy control standard deviation}}
\]

Thus, the healthy control group represented the zero point for all standardised scores to depict the standardised difference between groups across the multiple outcome variables. These are presented in Figures 7.2 to 7.16.
7.5.2 The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS).

7.5.2.1 RBANS classifications.

Figure 7.1 depicts the within group spread of performance according to overall RBANS classifications (i.e., RBANS Total scaled score). The majority of participants from all groups fell into the “average range”, except for PFTBI patients where only 30% were classified in this range. The remaining healthy control participants scored well, with 91.31% falling between “average”, “high average”, and “superior” ranges. TBIWP patients scored similarly, except that 20% of these (n =2) were within the “low average” range. Patients with schizophrenia performed more poorly overall, with the majority of the group scoring below average; 52.16% were classified between “extremely low”, “borderline”, or “low average”. Finally, the poorest overall neuropsychological performance was illustrated by PFTBI patients, with 70% classified in the “extremely low” or “borderline” categories.

7.5.2.2 RBANS indices and total score

Descriptive and inferential statistics for the RBANS indices and total scores are presented in Table 7.7. The ANOVA was significant at the .001 level for all group comparisons on RBANS index and total scores, with the exception of the Language Index Score (p = .07, see Table 7.7). Post hoc SNK/Dunnetts C comparisons confirmed that the PFTBI group performed consistently below the three comparison groups on all RBANS indices including the total scaled score, with the exception of the Visuo-spatial index (and the Language index where no group differences were shown). Figure 7.2 illustrates these differences according to standardised group means (i.e., z-scores). On the Visuo-spatial index the PFTBI and schizophrenia groups showed comparable performance which was poorer than that of the TBIWP cohort (although TBIWP and schizophrenia patients were not statistically different). All patient groups performed below the healthy cohort on this index. Patients with schizophrenia were the next poorest performers overall (i.e., RBANS Total) and on Immediate Memory, followed by the TBIWP and healthy groups which were not significantly different from each other. All three comparison groups showed equally superior performance relative to the PFTBI group on Delayed Memory. Finally, the schizophrenia and TBIWP groups were equally poor on Attention, and this was significantly below the performance of the healthy cohort, however TBIWP Attention was also matched to that of healthy controls. According to Levine and Hullett (2002) these effects are very large in size, ranging from .30 to .46 (where .25 is considered a large effect, see Table 7.7).
Figure 7.1. Neuropsychological classification (RBANS Total score) according to participant group.
### Table 7.7

*Group Comparisons across RBANS Indices and Total Score*

<table>
<thead>
<tr>
<th>Measure</th>
<th>HC</th>
<th>TBIWP</th>
<th>SCZ</th>
<th>PFTBI</th>
<th>$F^*$</th>
<th>$p$</th>
<th>Effect Size</th>
<th>Post hoc</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Immediate Memory</strong></td>
<td>113.57 (13.99)</td>
<td>104.80 (13.75)</td>
<td>91.65 (16.28)</td>
<td>76.10 (17.85)</td>
<td>16.44</td>
<td>&lt;.001</td>
<td>.44</td>
<td>PFTBI&lt;SCZ&lt;TBIWP=HC</td>
</tr>
<tr>
<td></td>
<td>[107.15, 119.99]</td>
<td>[95.06, 114.54]</td>
<td>[85.23, 98.07]</td>
<td>[66.36, 85.84]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Visuospatial</strong></td>
<td>116.91 (7.86)</td>
<td>105.60 (14.71)</td>
<td>96.35 (17.42)</td>
<td>91.10 (13.80)</td>
<td>16.16$^b$</td>
<td>&lt;.001</td>
<td>.37</td>
<td>PFTBI=SCZ&lt;SCZ=TBIWP&lt;HC</td>
</tr>
<tr>
<td></td>
<td>[111.19, 122.64]</td>
<td>[96.92, 114.28]</td>
<td>[90.62, 102.07]</td>
<td>[82.42, 99.78]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Language</strong></td>
<td>97.61 (9.30)</td>
<td>100.00 (12.55)</td>
<td>94.74 (13.39)</td>
<td>87.20 (11.54)</td>
<td>2.46</td>
<td>.07</td>
<td>.11</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>[92.74, 102.48]</td>
<td>[92.62, 107.39]</td>
<td>[89.87, 99.61]</td>
<td>[79.82, 94.59]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Attention</strong></td>
<td>107.00 (13.48)</td>
<td>98.40 (13.91)</td>
<td>91.09 (16.88)</td>
<td>77.20 (21.64)</td>
<td>8.82</td>
<td>&lt;.001</td>
<td>.30</td>
<td>PFTBI&lt;SCZ=TBIWP&lt;SCZ=TBIWP&lt;HC</td>
</tr>
<tr>
<td></td>
<td>[100.26, 113.74]</td>
<td>[88.18, 108.62]</td>
<td>[84.35, 97.83]</td>
<td>[66.98, 87.42]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Delayed Memory</strong></td>
<td>101.96 (14.70)</td>
<td>95.40 (10.57)</td>
<td>89.87 (14.65)</td>
<td>68.30 (21.88)</td>
<td>11.33</td>
<td>&lt;.001</td>
<td>.35</td>
<td>PFTBI&lt;SCZ=TBIWP=HC</td>
</tr>
<tr>
<td></td>
<td>[95.52, 108.40]</td>
<td>[85.64, 105.16]</td>
<td>[83.43, 96.31]</td>
<td>[58.54, 78.06]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>RBANS Total</strong></td>
<td>110.57 (10.79)</td>
<td>100.80 (13.11)</td>
<td>88.52 (16.56)</td>
<td>74.90 (16.84)</td>
<td>17.66</td>
<td>&lt;.001</td>
<td>.46</td>
<td>PFTBI&lt;SCZ&lt;TBIWP=HC</td>
</tr>
<tr>
<td></td>
<td>[104.60, 116.53]</td>
<td>[91.75, 109.85]</td>
<td>[82.56, 94.49]</td>
<td>[65.85, 83.95]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$^a$ Analysis of Variance (ANOVA).
$^b$ Welsh’s $F$ ratio.
$^c$ Dunnetts C post hoc test to account for unequal error variance.
Figure 7.2. Standardised participant group means (z-scores) for RBANS index and total scale scores. Healthy control data represents the zero point. Error bars represent standard error of the mean and are colour coded to enhance visibility.
7.5.2.3 Immediate versus delayed memory.

Descriptive data for the RBANS Immediate and Delayed Memory indices are contained in Table 7.7. The paired-sample t-test statistics are contained in Table 7.8. All groups illustrated better immediate versus delayed memory ability, except for the schizophrenia cohort whose performance was statistically matched (although, their means trended in the same direction as the other cohorts). All significant comparisons were considered large in effect (Green & Salkind, 2005).

<table>
<thead>
<tr>
<th>Group</th>
<th>t-statistic</th>
<th>p</th>
<th>Effect Size (Cohen’s d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HC (n = 23)</td>
<td>3.47</td>
<td>.002</td>
<td>0.72</td>
</tr>
<tr>
<td>TBIWP (n = 10)</td>
<td>2.74</td>
<td>.02</td>
<td>0.87</td>
</tr>
<tr>
<td>SCZ (n = 23)</td>
<td>0.58</td>
<td>.57</td>
<td>0.12</td>
</tr>
<tr>
<td>PFTBI (n = 10)</td>
<td>2.52</td>
<td>.03</td>
<td>0.80</td>
</tr>
</tbody>
</table>

Note. HC and SCZ, df = 22, TBIWP and PFTBI, df = 9.

7.5.2.4 RBANS subscales.

Descriptive and inferential data for normally distributed RBANS subscales are contained in Table 7.9. Table 7.10 contains the means and standard deviations for the non-normally distributed RBANS subscales, and Table 7.11 contains the t-test comparisons for these variables. Although performance on the individual RBANS subscales was not hypothesised (with the exception of semantic fluency covered in Section 7.5.4: Verbal Fluency), the results are reported here in the interest of completeness. Post hoc analyses (SNK/Dunnetts C/t-tests) on the twelve RBANS subscales showed no consistent pattern (Tables 7.9 and 7.10). Very generally, the PFTBI group showed either the poorest performance, or equally matched poorest performance with the schizophrenia group, while the TBIWP and healthy control cohorts showed matched performance across all subscales. These findings are depicted visually in Figure 7.3 according to standardised group means (i.e., z-scores). In only some circumstances did the subscale performance reflect group performance patterns shown at the related index score; Immediate/Delayed Memory and Language subscales reflected index patterns; however, the Visuo-spatial and Attention indices showed very different subscale patterns of performance.
Table 7.9
Group Comparisons across RBANS Subscales (Normally Distributed)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Mean (Standard Deviation) [95% confidence intervals]</th>
<th>F&lt;sup&gt;a&lt;/sup&gt; (df = 3,62)</th>
<th>p</th>
<th>Effect Size (partial η²)</th>
<th>Post Hoc</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HC (n = 23)</td>
<td>TBIWP (n = 10)</td>
<td>SCZ (n = 23)</td>
<td>PFTBI (n = 10)</td>
<td></td>
</tr>
<tr>
<td>--------------------</td>
<td>-------------------------------------------------</td>
<td>-----------------------------</td>
<td>-------------</td>
<td>-----------------------</td>
<td>-----------------------------</td>
</tr>
<tr>
<td>List Learning</td>
<td>35.13 (3.24) [33.26, 36.99]</td>
<td>33.10 (3.41) [30.27, 35.93]</td>
<td>28.48 (4.57) [26.61, 30.35]</td>
<td>22.70 (7.06) [19.87, 25.53]</td>
<td>16.60&lt;sup&gt;b&lt;/sup&gt; &lt; .001</td>
</tr>
<tr>
<td>Story Memory</td>
<td>19.83 (2.92) [18.21, 21.45]</td>
<td>17.40 (4.48) [14.94, 19.86]</td>
<td>15.65 (4.51) [14.03, 17.27]</td>
<td>12.90 (3.67) [10.44, 15.36]</td>
<td>8.72 &lt; .001  &lt; .001&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Semantic Fluency</td>
<td>20.70 (3.75) [18.59, 22.80]</td>
<td>21.50 (5.76) [18.30, 24.70]</td>
<td>19.17 (5.80) [17.07, 21.28]</td>
<td>16.30 (5.17) [13.10, 19.50]</td>
<td>2.30   &lt; .05  .09&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Digit Span</td>
<td>12.52 (2.56) [11.40, 13.64]</td>
<td>10.60 (2.46) [8.90, 12.30]</td>
<td>11.43 (2.95) [10.31, 12.56]</td>
<td>9.40 (2.55)  [7.70, 11.10]</td>
<td>3.47   &lt; .05  .02&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Coding</td>
<td>58.43 (9.56) [53.62, 63.26]</td>
<td>55.20 (7.69) [47.89, 62.51]</td>
<td>42.22 (12.34) [37.40, 47.04]</td>
<td>34.70 (16.34) [27.39, 42.01]</td>
<td>11.98 &lt; .001 &lt; .001&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>List Recall</td>
<td>7.96 (2.08) [7.02, 8.89]</td>
<td>6.90 (2.73) [5.48, 8.32]</td>
<td>5.35 (2.17) [4.41, 6.29]</td>
<td>3.60 (2.32)  [2.18, 5.02]</td>
<td>10.56 &lt; .001 &lt; .001&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Story Recall</td>
<td>10.43 (1.62) [9.41, 11.46]</td>
<td>8.90 (2.60) [7.34, 10.46]</td>
<td>8.52 (2.84) [7.50, 9.55]</td>
<td>5.70 (2.98)  [4.14, 7.26]</td>
<td>8.55&lt;sup&gt;b&lt;/sup&gt; &lt; .001 &lt; .001&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Figure Recall</td>
<td>15.87 (3.45) [14.21, 17.53]</td>
<td>14.60 (3.84) [12.08, 17.12]</td>
<td>11.61 (3.70) [9.95, 13.27]</td>
<td>7.80 (5.69)  [5.28, 10.32]</td>
<td>11.08 &lt; .001 &lt; .001&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Analysis of Variance (ANOVA).
<sup>b</sup> Welsh’s F ratio.
<sup>c</sup> Dunnetts C post hoc test to account for unequal error variance.
Table 7.10
Descriptive Statistics for the RBANS Subtests Variables with Non-normal Distribution

<table>
<thead>
<tr>
<th>Measure</th>
<th>Mean (Standard Deviation)</th>
<th>Summary of Group Differences (see Table 7.11)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HC ($n = 23$)</td>
<td>TBIWP ($n = 10$)</td>
</tr>
<tr>
<td>Figure Copy</td>
<td>19.74 (0.62)</td>
<td>19.00 (1.56)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Line Orientation</td>
<td>19.70 (0.63)</td>
<td>17.80 (3.16)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Picture Naming</td>
<td>10 (0)</td>
<td>10 (0)</td>
</tr>
<tr>
<td>List Recognition</td>
<td>19.65 (0.71)</td>
<td>19.70 (0.48)</td>
</tr>
</tbody>
</table>

For the Immediate Memory subscales (i.e., List Learning and Story Memory) the only exceptions were, (i) the TBIWP group showed superior performance relative to the schizophrenia group on the List Learning task (reflected at the index score), however, their Story Memory performance was matched, and (ii) the PFTBI group showed matched performance with the schizophrenia group on both subscales, however, the index score identified the PFTBI group as inferior on Immediate Memory recall. The Language index subscales (i.e., Picture Naming and Semantic Fluency) reflected the Language index exactly, with no significant differences in performance shown from the groups. Delayed Memory index differences included, (i) superior performance was shown by healthy controls relative to schizophrenia in the List Recall, Story Recall, and Figure Recall subscales, whereas these groups showed matched performance (along with TBIWP) on the index score, (ii) the PFTBI patients showed the poorest performance on the List Recall and Figure Recall subscales (i.e., reflected in the Delayed Memory Index score); however, their performance was matched with that of schizophrenia patients on the Story Recall subscale, and (iii) List Recognition showed no significant group differences (see Table 7.7 for Index score performance patterns).

Significant differences according to the Visuo-Spatial index subscales (i.e., Figure Copy and Line Orientation) were shown only between the healthy control and PFTBI, and healthy control and schizophrenia groups’ performance. Comparisons on the Visuo-Spatial index; however, reached statistical significance between head injured groups as well (i.e., PFTBI and TBIWP). Finally, only the matched TBIWP and healthy control performance on the Attention index score was shown on the Digit Span and Coding subscales. Significantly different Digit Span abilities were identified between healthy control and PFTBI groups only,
Table 7.11
Multiple Group Comparisons for RBANS Subtest Variables with Non-normal Distribution; Significance of T-tests, Cohen’s d and 95% Confidence Intervals

<table>
<thead>
<tr>
<th></th>
<th>HC &amp; TBIWP (df=31)</th>
<th>HC &amp; SCZ (df=44)</th>
<th>HC &amp; PFTBI (df=31)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Figure Copy*</td>
<td>Line Orientation*</td>
<td>Picture Naming</td>
</tr>
<tr>
<td>t*</td>
<td>1.45</td>
<td>1.88</td>
<td>-</td>
</tr>
<tr>
<td>p</td>
<td>.18</td>
<td>.09</td>
<td>-</td>
</tr>
<tr>
<td>d</td>
<td>0.25</td>
<td>0.33</td>
<td>-</td>
</tr>
<tr>
<td>95% CI</td>
<td>-0.40</td>
<td>-0.37</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>1.87</td>
<td>4.16</td>
<td>0.46</td>
</tr>
</tbody>
</table>

Table 7.11 (continued)
Multiple Group Comparisons for RBANS Subtest Variables with Non-normal Distribution; Significance of T-tests, Cohen’s d and 95% Confidence Intervals

<table>
<thead>
<tr>
<th></th>
<th>SCZ &amp; TBIWP (df=31)</th>
<th>SCZ &amp; PFTBI (df=31)</th>
<th>TBIWP &amp; PFTBI (df=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Figure Copy*</td>
<td>Line Orientation*</td>
<td>Picture Naming</td>
</tr>
<tr>
<td>t*</td>
<td>-1.10</td>
<td>-0.84</td>
<td>-0.89</td>
</tr>
<tr>
<td>p</td>
<td>.28</td>
<td>.41</td>
<td>.38</td>
</tr>
<tr>
<td>d</td>
<td>-0.19</td>
<td>-0.15</td>
<td>-0.14</td>
</tr>
<tr>
<td>95% CI</td>
<td>-3.22</td>
<td>-3.63</td>
<td>-0.43</td>
</tr>
<tr>
<td></td>
<td>0.96</td>
<td>1.51</td>
<td>0.17</td>
</tr>
</tbody>
</table>

*a Independent Samples t-test Statistic.
bCohen’s d effect size.
*Equal variances not assumed.
Figure 7.3. Standardised participant group means (z-scores) for RBANS subscale scores. Healthy control data represents the zero point. Error bars represent standard error of the mean and are colour coded to enhance visibility.
with healthy controls showing superior performance. On the Coding task, PFTBI and schizophrenia patients showed matched performance, which was reduced compared to TBIWP and healthy controls (who were also matched). However the Attention index score identified differences between PFTBI and schizophrenia performance, which was reduced compared to healthy controls (i.e., TBIWP patient performance was matched with that of both schizophrenia and healthy controls).

Effect sizes for these differences on the RBANS subscales ranged from 0.14 to 0.51 for normally distributed variables (partial Eta squared), and from 0.42 to 0.77 for variables with a non-normal distribution (Cohen’s d). These were generally considered medium to very large in size (see Tables 7.9 and 7.11, Green & Salkind, 2005; Tabachnick & Fidell, 1996).

### 7.5.3 Gabor Elements Contour Integration Task (GECIT).

Descriptive and inferential data for the GECIT task is contained in Table 7.12, and the \( z \)-score comparison in Figure 7.4. All four groups reached a similar number of (mean) card trials on the GECIT task (i.e., between the ninth and tenth card). However, while the means are close together, a tendency for the psychosis cohorts (i.e., PFTBI and schizophrenia patients) to reach an average of approximately one less card was observed (see Figure 7.4). Nonetheless, this trend was not significant, and nor were any other group comparisons on the GECIT task.

#### Table 7.12

*Group Comparisons on the GECIT task*

<table>
<thead>
<tr>
<th>Measure</th>
<th>Mean (Standard Deviation) [95% confidence intervals]</th>
<th>( F^a )</th>
<th>( p )</th>
<th>Effect Size (partial ( \eta^2 ))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HC ( (n = 23) )</td>
<td>TBIWP ( (n = 10) )</td>
<td>SCZ ( (n = 23) )</td>
<td>PFTBI ( (n = 10) )</td>
</tr>
<tr>
<td>GECIT</td>
<td>10.17 (2.08) ([9.32, 11.03])</td>
<td>10.60 (2.50) ([9.30, 11.90])</td>
<td>9.35 (1.75) ([8.49, 10.20])</td>
<td>9.10 (2.18) ([7.80, 10.40])</td>
</tr>
</tbody>
</table>

\( ^a \) Analysis of Variance (ANOVA).

### 7.5.4 Verbal fluency (phonological and semantic).

#### 7.5.4.1 Participant group comparisons.

Descriptive and inferential statistics for the verbal fluency data are contained in Table 7.13. Data from the RBANS Semantic Fluency subtest is repeated for comparison. The PFTBI group showed the lowest mean production of words across all five tests of verbal
fluency. Conversely, the healthy cohort produced the largest mean words across trials, except for in the semantic fluency task where the TBIWP group illustrated greater word production. Interestingly, schizophrenia patients produced the second largest mean words for all three phonological fluency trials (and their cumulative total), followed by the TBIWP group (see Figure 7.5 for z-score comparison). However, with a conservative cutoff of \( p < .01 \) (Green & Salkind, 2004), group means were statistically different for the phonological fluency (a) trial, and cumulative total alone. According to Levine and Hullett (2002) both of these effects were medium to large in size (Table 7.13). For phonological fluency (a), post hoc SNK tests showed that word production from the PFTBI group was reduced relative to word production from the schizophrenia and healthy controls, who were comparable. Word production for the
Table 7.13  
*Group Comparisons on Phonological and Semantic Fluency*

<table>
<thead>
<tr>
<th>Measure</th>
<th>HC</th>
<th>TBIWP</th>
<th>SCZ</th>
<th>PFTBI</th>
<th>$F^a$</th>
<th>$P$</th>
<th>Effect Size (partial $\eta^2$)</th>
<th>Post Hoc (SNK)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phonological Fluency (f)</td>
<td>16.39 (4.25)</td>
<td>14.50 (5.15)</td>
<td>14.91 (5.50)</td>
<td>11.20 (5.79)</td>
<td>2.44</td>
<td>.07</td>
<td>.11</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>[14.27, 18.51]</td>
<td>[11.29, 17.72]</td>
<td>[12.79, 17.03]</td>
<td>[7.99, 14.42]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phonological Fluency (a)</td>
<td>15.35 (3.65)</td>
<td>11.40 (4.01)</td>
<td>14.04 (5.21)</td>
<td>9.70 (4.19)</td>
<td>4.74</td>
<td>.005</td>
<td>.19</td>
<td>PFTBI=TBIWP&lt;SCZ=HC</td>
</tr>
<tr>
<td></td>
<td>[13.52, 17.18]</td>
<td>[8.63, 14.17]</td>
<td>[12.22, 15.87]</td>
<td>[6.93, 12.47]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phonological Fluency (s)</td>
<td>19.21 (5.33)</td>
<td>14.20 (4.94)</td>
<td>16.00 (5.97)</td>
<td>13.50 (5.68)</td>
<td>3.43</td>
<td>.02</td>
<td>.14</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>[16.90, 21.54]</td>
<td>[10.68, 17.72]</td>
<td>[13.68, 18.32]</td>
<td>[9.98, 17.02]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phonological Fluency Total</td>
<td>50.96 (11.41)</td>
<td>40.10 (13.33)</td>
<td>45.78 (14.30)</td>
<td>34.40 (14.08)</td>
<td>4.22</td>
<td>.009</td>
<td>.17</td>
<td>PFTBI&lt;HC</td>
</tr>
<tr>
<td></td>
<td>[45.47, 56.44]</td>
<td>[31.78, 48.42]</td>
<td>[40.30, 51.27]</td>
<td>[26.08, 42.72]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Semantic Fluency Total</td>
<td>20.70 (3.75)</td>
<td>21.50 (5.76)</td>
<td>19.17 (5.80)</td>
<td>16.30 (5.17)</td>
<td>2.30</td>
<td>.09</td>
<td>.10</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>[18.59, 22.80]</td>
<td>[18.30, 24.70]</td>
<td>[17.07, 21.28]</td>
<td>[13.10, 19.50]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$^a$ Analysis of Variance (ANOVA).
Figure 7.5. Standardised participant group means (z-scores) for phonological (‘f’, ‘a’, ‘s’) and total words produced and semantic fluency. Healthy control data represents the zero point. Error bars represent standard error of the mean and are colour coded to enhance visibility.
The total phonological fluency data indicated that the PFTBI group showed significantly reduced word production relative to healthy controls, whereas the TBIWP and schizophrenia performance was statistically comparable to all other groups. No other statistically significant differences were shown to verbal fluency.

### 7.5.4.2 Fluency type.

Descriptive and inferential statistics for the paired-sample t-test comparisons are contained in Table 7.14. All groups illustrated greater semantically-driven fluency relative to their performance on phonologically-driven fluency, and these were all large in effect, except for the healthy comparisons which were medium to large in size (Green & Salkind, 2005).

### Table 7.14

**Paired Sample t-test Comparisons for Fluency Type**

<table>
<thead>
<tr>
<th></th>
<th>Mean (Standard Deviation)</th>
<th>t-statistic</th>
<th>p</th>
<th>Effect Size (Cohen’s d)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Phonological Fluency*</td>
<td>Semantic Fluency</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HC (n = 23)</td>
<td>16.99 (3.80)</td>
<td>20.70 (3.75)</td>
<td>-3.16</td>
<td>.005</td>
</tr>
<tr>
<td>TBIWP (n = 10)</td>
<td>13.37 (4.44)</td>
<td>21.50 (5.76)</td>
<td>-6.07</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>SCZ (n = 23)</td>
<td>15.26 (4.77)</td>
<td>19.17 (5.80)</td>
<td>-3.84</td>
<td>.001</td>
</tr>
<tr>
<td>PFTBI (n = 10)</td>
<td>11.47 (4.69)</td>
<td>16.30 (5.17)</td>
<td>-4.19</td>
<td>.002</td>
</tr>
</tbody>
</table>

*Phonological fluency score here was the total divided by three (i.e., originally derived from three trials) to be compatible with semantic fluency totals (i.e., only one trial).*

### 7.5.4.3 Clustering and switching.

Descriptive and inferential statistics for the analysis of clusters and switches produced by the cohorts on the phonological and semantic fluency task are contained in Table 7.15. Total clusters and mean cluster size from all cohorts was similar; approximately one and a half clusters with two words per cluster on the phonological task, and four clusters with three words per cluster on the semantic task. Accordingly, there were no group-wise differences shown to the number of clusters or the mean cluster size produced for either fluency trial. However, a greater group distinction was shown to the mean number of switches, with PFTBI patients switching between clusters the least of any cohort during both fluency trials. This was followed by TBIWP, schizophrenia, and the healthy cohort on the phonological fluency trial, and by the schizophrenia, TBIWP, and healthy cohort on the semantic fluency trial (see Figure 7.6 for these patterns). Post Hoc Dunnett C tests indicated that PFTBI patients made fewer switches relative to the healthy
Table 7.15

*Group Comparisons on Fluency Clustering and Switching*

<table>
<thead>
<tr>
<th>Measure</th>
<th>Mean (Standard Deviation) [95% confidence intervals]</th>
<th>F* (df = 3.62)</th>
<th>P</th>
<th>Effect Size (partial η²)</th>
<th>Post Hoc (Dunnett C)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HC (n = 23)</td>
<td>TBIWP (n = 10)</td>
<td>SCZ (n = 23)</td>
<td>PFTBI (n = 10)</td>
<td></td>
</tr>
<tr>
<td><strong>Phonological Fluency</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Clusters</td>
<td>1.51 (0.41)</td>
<td>1.25 (0.56)</td>
<td>1.44 (0.51)</td>
<td>1.25 (0.48)</td>
<td>2.61</td>
</tr>
<tr>
<td></td>
<td>[1.33, 1.69]</td>
<td>[0.84, 1.65]</td>
<td>[1.22, 1.66]</td>
<td>[0.90, 1.59]</td>
<td>.06</td>
</tr>
<tr>
<td>Mean Cluster Size</td>
<td>3.10 (1.24)</td>
<td>2.13 (1.41)</td>
<td>2.68 (1.11)</td>
<td>2.13 (1.15)</td>
<td>1.31†</td>
</tr>
<tr>
<td></td>
<td>[2.57, 3.64]</td>
<td>[1.13, 3.14]</td>
<td>[2.20, 3.16]</td>
<td>[1.31, 2.95]</td>
<td>.30</td>
</tr>
<tr>
<td>Switches</td>
<td>10.78 (2.51)</td>
<td>9.20 (2.87)</td>
<td>9.68 (3.48)</td>
<td>7.67 (3.43)</td>
<td>2.73</td>
</tr>
<tr>
<td></td>
<td>[9.70, 11.87]</td>
<td>[7.15, 11.25]</td>
<td>[8.18, 11.19]</td>
<td>[5.21, 10.12]</td>
<td>.05</td>
</tr>
<tr>
<td><strong>Semantic Fluency</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Clusters</td>
<td>4.35 (1.03)</td>
<td>3.70 (1.34)</td>
<td>3.83 (1.47)</td>
<td>3.50 (0.97)</td>
<td>1.51</td>
</tr>
<tr>
<td></td>
<td>[3.90, 4.79]</td>
<td>[2.74, 4.66]</td>
<td>[3.19, 4.46]</td>
<td>[2.80, 4.20]</td>
<td>.22</td>
</tr>
<tr>
<td>Mean Cluster Size</td>
<td>3.01 (1.12)</td>
<td>3.09 (1.15)</td>
<td>3.80 (2.58)</td>
<td>3.00 (1.10)</td>
<td>0.41†</td>
</tr>
<tr>
<td></td>
<td>[2.52, 3.49]</td>
<td>[2.67, 3.91]</td>
<td>[2.68, 4.91]</td>
<td>[2.22, 3.79]</td>
<td>.75</td>
</tr>
<tr>
<td>Switches</td>
<td>6.83 (2.37)</td>
<td>6.60 (2.17)</td>
<td>5.70 (2.82)</td>
<td>4.10 (0.74)</td>
<td>9.48†</td>
</tr>
<tr>
<td></td>
<td>[5.80, 7.85]</td>
<td>[5.05, 8.15]</td>
<td>[4.48, 6.91]</td>
<td>[3.57, 4.63]</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

*a Analysis of Variance (ANOVA)
†Welsh F statistic.
Figure 7.6. Standardised participant group means (z-scores) for clusters and switches produced on the phonological and semantic fluency tasks. Healthy control data represents the zero point. Error bars represent standard error of the mean and are colour coded to enhance visibility.
cohort during the phonological task. However, on the semantic fluency task the psychotic cohorts had matched and fewer switches relative to the remaining comparison cohorts. Patients with schizophrenia were also matched with the TBIWP and healthy cohort on this trial.

7.5.5 Semantic priming.

7.5.5.1 Reaction times and percentage accuracy.

Descriptive statistics for the semantic priming task are presented in Table 7.16. At the short SOA, RTs were fastest from the healthy cohort, followed by the psychosis cohorts (i.e., schizophrenia and PFTBI patients with similar RT’s), then followed by the TBIWP group who were the slowest. The same pattern was shown for RTs at the long SOA, except that patients with schizophrenia illustrated almost identical performance to the healthy cohort in the related condition, with poorer performance from PFTBI patients. Despite the largest RT difference arising from healthy and TBIWP patient comparisons, these groups alone showed hypopriming at the long SOA, that is, faster (mean) responses to unrelated versus related word pairs (hypopriming is discussed in the following Section 7.5.5.2: Derived Priming). Figure 7.7 illustrates these patterns in standardised scores.

Nonetheless, repeated measures analysis of variance revealed that the patterns in mean RTs across cohorts were not statistically different; no RT main effect was shown for participant group (p= .10). Reaction times (RTs) were faster overall at the short SOA (M = 895.89ms, SD = 92.48) relative to the long SOA (M = 1,385.42ms, SD = 96.72) with a large effect size (Levine & Hullett, 2002); main effect for SOA, $F (1, 51) = 1251.44, p < .001$, partial $\eta^2 = .96$. RTs were also faster to semantically related (M =1,134.401ms, SD = 84.17), relative to unrelated (M =1,147.30ms, SD = 85.29) word pairs; main effect for word pair relationship, $F (1, 51) = 5.43, p = .02$, partial $\eta^2 = .10$ (a medium effect size; Levine & Hullett, 2002). No interaction effects were demonstrated for the RT data.

The poorest accuracy was shown by the PFTBI group to both related and unrelated word pair conditions, and at both short and long SOAs. Although the differences are small, the schizophrenia group actually showed the greatest accuracy to related word pairs at the short SOA, followed by TBIWP and healthy control cohorts. However, at the long SOA (i.e., controlled processing), the healthy and TBIWP groups showed equal greatest accuracy, followed by schizophrenia patients. For the unrelated conditions the pattern of accuracy scores was identical at both SOAs; greatest accuracy was shown by the healthy group,
<table>
<thead>
<tr>
<th></th>
<th>HC (n = 18)</th>
<th>TBIWP (n = 10)</th>
<th>SCZ (n = 18)</th>
<th>PFTBI (n = 9)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Related</td>
<td>Unrelated</td>
<td>Related</td>
<td>Unrelated</td>
</tr>
<tr>
<td><strong>Short SOA (250ms)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RT (ms)</td>
<td>866.97</td>
<td>877.73</td>
<td>922.44</td>
<td>945.66</td>
</tr>
<tr>
<td>(SD)</td>
<td>(75.09)</td>
<td>(55.95)</td>
<td>(97.28)</td>
<td>(91.72)</td>
</tr>
<tr>
<td>95% CI</td>
<td>[820.01, 913.92]</td>
<td>[859.44, 887.15]</td>
<td>[827.59, 855.04]</td>
<td>[815.86, 837.17]</td>
</tr>
<tr>
<td>% Acc.</td>
<td>93.29</td>
<td>93.05</td>
<td>94.58</td>
<td>94.02</td>
</tr>
<tr>
<td>(SD)</td>
<td>(8.47)</td>
<td>(8.69)</td>
<td>(5.91)</td>
<td>(6.82)</td>
</tr>
<tr>
<td>95% CI</td>
<td>[89.37, 97.20]</td>
<td>[89.23, 98.33]</td>
<td>[89.33, 95.55]</td>
<td>[90.05, 95.96]</td>
</tr>
<tr>
<td><strong>Long SOA (750 ms)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RT (ms)</td>
<td>1352.30</td>
<td>1349.37</td>
<td>1437.13</td>
<td>1434.39</td>
</tr>
<tr>
<td>(SD)</td>
<td>(63.10)</td>
<td>(63.58)</td>
<td>(79.51)</td>
<td>(81.08)</td>
</tr>
<tr>
<td>95% CI</td>
<td>[1309.73, 1394.87]</td>
<td>[1303.05, 1380.02]</td>
<td>[1372.24, 1309.95]</td>
<td>[1332.02, 1323.74]</td>
</tr>
<tr>
<td>% Acc.</td>
<td>95.83</td>
<td>95.13</td>
<td>95.83</td>
<td>94.02</td>
</tr>
<tr>
<td>(SD)</td>
<td>(4.04)</td>
<td>(4.79)</td>
<td>(3.93)</td>
<td>(8.80)</td>
</tr>
<tr>
<td>95% CI</td>
<td>[92.06, 99.61]</td>
<td>[90.26, 99.83]</td>
<td>[90.77, 100.90]</td>
<td>[91.37, 96.04]</td>
</tr>
</tbody>
</table>

*Note.* RT data reflects correct responses only.
Figure 7.7. Standardised participant group means (z-scores) for reaction time (RT) data for related and unrelated conditions at both the short (250ms) and long (550ms) SOA. Healthy control data represents the zero point. Error bars represent standard error of the mean and are colour coded to enhance visibility.
Figure 7.8. Standardised participant group means (z-scores) for the accuracy data for related and unrelated conditions at both the short (250ms) and long (550ms) SOA. Healthy control data represents the zero point. Error bars represent standard error of the mean and are colour coded to enhance visibility.
followed by schizophrenia, TBIWP, and finally, PFTBI patients. Accuracy to the unrelated conditions also showed a greater variation in group means, especially at the long SOA (see Figure 7.8 for this illustration in standardised scores). Interestingly, the PFTBI cohort illustrated accuracy hypopriming at both SOAs, not demonstrated by any of the three comparison groups.

No main effect for participant group was illustrated in the accuracy data ($p = .09$), nor was there a main effect for SOA ($p = .79$). However, greater response accuracy was shown to words in the semantically related condition ($M = 93.04, SD = 7.47$) relative to the unrelated condition ($M = 90.95, SD = 7.38$); main effect for word pair relationship, $F(1, 51) = 10.34, p = .01$, partial $\eta^2 = .17$ (a medium to large effect size; Levine & Hullett, 2002).

A participant group x word pair interaction was also illustrated that acknowledges the accuracy hypopriming shown by the PFTBI group, $F(3, 51) = 3.65, p = .019$, partial $\eta^2 = .18$. That is, all three comparison groups showed greater accuracy to semantically related word pairs relative to unrelated word pairs, whereas the PFTBI group showed the opposite pattern. The effect is considered medium to large in size (Levine & Hullett, 2002) and is illustrated in Figure 7.9. However, once the reduced alpha level ($p < .01$) was applied to account for the potential inequality of variance-covariance matrices, this interaction was no longer significant.

![Figure 7.9](image.png)

*Figure 7.9.* Participant group x word (pair) relationship interaction. Error bars represent standard error of the mean and are colour coded to enhance visibility. Note that the y-axis spans ~80-100% accuracy for illustration of the interaction, and group differences in percentage accuracy are therefore overemphasised.
7.5.5.2 Derived priming (RTs and accuracy).

RT and accuracy derived priming means and standard error scores across the four groups are presented in Figures 7.10 and 7.11 respectively. At the short SOA, the greatest degree of RT priming was shown by the schizophrenia group, followed by the TBIWP, PFTBI, and healthy groups respectively. Accuracy priming was the greatest for TBIWP patients, followed by schizophrenia, PFTBI, and healthy groups respectively. Again, as noted, the PFTBI group illustrated hypopriming in this condition.

At the long SOA, derived RT priming was again the greatest for schizophrenia patients, followed by PFTBI, TBIWP, and healthy cohorts respectively. Hypopriming was demonstrated here by the healthy and TBIWP groups as previously noted. Accuracy priming at the long SOA followed the same pattern as at the short SOA; the greatest priming shown by TBIWP patients, followed by schizophrenia, PFTBI, and healthy groups respectively, with hypopriming demonstrated by the PFTBI cohort alone in this condition.

Despite the variable patterns of derived priming across groups, multivariate analysis of variance (MANOVA) indicated that no significant participant group differences were demonstrated by derived priming scores; Wilks’s Λ = .77, F (12, 127.29) = 1.12, p = .35, partial η² = .09. Significance values for the tests of between-subjects effects were as follows: Short SOA; RT priming, p = .92, and accuracy priming, p = .20. Long SOA; RT priming, p = .61, and accuracy priming, p = .07.

7.5.6 Probabilistic reasoning.

7.5.6.1 Participant group comparisons.

Group means and standard deviations for the probabilistic reasoning task are shown in Table 7.17. The descriptive trends are discussed first, followed by the outcome of group comparisons.

7.5.6.1.1 Initial prediction.

For the first condition (i.e., ratio 85:15) the TBIWP group were best at estimating the probability that a pink bead would be drawn at random (i.e., 85% likelihood), followed by the healthy cohort (although the standard deviation for the healthy group indicated moderate variability in their individual responses on this task). The schizophrenia and PFTBI patients tended to underestimate the likelihood of a pink bead, with the largest mean underestimation illustrated by the PFTBI group. Substantial variability was also shown by both psychotic cohorts.
Figure 7.10. Mean reaction time priming across the four participant groups at both short and long stimulus onset asynchrony (SOA) conditions. Error bars represent standard error of the mean. *Negative values indicate hypopriming (i.e., decrease in reaction times to semantically unrelated relative to related stimulus pairs). Note. n = 18, 18, 10, and 9 for healthy control, schizophrenia, TBIWP, and PFTBI groups respectively.
Figure 7.11. Mean accuracy priming across the four participant groups at both short and long stimulus onset asynchrony (SOA) conditions. Error bars represent standard error of the mean. *Negative values indicate hypopriming (i.e., decrease in percentage accuracy to semantically related relative to unrelated stimulus pairs). Note. n = 18, 18, 10, and 9 for healthy control, schizophrenia, TBIWP, and PFTBI groups respectively.
on this index, with the PFTBI cohort also most variable in their estimates. However, in the more difficult condition where the ratio is 60:40, there was much less variability across all groups and closer estimations between groups. Nonetheless, the PFTBI group still showed the poorest estimation and the largest variability, followed by the healthy cohort, with the TBIWP and schizophrenia groups performing quite well and similarly.

Table 7.17
Descriptive Statistics for the Probabilistic Reasoning Task

<table>
<thead>
<tr>
<th>Measure</th>
<th>Mean (Standard Deviation)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HC (n = 23)</td>
</tr>
<tr>
<td>Prediction (C1)</td>
<td>81.96 (14.60)</td>
</tr>
<tr>
<td>Prediction (C2)</td>
<td>58.26 (5.76)</td>
</tr>
<tr>
<td>Draws-to-Decision (C1)</td>
<td>4.78 (2.19)</td>
</tr>
<tr>
<td>Draws-to-Decision (C2)</td>
<td>17.22 (5.44)</td>
</tr>
<tr>
<td>Decision Confidence (C1)</td>
<td>89.43 (5.44)</td>
</tr>
<tr>
<td>Decision Confidence (C2)</td>
<td>74.13 (13.03)</td>
</tr>
</tbody>
</table>

*Note. C1 = Condition 1 (ratio 85:15); C2 = Condition 2 (ratio 60:40).*

7.5.6.1.2 Draws-to-decision.

In the first condition (i.e., ratio 85:15) healthy controls were fastest to make a decision. This was followed by the TBIWP, PFTBI, and finally the schizophrenia patients who were most conservative, making a decision, on average, at the seventh or eighth trial. Note, however, that there was some moderate variability from both psychotic cohorts. Yet, in the more difficult condition (i.e., ratio 60:40) patients with schizophrenia tended to make the earliest decision, followed by the PFTBI, healthy, and TBIWP groups (albeit, again, some moderate variability was shown from both psychotic groups, as well as the healthy group in this condition).

7.5.6.1.3 Percentage confidence.

Finally, self-estimated confidence followed the same pattern over both conditions; the PFTBI patients were most confident, followed by TBIWP patients, and then by schizophrenia and healthy cohorts who were quite similar in their degree of certainty for both conditions. However, self-estimated confidence was quite variable in the second and more difficult condition for all groups (see Figure 7.12 for an illustration of these patterns).
Figure 7.12. Standardised participant group means (z-scores) for probabilistic reasoning (bead-colour prediction, draws-to-decision, and degree of certainty upon decision) in Condition 1 (C1; ratio 85:15) and Condition 2 (C2; ratio 60:40). Healthy control data represents the zero point. Error bars represent standard error of the mean and are colour coded to enhance visibility.
Table 7.18

Multiple Group Comparisons for the Prediction Data (Probabilistic Reasoning) Conditions One and Two; Significance of T-tests, Effect Size and 95% Confidence Intervals

<table>
<thead>
<tr>
<th></th>
<th>HC &amp; TBIWP (df=31)</th>
<th>HC &amp; SCZ (df=44)</th>
<th>HC &amp; PFTBI (df=31)</th>
<th>SCZ &amp; TBIWP (df=31)</th>
<th>SCZ &amp; PFTBI (df=31)</th>
<th>TBIWP &amp; PFTBI (df=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>C1</td>
<td>C2</td>
<td>C1</td>
<td>C2</td>
<td>C1</td>
<td>C2</td>
</tr>
<tr>
<td>$t^a$</td>
<td>-.76</td>
<td>-.38</td>
<td>.51</td>
<td>-.59</td>
<td>.77</td>
<td>.28</td>
</tr>
<tr>
<td>$p$</td>
<td>.45</td>
<td>.71</td>
<td>.61</td>
<td>.56</td>
<td>.45</td>
<td>.78</td>
</tr>
<tr>
<td>$d^b$</td>
<td>-0.13</td>
<td>-0.07</td>
<td>0.08</td>
<td>-0.09</td>
<td>0.13</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Note. C1 = ratio 85.15; C2 = ratio 60.40.

$a$ Independent Samples $t$-test Statistic.

$b$ Cohen’s $d$ effect size.

*Equal variances not assumed.
7.5.6.1.4 Group-wise comparisons.

Table 7.18 presents the group comparison data for the initial predictions, including significance of the t-tests, effect size, and 95% confidence intervals. Despite the aforementioned trends, no significant differences were demonstrated from the independent samples t-tests (i.e., initial prediction data, Table 7.18), nor were any main effects demonstrated for cohort membership on the repeated measures analysis (i.e., draws-to-decision and self-rated confidence, \( p = .23 \)). The repeated measures ANOVA revealed a main effect for “index”, where draws-to-decision (choices from 1-20, \( M = 11.33, SD = 7.43 \)) were consistently smaller in value than the self-rated percentage confidence associated with a participants’ decision (\( M = 83.03\%, SD = 13.37 \)); \( F(1, 62) = 2.446.86, p < .001, \) partial \( \eta^2 = .98. \) A ratio x “index” interaction was also shown where participants made a decision earlier (\( M = 6.03, SD = 4.63 \)) and were more sure of their judgement (\( M = 89.77\%, SD = 5.61 \)) for the first trial (i.e., 85:15), relative to the more difficult second trial (i.e., 60:40) where they decided later (\( M = 16.64, SD = 5.71 \)) and were less sure of their decision (\( M = 76.29, SD= 15.38 \)); \( F(1, 62) = 89.79, p < .001, \) partial \( \eta^2 = .59. \) Both the main effect and interaction effect demonstrated by this data have large effect sizes associated with them (Levine & Hullett, 2002).

7.5.6.1.5 JTC behaviour.

The JTC behaviour of each participant group is contained in Table 7.19 along with the inferential statistics for the group comparisons. Patients with schizophrenia showed the greatest amount of JTC behaviour across both conditions. For condition one (i.e., 85:15) this was followed by healthy, PFTBI, and finally TBIWP cohorts. However, for condition two (i.e., 60:40) no other cohort showed JTC behaviour. Nonetheless, statistical group comparisons determined that JTC behaviour was not significantly different across the cohorts for either condition (see Table 7.19).

### Table 7.19

**Group Comparisons on JTC Behaviour**

<table>
<thead>
<tr>
<th>Condition</th>
<th>HC (n = 23)</th>
<th>TBIWP (n = 10)</th>
<th>SCZ (n = 23)</th>
<th>PFTBI (n = 10)</th>
<th>Chi-Square Statistic</th>
<th>( p )</th>
<th>Effect Size (Cramer’s V)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ratio 85:15 (C1)</td>
<td>21.74%</td>
<td>10%</td>
<td>26.09%</td>
<td>20%</td>
<td>( \chi^2(3, N=66)=1.09 )</td>
<td>.78</td>
<td>.13</td>
</tr>
<tr>
<td>Ratio 60:40 (C2)</td>
<td>0%</td>
<td>0%</td>
<td>4.35%</td>
<td>0%</td>
<td>( \chi^2(3, N=66)=1.90 )</td>
<td>.59</td>
<td>.17</td>
</tr>
</tbody>
</table>
7.5.6.2 *Presence/absence of delusions.*

Group means and standard deviations for the probabilistic reasoning data according to the presence/absence of delusions are contained in Table 7.20.

7.5.6.2.1 *Initial prediction.*

Descriptive statistics indicated a tendency for patients with delusions to underestimate the likelihood of a pink bead being drawn on the first trial (i.e., condition one; ratio 85:15), whereas predictions were almost matched exactly for condition two (i.e., ratio 60:40). However, there was quite large variability in the responses for both conditions, especially from the patients with delusions.

7.5.6.2.2 *Draws-to-decision.*

For the first condition (i.e., ratio 85:15), patients with delusions tended to be more conservative in their “draws-to-decision” relative to the group without delusions. However, deluded patients tended to decide sooner during the second, and more difficult, condition (i.e., ratio 60:40).

7.5.6.2.3 *Percentage confidence.*

Self-rated confidence for both conditions was comparable across deluded and non-deluded groups. However, quite a large variability in confidence was shown for the second condition, especially from patients with delusions. These descriptive trends are illustrated in Figure 7.13.

Table 7.20

<table>
<thead>
<tr>
<th>Measure</th>
<th>Mean (Standard Deviation)</th>
<th>Delusions (n = 31)</th>
<th>No Delusions (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prediction (C1)</td>
<td>78.23 (20.56)</td>
<td>82.20 (14.00)</td>
<td></td>
</tr>
<tr>
<td>Prediction (C2)</td>
<td>58.58 (5.40)</td>
<td>58.40 (5.54)</td>
<td></td>
</tr>
<tr>
<td>Decision Trial No. (C1)</td>
<td>7.16 (6.13)</td>
<td>5.00 (2.27)</td>
<td></td>
</tr>
<tr>
<td>Decision Trial No. (C2)</td>
<td>15.42 (6.58)</td>
<td>17.44 (5.27)</td>
<td></td>
</tr>
<tr>
<td>Decision Confidence (C1)</td>
<td>89.81 (6.12)</td>
<td>89.44 (5.37)</td>
<td></td>
</tr>
<tr>
<td>Decision Confidence (C2)</td>
<td>76.13 (17.88)</td>
<td>75.20 (13.03)</td>
<td></td>
</tr>
</tbody>
</table>

*Note.* C1 = ratio 85:15; C2 = ratio 60:40.
Figure 7.13. Standardised group means (z-scores) according to scores on the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987) for probabilistic reasoning (bead-colour prediction, draws-to-decision, and degree of certainty upon decision) in Condition 1 (C1; ratio 85:15) and Condition 2 (C2; ratio 60:40). Data from non-deluded participants represents the zero point. Error bars represent standard error of the mean and are colour coded to enhance visibility.
7.5.6.2.4 JTC behaviour.

Descriptive and inferential statistics for the JTC analysis are contained in Table 7.21. Patients with delusions demonstrated the greatest amount of JTC behaviour across both conditions, however, the mean difference between the groups was small.

Table 7.21
JTC Behaviour According to the Presence of Delusions on the PANSS

<table>
<thead>
<tr>
<th>Condition</th>
<th>Delusions (n = 31)</th>
<th>No Delusions (n = 25)</th>
<th>Chi-Square Statistic</th>
<th>p</th>
<th>Effect Size (Cramer’s V)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ratio 85:15</td>
<td>25.81%</td>
<td>20%</td>
<td>$\chi^2$ (1, N=56)=.26</td>
<td>.61</td>
<td>.07</td>
</tr>
<tr>
<td>Ratio 60:40</td>
<td>3.23%</td>
<td>0%</td>
<td>$\chi^2$ (1, N=56)=.82</td>
<td>.37</td>
<td>.12</td>
</tr>
</tbody>
</table>

The independent samples $t$-tests (i.e., initial prediction data) indicated that there were no significant differences in the prediction data according to the presence/absence of delusions: Condition one, $t (54) = .82, p = .41, d = 0.22$; Condition two, $t (54) = -.12, p = .90, d = -.03$. Moreover, no main effect was illustrated according to the presence/absence of delusions on the repeated measures analysis, $F (1, 54) = .14, p = .71$, partial $\eta^2 = .003$, nor were any group-based interaction effects found, $p = .35-.85$. Similarly, there was no statistically significant difference in JTC behaviour between patients with delusions versus those without.

7.5.7 The Stroop task.

The Stroop task descriptive and inferential data is presented in Table 7.22. The group means for all Stroop trials and derived scores adhered to the same pattern. That is, patients with PFTBI showed the poorest performance, followed by schizophrenia, TBIWP, and finally the healthy group who showed superior performance across all trials (see Figure 7.14).

Group-wise analyses confirmed that the PFTBI patients were the poorest performers. For the colour, word, inhibition, and derived inhibition data, this was followed by schizophrenia, and then the healthy cohort, with TBIWP patients showing matched performance with both the schizophrenia and healthy groups. However, for the switching trial and the derived interference/switching score, all three comparison groups (i.e., healthy, TBIWP, and schizophrenia) showed equally superior performance relative to PFTBI patients. These effects were all quite large in size, ranging from .26-.38 (Levine & Hullett, 2002, see Table 7.22).

Total errors on the Stroop colour, and word, trials were assessed for group-wise differences, to investigate evidence for a speed-accuracy trade-off in the measurement of
Table 7.22

*Group Comparisons on the Stroop*

<table>
<thead>
<tr>
<th>Measure</th>
<th>Measure</th>
<th>HC</th>
<th>TBIWP</th>
<th>SCZ</th>
<th>PFTBI</th>
<th>F*</th>
<th>p</th>
<th>Effect Size (partial η²)</th>
<th>Post Hoc SNK/Dunnetts C Post Hoc Test to Account for Unequal Error Variance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroop Colour</td>
<td></td>
<td>25.52 (4.95)</td>
<td>28.10 (5.02)</td>
<td>34.45 (9.44)</td>
<td>48.10 (22.22)</td>
<td>8.99</td>
<td>&lt;.001</td>
<td>.37</td>
<td>HC=TBIWP&lt;TBIWP&lt;SCZ&lt;PFTBI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>[21.03, 30.01]</td>
<td>[21.29, 34.91]</td>
<td>[29.86, 39.05]</td>
<td>[41.29, 54.91]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroop-Word</td>
<td></td>
<td>18.48 (4.03)</td>
<td>21.40 (2.41)</td>
<td>23.32 (4.92)</td>
<td>30.60 (10.37)</td>
<td>11.54</td>
<td>&lt;.001</td>
<td>.36</td>
<td>HC=TBIWP&lt;TBIWP&lt;SCZ&lt;PFTBI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>[16.16, 20.80]</td>
<td>[17.88, 24.92]</td>
<td>[20.95, 25.69]</td>
<td>[27.08, 34.12]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroop-Inhibition</td>
<td></td>
<td>44.83 (10.35)</td>
<td>53.10 (21.23)</td>
<td>69.18 (26.32)</td>
<td>109.30 (66.09)</td>
<td>10.20</td>
<td>&lt;.001</td>
<td>.38</td>
<td>HC=TBIWP&lt;TBIWP&lt;SCZ&lt;PFTBI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>[31.72, 57.93]</td>
<td>[33.22, 72.98]</td>
<td>[55.78, 82.58]</td>
<td>[89.42, 129.18]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroop-Switching</td>
<td></td>
<td>54.65 (14.32)</td>
<td>67.40 (24.15)</td>
<td>72.59 (21.43)</td>
<td>112.30 (66.40)</td>
<td>8.51</td>
<td>&lt;.001</td>
<td>.30</td>
<td>HC=TBIWP=SCZ&lt;PFTBI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>[41.68, 67.63]</td>
<td>[47.72, 87.08]</td>
<td>[59.32, 85.86]</td>
<td>[92.62, 131.98]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroop-Interference</td>
<td></td>
<td>34.16 (9.05)</td>
<td>40.99 (20.27)</td>
<td>55.35 (23.69)</td>
<td>90.94 (60.33)</td>
<td>10.21</td>
<td>&lt;.001</td>
<td>.36</td>
<td>HC=TBIWP&lt;TBIWP=SCZ&lt;PFTBI</td>
</tr>
<tr>
<td>(derived)</td>
<td></td>
<td>[22.22, 46.11]</td>
<td>[22.88, 59.10]</td>
<td>[43.14, 67.56]</td>
<td>[72.83, 109.05]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroop-Switching/</td>
<td></td>
<td>43.99 (12.95)</td>
<td>55.29 (24.06)</td>
<td>58.76 (19.37)</td>
<td>93.94 (60.24)</td>
<td>7.26</td>
<td>&lt;.001</td>
<td>.26</td>
<td>HC=TBIWP=SCZ&lt;PFTBI</td>
</tr>
<tr>
<td>Interference (derived)</td>
<td></td>
<td>[32.12, 55.86]</td>
<td>[37.28, 73.29]</td>
<td>[46.62, 70.89]</td>
<td>[75.94, 111.95]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*a* Analysis of Variance (ANOVA).

*b* Welsh’s *F* statistic.

*c* Dunnetts C post hoc test to account for unequal error variance.
Figure 7.14. Standardised participant group means ($z$-scores) for the Stroop trials (colour, word, inhibition, and switching) and derived interference and switching-interference scores. Healthy control data represents the zero point. Error bars represent standard error of the mean and are colour coded to enhance visibility.
processing speed taken from these trials. Errors on both trials were the greatest from the PFTBI patients. This was followed by schizophrenia, healthy, and TBIWP patients on the Stroop colour trial, and TBIWP, schizophrenia, and healthy controls on the Stroop word trial. Errors rates were not significantly greater from any of the cohorts. These data are contained in Table 7.23.

Table 7.23

<table>
<thead>
<tr>
<th>Group</th>
<th>Stroop Colours</th>
<th>Stroop Words</th>
</tr>
</thead>
<tbody>
<tr>
<td>HC</td>
<td>0.43 (0.79)</td>
<td>0.09 (0.29)</td>
</tr>
<tr>
<td>TBIWP</td>
<td>0.30 (0.48)</td>
<td>0.40 (0.70)</td>
</tr>
<tr>
<td>SCZ</td>
<td>0.59 (0.96)</td>
<td>0.27 (0.55)</td>
</tr>
<tr>
<td>PFTBI</td>
<td>1.30 (1.34)</td>
<td>0.50 (0.97)</td>
</tr>
</tbody>
</table>

Kruskal-Wallis H: χ²(3, N=65) = 6.04, p = .11, Effect Size*: .09

Table 7.24

<table>
<thead>
<tr>
<th>Group</th>
<th>Stroop Colours</th>
<th>Stroop Words</th>
</tr>
</thead>
<tbody>
<tr>
<td>HC</td>
<td>0.43 (0.79)</td>
<td>0.09 (0.29)</td>
</tr>
<tr>
<td>TBIWP</td>
<td>0.30 (0.48)</td>
<td>0.40 (0.70)</td>
</tr>
<tr>
<td>SCZ</td>
<td>0.59 (0.96)</td>
<td>0.27 (0.55)</td>
</tr>
<tr>
<td>PFTBI</td>
<td>1.30 (1.34)</td>
<td>0.50 (0.97)</td>
</tr>
</tbody>
</table>

Kruskal-Wallis H: χ²(3, N=65) = 3.40, p = .33, Effect Size*: .05

* Chi-square statistic divided by N-1.

7.5.8 The Trail Making Test (TMT).

Table 7.24 presents the descriptive and inferential statistics for the TMT data. Group means for both the TMT trials and the derived difference score illustrated a similar pattern; the poorest performance from PFTBI patients, followed by schizophrenia, TBIWP, and the healthy cohort who showed the best performance (Figure 7.15). Means for the derived ratio score were much closer together, and although the PFTBI group still illustrated the furthest deviation from healthy performance, the F-test was not significant (i.e., no significant differences were shown between groups for the derived ratio score, see Table 7.24). It is noted, however, that the PFTBI ratio score is almost at the cut-off of 3 (i.e., 2.99), suggested by Arbuthnott and Frank (2000) as indicative of substantial set-switching dysfunction.

Group-wise comparisons confirmed that all three control groups performed equally better than PFTBI patients on the TMT Form B, and according to the derived difference score, and these effects were considered quite large (i.e., .25, and .20 respectively, Levine and Hullett, 2002). However, on Form A, SNK tests showed that PFTBI patients illustrated significantly reduced performance relative to the healthy cohort alone, while the TBIWP and schizophrenia patient performance was statistically comparable to all other cohorts. Similarly, this effect was considered to be of a medium to large size (Levine & Hullett, 2002, see Table 7.24).
<table>
<thead>
<tr>
<th>Measure</th>
<th>Mean (Standard Deviation) [95% confidence intervals]</th>
<th>$F^a$</th>
<th>$p$</th>
<th>Effect Size (partial $\eta^2$)</th>
<th>Post Hoc SNK</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HC $(n = 23)$</td>
<td>TBIWP $(n = 10)$</td>
<td>SCZ $(n = 23)$</td>
<td>PFTBI $(n = 10)$</td>
<td>(df = 3,62)</td>
</tr>
<tr>
<td>TMT Form A</td>
<td>27.17 (10.65) [14.74, 39.61]</td>
<td>28.90 (7.62) [10.04, 47.76]</td>
<td>42.91 (27.28) [30.48, 55.35]</td>
<td>62.30 (63.06) [43.44, 81.16]</td>
<td>4.22</td>
</tr>
<tr>
<td>TMT Form B</td>
<td>57.30 (24.19) [17.78, 96.83]</td>
<td>65.40 (19.85) [5.46, 125.34]</td>
<td>110.61 (122.30) [71.09, 150.13]</td>
<td>163.30 (153.47) [103.36, 223.24]</td>
<td>6.93</td>
</tr>
<tr>
<td>TMT Difference Score</td>
<td>30.13 (18.78) [0.75, 59.51]</td>
<td>36.50 (20.34) [-8.06, 81.06]</td>
<td>67.70 (97.09) [38.31, 97.08]</td>
<td>101.00 (99.60) [56.44, 145.56]</td>
<td>5.17</td>
</tr>
<tr>
<td>TMT Ratio Score (derived)</td>
<td>2.20 (.60) [1.87, 2.52]</td>
<td>2.37 (.83) [1.88, 2.87]</td>
<td>2.31 (.79) [1.98, 2.64]</td>
<td>2.99 (1.06) [2.50, 3.49]</td>
<td>1.66</td>
</tr>
</tbody>
</table>

$^a$Analysis of Variance (ANOVA).

$^b$In spite of the close raw scores shown between healthy controls and TBIWP, and the intermediate score shown in schizophrenia, only the healthy control cohort illustrated statistically significant differences relative to PFTBI patients when analyses were run using the transformed means and standard deviations.
Figure 7.15. Standardised participant group means (z-scores) for the Trail Making Test; Trials A and B, as well as total time difference between trials and derived trial ratio score. Healthy control data represents the zero point. Error bars represent standard error of the mean and are colour coded to enhance visibility.
7.5.9 Intelligence quotient (premorbid and current).

Descriptive and inferential statistics for NART (premorbid) and WASI (current) IQ are contained in Table 7.25, and a visual plot of the standardised data is presented in Figure 7.16. Mean scores on the NART were relatively similar for all groups, with the healthy cohort illustrating the highest score, followed by schizophrenia and PFTBI patients who were almost identical (i.e., $M=102.69$ and $M=102.47$ respectively), and TBIWP patients who demonstrated the lowest score. As discussed in Chapter 6.7: General Demographics, all four cohorts were classified as having a premorbid IQ score in the average range as defined by the NART.

Scores on the WASI (full scale equivalent and subscales) showed greater variability. The WASI full scale IQ and Matrix Reasoning subscale illustrated the same pattern across groups; that is, the largest score was shown by the healthy group, followed by TBIWP, schizophrenia, and PFTBI patients respectively. However, the Vocabulary subscale showed a pattern that reflected NART performance from the TBIWP patients. Healthy participants showed the highest score once again, followed by the schizophrenia, TBIWP, and PFTBI patient groups respectively. The breakdown of these scores according to WASI classifications was detailed in Chapter 6.7 General Demographics. Healthy controls were the only group that showed consistency in classifications; that is, they generally performed within the “average” range on measures of both “premorbid” and current IQ. The TBIWP and schizophrenia patients were classified instead as “low average”, and PFTBI patients were classified in the category below, as “borderline”.

As mentioned in Chapter Six (Section 6.7: General Demographics), mean scores on the NART were not statistically different across cohorts, indicating that they were matched on premorbid IQ. However, even with a conservative cut-off of $p < .01$, group means were statistically different on all three WASI scales (i.e., full scale IQ, Matrix Reasoning and Vocabulary, see Table 7.25). Post hoc SNK analysis revealed that on the WASI measurement of full scale IQ, as well as the Vocabulary subscale, PFTBI patients obtained the lowest score, followed by schizophrenia and TBIWP patients who were statistically comparable and healthy controls who obtained the highest score. On the Matrix Reasoning subscale, however, the psychosis cohorts (i.e., PFTBI and schizophrenia) performed similarly and statistically below the TBIWP and healthy cohorts, who were also statistically matched. These patterns are illustrated in the $z$-score plot in Figure 7.16.
Table 7.25
Group Comparisons on Premorbid and Current IQ

<table>
<thead>
<tr>
<th>Measure</th>
<th>HC (n = 23)*</th>
<th>TBIWP (n = 10)</th>
<th>SCZ (n = 23)</th>
<th>PFTBI (n = 10)</th>
<th>F^a</th>
<th>p</th>
<th>Effect Size (partial η²)</th>
<th>Post Hoc SNK</th>
</tr>
</thead>
<tbody>
<tr>
<td>NART IQ</td>
<td>105.00 (7.04)</td>
<td>100.40 (9.07)</td>
<td>102.69 (6.48)</td>
<td>102.47 (4.74)</td>
<td>F(3, 62)=1.15</td>
<td>.34</td>
<td>.05</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>[102.12, 107.88]</td>
<td>[96.04, 104.77]</td>
<td>[99.81, 105.57]</td>
<td>[98.10, 106.83]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WASI IQ</td>
<td>98.18 (11.20)</td>
<td>87.00 (10.15)</td>
<td>84.78 (11.96)</td>
<td>72.20 (16.50)</td>
<td>F(3, 61)=11.15</td>
<td>&lt;.001</td>
<td>.35</td>
<td>PFTBI&lt;SCZ=TBIWP&lt;HC</td>
</tr>
<tr>
<td></td>
<td>[92.96, 103.41]</td>
<td>[79.25, 94.75]</td>
<td>[79.67, 89.89]</td>
<td>[60.45, 79.95]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Matrix Reasoning</td>
<td>45.36 (7.31)</td>
<td>44.30 (8.86)</td>
<td>38.00 (7.60)</td>
<td>33.90 (8.81)</td>
<td>F(3, 61)=6.62</td>
<td>.001</td>
<td>.25</td>
<td>PFTBI=SCZ&lt;TBIWP=HC</td>
</tr>
<tr>
<td></td>
<td>[42.00, 48.73]</td>
<td>[39.31, 49.20]</td>
<td>[34.71, 41.29]</td>
<td>[28.91, 38.89]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vocabulary</td>
<td>51.86 (9.08)</td>
<td>38.80 (8.44)</td>
<td>43.43 (9.47)</td>
<td>30.90 (11.68)</td>
<td>F(3, 61)=12.21</td>
<td>&lt;.001</td>
<td>.38</td>
<td>PFTBI&lt;TBIWP=SCZ&lt;HC</td>
</tr>
<tr>
<td></td>
<td>[47.79, 55.94]</td>
<td>[32.76, 44.85]</td>
<td>[39.45, 47.42]</td>
<td>[24.86, 36.95]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

^a Analysis of Variance (ANOVA).

* n = 22 (healthy control WASI IQ, and Matrix Reasoning and Vocabulary Subscales).
Figure 7.16. Standardised participant group means (z-scores) for measures of premorbid and current IQ. Full scale and subscale data are shown for current (WASI) IQ. Healthy control data represents the zero point. Error bars represent standard error of the mean and are colour coded to enhance visibility.
### 7.5.10 Summary of group differences.

*Table 7.26* lists the measures where statistically significant differences were shown following group-wise comparisons performed in this chapter. Measures on which the PFTBI patients demonstrated isolated inferior performance are highlighted, and where this was not the case, equal inferior performance from one or both of the comparison patient groups is indicated. Significant group differences were shown to 30 of 52 individual cognitive neuropsychological measurements applied in this research. Of these 30, isolated inferior performance was shown by PFTBI patients 63.33% of the time. Equal inferior performance was shown by patients with psychosis (i.e., PFTBI and schizophrenia) on 13.33% of the remaining measurements, patients with TBI (i.e., PFTBI and TBIWP) on 3.57%, and by all patient comparisons relative to healthy performance on 21.43%.

#### Table 7.26

*Summary of Measures Illustrating Significant Group-wise Differences and Inferior Performance in PFTBI*

<table>
<thead>
<tr>
<th>Measures Illustrating Group Differences</th>
<th>Isolated Inferior Performance in PFTBI</th>
<th>Equal Inferior Performance in Psychosis (PFTBI and SCZ)</th>
<th>Equal Inferior Performance in TBI (PFTBI and TBIWP)</th>
<th>Equal Inferior Performance from all Patient Cohorts</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBANS</td>
<td>✓</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Immediate Memory Index</td>
<td>✗</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visuo-Spatial Index</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attention Index</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delayed Memory Index</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RBANS Total</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>List Learning Subscale</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Story Memory Subscale</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Figure Copy Subscale</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Line Orientation Subscale</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digit Span Subscale</td>
<td>✗</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coding Subscale</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>List Recall Subscale</td>
<td>✗</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Story Recall Subscale</td>
<td>✗</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Figure Recall Subscale</td>
<td>✗</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Verbal Fluency</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phonological Fluency (a)</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phonological Fluency</td>
<td>✗</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phonological switches</td>
<td>✗</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Semantic switches</td>
<td>✗</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stroop</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colour Trial</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Word Trial</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(continued)
Table 7.26  
**Summary of Measures Illustrating Significant Group-wise Differences and Inferior Performance in PFTBI**  
(Continued)

<table>
<thead>
<tr>
<th>Measures Illustrating Group Differences</th>
<th>Isolated Inferior Performance in PFTBI</th>
<th>Equal Inferior Performance in Psychosis (PFTBI and SCZ)</th>
<th>Equal Inferior Performance in TBI (PFTBI and TBIWP)</th>
<th>Equal Inferior Performance from all Patient Cohorts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhibition Trial</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Switching Trial</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Derived Interference Score</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Derived Switching/Interference Score</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trail Making Task (TMT)</td>
<td></td>
<td>X</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>TMT Form A</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TMT Form B</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TMT Difference Score</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WASI IQ</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WASI Full Scale IQ</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Matrix Reasoning Subscale</td>
<td>X</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vocabulary Subscale</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (carried over)</td>
<td>19 (63.33%)</td>
<td>4 (13.33%)</td>
<td>1 (3.57%)</td>
<td>6 (21.43%)</td>
</tr>
</tbody>
</table>

7.6 **Discussion**

A discussion pertaining to the results of group-wise comparisons detailed in this chapter follows. Findings are discussed according to the format of hypotheses (i.e., by cognitive neuropsychological domain, see Section 7.2: Hypotheses). Discussion is based primarily on the PFTBI patient data, except where hypotheses particular to another cohort were made. In general, PFTBI patients were expected to illustrate inferior performance on all measures relative to the three comparison cohorts, given their dual morbidity. As illustrated in Table 7.24 (in the previous results section), the PFTBI cohort illustrated the poorest performance 64.29% of the time on measures where group differences were shown. Where PFTBI patients did not demonstrate isolated inferior performance, they instead showed equal inferior performance with schizophrenia patients (10.71%), equal inferior performance with TBIWP patients (3.57%; one task), or equal inferior performance with both patient groups (21.43%). Accordingly, on all measures where group differences were shown, the healthy cohort illustrated superior performance as hypothesised.

7.6.1 **Visual-perceptual organisation.**

All three patient groups were expected to illustrate reduced visual-perceptual abilities, including both visuo-spatial and Gestalt abilities, relative to the healthy cohort.
7.6.1.1 RBANS visuo-spatial index.

Results from the RBANS Visuo-spatial index support hypothesised reductions in visuo-spatial processing from the patient groups. Superior performance was shown by the healthy cohort, followed by TBIWP, schizophrenia, and PFTBI patients who demonstrated the poorest performance. An expected, and relatively pronounced, decline in visuo-spatial processing was further illustrated by the PFTBI cohort. This is an important finding given that the nature of visuo-spatial processing in PFTBI is unclear from existing research (e.g., in Burg et al., 2000; Fujii & Ahmed, 2002; Fujii et al., 2004). These data also reflect selected literature that has established visuo-spatial deficits in patients with both TBIWP and schizophrenia (e.g., Joshua & Rossell, 2009; McKenna et al., 2006; Parnas et al., 2001; Patel et al., 2011; Ponsford et al., 2011; Shum et al., 2000; Silverstein et al., 2000).

Although significant reductions in visuo-spatial performance were illustrated by all three patient groups, it is imperative to acknowledge that the mean scores on this index from all four cohorts fell within the “average” range according to RBANS norms (Randolph, 1998). This may help to explain existing PFTBI literature that has relied on norm comparisons, and subsequently, reported intact visuo-spatial processing; similarly, the deficit in PFTBI was only apparent here relative to the comparison cohorts. The distinction between PFTBI and injury-matched TBIWP performance is especially striking, and suggests that the psychosis in PFTBI may be exerting a greater influence over visuo-spatial processing deficits than the effects of the injury. As such, the assessment of PFTBI against RBANS standardised norms, as an isolated procedure in the determination of patient visual-spatial proficiency, is discouraged.

With the above argument in mind, 30% of the PFTBI patient group demonstrated mean scores at two standard deviations below the RBANS normative scores. This finding reflects data from Fujii and Ahmed (2002) who reported that 41% of their case-reviewed PFTBI’s showed impaired visuo-spatial abilities relative to norm data. This represents a rare consistency in the literature, and may thereby offer a preliminary indication of the prevalence of visuo-spatial impairment in PFTBI. On the other hand, Fujii and Ahmed (2002) relied on case studies identified by literature search, and thus the comparison of various, and likely incompatible, measurements of visuo-spatial ability cannot be discounted.

Patients from the schizophrenia cohort performed up to four standard deviations below the normative data (i.e., 26.11% at two SD’s, 4.35% at three SD’s, 4.35% at four SD’s). Essentially the schizophrenia literature points to a perceptual organisation deficit that may be somewhat
heterogeneous in its degree (e.g., Passerieux et al., 1997; Schwartz-Place & Gilmore, 1980), and these findings support established heterogeneity further. A subset of the schizophrenia patient sample appeared to have more pronounced visuo-spatial deficits akin to those illustrated by the dual-diagnosis PFTBI group (i.e., as mentioned, one schizophrenia patient performed at 4 SD’s below the norm). At the other end of the spectrum, however, a subset of patients showed milder deficits akin to those illustrated by TBIWP patients. In fact, two schizophrenia patients performed at 2 SD’s above the norms on this index. This variation explains the intermediate but matched performance of the schizophrenia cohort with both superior TBIWP performance, and inferior PFTBI performance.

Overall these data indicate that PFTBI patients do in fact illustrate reduced visuo-spatial abilities, the extent of which appears to be heterogeneous, a feature of psychosis generally. Given statistically indistinguishable performance from the psychotic cohorts, these findings suggest that the spectrum of psychosis may be broadly associated with visuo-spatial deficits. However, whether the reduction in visuo-spatial processing is considered an impairment in PFTBI, especially where performance is assessed on the RBANS index relative to RBANS norms, may only be accurately determined on a patient by patient basis with reference to alternate complementary assessments.

7.6.1.2 Gabor Elements Contour Integration Task (GECIT).

Hypothesised differences in Gestalt processing were not supported by these data; no significant group-wise differences were shown on the GECIT task. Nonetheless, a non-significant tendency was shown by the psychosis cohorts (i.e., PFTBI and schizophrenia patients) to solve approximately one less card than the healthy and TBIWP cohorts.

The existing literature suggests that differences in task performance should be larger. For instance, poor Gestalt processing has been shown following even mild TBI (Rohling et al., 2011), and holistic/Gestalt processing is lateralised whereby patients with lesions in their right hemisphere demonstrate pronounced deficits in recalling and reproducing the global aspects of visual images (Delis et al., 1986; Robertson & Lamb, 1991). Injury to the right hemisphere was statistically matched across brain-injured cohorts in this research; 50% of TBIWP patients and 60% of PFTBI patients sustained a right hemisphere lesion, and 30% of TBIWP and 40% of PFTBI patients sustained a dual (i.e., both left and right) hemispheric injury. However, these figures indicate that an additional two PFTBI patients had sustained injury to their right hemisphere, and this may account for their observed trend in solving a mean of one less card than their injury counterparts.
This explanation does not, however, account for the same tendency demonstrated by patients with schizophrenia, suggesting once again that the presence of psychosis exerts the greater influence.

The findings are also inconsistent with the large literature indicating disruptions to Gestalt processing in schizophrenia (Joshua & Rossell, 2009; Parnas et al., 2001; Rief, 1991; Schwartz-Place & Gilmore, 1980; Silverstein et al., 2000). However, some authors have illustrated that deficits in schizophrenia are mediated by task difficulty, where patients are capable of employing global processing strategies when the salience of the Gestalt properties are strong (Landgraf et al., 2011; Rief, 1991). Thus, one explanation for statistically comparable group performance may relate to the salience of the Gestalt properties on the GECIT cards. The GECIT task was originally designed to assess perceptual grouping impairment in amblyopia (i.e., a vision deficiency such as blurriness, usually in one eye; Kovacs, Polat, & Norcia, 1996), and may therefore be less sensitive in schizophrenia. That is, the Gestalt properties may be too prominent on stimulus cards prior to the tenth card to adequately distinguish between healthy and compromised Gestalt processing in psychosis. However, Green et al. (2009) highlighted that at least six research projects have shown significant Gestalt processing impairment in schizophrenia using the GECIT task, with good test-retest reliability and minimal practice effects (Silverstein et al., 2000).

Studies have also reported that performance on the GECIT task appears to be influenced by the presence of disorganised symptoms, but not positive or negative symptoms (Silverstein, Kovacs, Corry, & Valone, 2000; Uhlhaas et al., 2005; Uhlhaas & Silverstein, 2005; Uhlhaas et al., 2006). In fact, the attenuation of disorganised symptoms has been associated with significant improvement on the GECIT (Uhlhaas et al., 2005; Uhlhaas & Silverstein, 2005). This is the most likely explanation for the matched performance shown here. Uhlaas et al. (2006) identified disorganised schizophrenia according to a PANSS conceptual disorganisation score of more than three (i.e., above the ‘mild’ classification, where thinking is circumstantial, tangential or paralogical, and there is some difficulty in goal-directed thoughts and/or some loosening of associations). By comparison, both psychosis cohorts in this research had mean scores on the PANSS conceptual disorganisation item below three (i.e., schizophrenia, $M = 2.87$, $SD = 1.74$; PFTBI, $M = 2.40$, $SD = 1.07$), classifying them as non-disorganised types, in accordance with their relatively unimpaired GECIT performance. As such, these findings appear to support the state rather than trait account of perceptual Gestalt disorganisation. Given that GECIT performance was comparable across psychotic groups, and with consideration for the visuo-spatial results on the RBANS index, these data provide further preliminary evidence that visual-perceptual processing of
a visuo-spatial and Gestalt nature may be deficient as a characteristic of the psychosis spectrum generally, rather than uniquely impaired in PFTBI relative to schizophrenia.

7.6.2 Language

7.6.2.1 RBANS language index.

Hypothesised impairments in language from the patient cohorts were not supported by data from the RBANS Language tasks. Instead, patient performance was matched with the healthy cohort on the overall Language Index score. The existing literature pertaining to all three patient groups suggests substantial language and communication deficits should be shown (DeLisi, 2001; Fujii & Ahmed, 2002; Fujii et al., 2004; Hinchliffe et al., 1998; LeBlanc et al., 2006; Levy et al., 2010; Rossell et al., 2010; Rossell & David, 2006; Sachdev et al., 2001). There is some evidence in the brain injury literature to suggest that the extent of damage to the language system post injury is mediated by the relative stability of verbal skills prior to the injury (LeBlanc et al., 2006). Elevated premorbid language may thus serve to protect the language skill set post injury. However, although this may be true for some cases, it was not supported by premorbid IQ (a language-based task) and relative performance on the RBANS Language index from the TBIWP cohort in this study.

Proficiency according to the RBANS Language index from all three patient cohorts was also contradictory to statistically impaired vocabulary, as indicated by their decreased performance on the WASI vocabulary subtest (discussed in Section 7.6.6). As such, failure to find group differences in RBANS Language may instead reflect the limited sensitivity of the relevant subtests, including; (i) inadequate task difficulty on the Picture Naming subtest, and (ii) inadequate power on the Semantic Fluency subtest. One hundred per cent of individuals from both the healthy and TBIWP cohorts performed at ceiling on the Picture Naming subtest, and the psychotic cohorts were not far behind: schizophrenia and PFTBI groups performed identically with only two patients below 100%; one at 80% (two errors) and one at 90% (one error). Because ceiling performance reduces task validity in the measurement of the desired construct, language ability, as indicated by the Picture Naming subtest, is likely to be inaccurate. Results from the Semantic Fluency subtest are discussed in more detail in the following section (i.e., verbal fluency). Briefly, the semantic fluency data illustrated graded performance, with a downward trend from the psychotic cohorts in the hypothesised direction. This is complementary to the existing, and substantial, semantic processing literature in psychosis (Henry & Crawford, 2005; Kremen et al., 2003; Landro & Ueland, 2008; Rossell et al., 1999). However, all three patient cohorts also demonstrated considerable variability on this task and, as such, failure to detect significantly meaningful
7.6.2.2 *Verbal fluency.*

Participants in both the healthy and TBIWP cohorts produced a greater mean number of semantic, relative to phonological, category words as expected. TBIWP patients were further expected to illustrate a general verbal fluency deficit by generating fewer words for both category types relative to the healthy cohort. This was true for the phonological fluency trials, although not statistically significant. However, mean semantic fluency was instead marginally increased from TBIWP patients (albeit, this amounted to a mean of less than one additional word). Prior research has illustrated impairments in both phonemic and semantic fluency post injury (Baldo & Shimamura, 1998; Grossman, 1981; Jurado et al., 1997; Jurado et al., 2000; Kave et al., 2011; Martin et al., 1990). Reduced phonological fluency from the TBIWP cohort demonstrate a trend reflecting this literature, however, deficient networks of attention and speeded cognition (e.g., executive function) may not have been impaired enough to impede verbal fluency in statistical analysis (Beauchamp et al., 2011; Madigan et al., 2000; Ponsford & Kinsella, 1992, Rios et al., 2004). The same may not be shown to the semantically-driven task because demands on the cognitive load are not as substantial when retrieval is semantically driven. Brain regions may also be specialised for fluency types; frontal regions for phonological fluency and temporal regions for semantic fluency (Henry & Crawford, 2004; Mummery et al., 2000; Pujol et al., 1996). Analysis according to lesion location was not possible due to sample size, however, lesion location does not appear to be driving the fluency data; greater injuries were sustained to temporal versus frontal regions in TBIWP, which implicate semantic, rather than phonological, fluency deficits. Nonetheless, given that mean differences did not reach significance, comparable executive (indicated by phonological fluency) and semantic processes in injured and healthy cohorts are supported by these fluency data.

It is worth noting that raw scores from the TBIWP cohort were below those of the schizophrenia cohort on all phonological fluency measures, with the opposite shown to the semantic fluency trial. TBIWP and schizophrenia patients have not been compared on verbal fluency to date, and this novel data demonstrates that executive processing deficits (e.g., attention, processing speed, effortful retrieval etc.) may be proportionately greater post injury, relative to
those associated with psychosis. The reverse shown for semantic fluency suggests that the semantic system appears to be more disorganised in schizophrenia, even with the higher likelihood of memory retrieval deficits in TBIWP. However, in light of the substantial overlap from the cohorts on these fluency measures, this interpretation is preliminary.

Impaired fluency from the schizophrenia cohort was illustrated descriptively for both fluency types, although the mean differences did not reach statistical significance. Reduced verbal fluency in schizophrenia is well established (Bozikas et al., 2005; Elvevag et al., 2001; Kremen et al., 2003; Landro & Ueland, 2008; Prescott et al., 2006; Vinogradov et al., 2002), however deficits are especially prominent for patients with substantial negative symptoms (Bowie et al., 2004; Sumiyoshi et al., 2005). The absence of statistical differences here may thus be explained by the clinical symptom profile of this group, given that the PANSS data from the schizophrenia cohort indicated minimal negative pathology. On the other hand, the poorest fluency performance was illustrated by the PFTBI cohort who also demonstrated the least amount of negative pathology.

Reduced fluency in PFTBI was shown to both tasks as hypothesised; they produced the smallest number of words relative to all comparison cohorts on all verbal fluency trials. However, differences only reached statistical significance in phonological fluency “a” and “total” trials. Furthermore, their performance was statistically comparable to TBIWP, and TBIWP/schizophrenia for the two trials respectively, essentially indicating that PFTBI patients share deficits with their single diagnosis counterparts. Accordingly, these findings support prior work from Burg et al. (2000) who showed matched PFTBI and psychosis fluency, but are inconsistent with Fujii et al. (2004) who reported performance indistinguishable from healthy participants. With regard to the descriptive patterns of performance, it is also noted that PFTBI fluency was more like TBIWP fluency on the phonological task, yet more like fluency in schizophrenia on the semantic task; PFTBI patients generated approximately two to three words below these cohorts in both examples. It is hypothesised that phonological fluency deficits in PFTBI, then, may stem primarily from the consequences of the traumatic brain injury (i.e., executive dysfunction), whereas semantic fluency deficits may instead stem from the effects of the existing psychosis.

Neither psychotic cohort demonstrated disproportionally greater impairment to semantically-driven fluency as hypothesised. Instead, semantic fluency was significantly increased.

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6 Memory deficits were not demonstrated by the TBIWP or schizophrenia patients on the RBANS Delayed Memory Scale beyond trend level. However, poor memory has been established in both cohorts by prior research (i.e., Broome et al., 2010; Lezak, 1979; Silver et al., 2001; Tate et al., 1991).
compared to phonological fluency from all cohorts. There is a large literature supporting relatively greater deficits in semantic fluency from patients with psychosis (e.g., Gouzoulis-Mayfrank et al., 2003; Henry & Crawford, 2005; Kremen et al., 2003; Rossell et al., 2010; Rossell et al., 1999), however, this is not supported in all studies (e.g., Landro & Ueland, 2008). Further, Rossell et al. (1999) found disproportionate and reduced semantic fluency to be true for patients with delusions alone. According to the PANSS and SAPS rating scales, delusions were matched for the psychotic cohorts, and within the mild to moderate range. This rating generally refers to delusions that are not held with conviction, or interfere little with cognition and behaviour. By contrast, Rossell et al. (1999) investigated patients with delusions rated between mild to severe on the SAPS rating scale, indicating firmly held, complex, pervasive and/or bizarre delusions with a major effect on behaviour (although it is not clear how many of the patients fit this category). Accordingly, reductions in the presence and degree of delusions in the PFTBI and schizophrenia patients in this research may underpin the apparently enhanced organisation of the semantic network suggested by these data.

Another speculation is that this result may reflect the type of fluency task used in this research. Studies typically use animal category fluency, whereas the RBANS Semantic Fluency subtest requires participants to generate lists of fruits and vegetables. Following administration of the task many participants indicated that during the production of their list they had mentally walked through the supermarket fruit/vegetable isle, and/or mentally scanned the contents of their refrigerator. Although a cognitive technique of this nature can be applied to most category types used to measure semantic fluency (e.g., animals, body parts), it may not be as readily applicable to animal category fluency, from which the majority of findings have been drawn. Most individuals would be more familiar with their supermarket/refrigerator than their closest farm or zoo, allowing the former to be more easily visualised. It is possible that the RBANS subtest may thus be confounded by the propensity of an individual to employ a cognitive strategy of this kind during the task. On the other hand, the failure to find statistically significant group differences in semantic fluency may reflect a lack of statistical power in the current dataset. The RBANS fluency subtest has been used to demonstrate poor semantic fluency in schizophrenia in the past, despite comparable fluency means and group variability to the data acquired here (e.g., Gogos et al., 2010). However, Gogos et al. (2010) incorporated group sizes of thirty-eight and forty-three for their schizophrenia and healthy cohorts respectively. Thus, larger group sizes may be required to account statistically for within group variability in semantic fluency in psychosis.
7.6.2.3 Clustering and switching.

Reductions in the number of clusters and switches (i.e., theoretically executive functions) produced during both fluency tasks were expected from TBIWP patients, however, the size of their clusters (i.e., theoretically a semantic ability) were predicted to match those from the healthy cohort. Instead, TBIWP performance was statistically matched to all three comparison cohorts across all clustering and switching measures. This is inconsistent with research indicating diminished cognitive switching (Kave et al., 2011; Stuss et al., 1998 Zakzanis et al., 2011) and clustering (Kave et al., 2011) post injury. However, intact clustering ability has also been reported by others for both fluency types (Raskin & Rearick, 1996; Zakzanis et al., 2011), as well as intact switching during semantic fluency (Zakzanis et al., 2011). Although TBIWP cluster sizes were comparable with the healthy cohort as expected, this is not considered evidence of intact semantic processing given the statistical comparability of all cohorts on this measure.

The greatest impairments in clustering and switching post injury were shown by Kave et al. (2011) who assessed patients with moderate to severe TBI at a maximum of 24 months post-injury. Evidence exists to suggest that fluency impairment, at least to switching between clusters, is worse following more severe injury (e.g., Zakzanis et al., 2011). Cognition also tends to improve gradually from one to 24 months post injury, with the most accurate picture of lasting deficits becoming apparent after the two year mark (for example see Schretlen and Shapiro [2003]). Thus, the cohort assessed by Kave et al. (2011) would be expected to show exceptional deficiency given their injury demographics. By contrast, the sample assessed by Zakzanis et al. (2011) had milder injury (i.e., 50% mTBI), and a greater latency between their injury and assessment ($M = 4.6$ yrs post injury), and deficits were found to semantic switching alone. Inconsistencies in the literature may therefore stem from variations in injury demographics. The absence of statistical differences in the current study may be attributed to injury variables in the same way. Mild injury had been sustained by 40% of TBIWP patients, and the cohort was assessed at a mean of 9.8 years following their TBI. As such, negligible impairment in mental clustering and switching might be expected from them as a group. Strictly then, these findings indicate intact executive and semantic processing in this TBIWP cohort.

Descriptively, however, TBIWP patients performed consistently below both healthy and schizophrenia cohorts, except for their total number of semantic switches where they outperformed patients with schizophrenia. As expected, this mirrors the descriptive trends previously discussed for verbal fluency, and is a further novel finding regarding the relative impairment of clustering and
switching capabilities in TBIWP and schizophrenia patients. However, bearing in mind that this
discussion pertains to non-significant trends, and injury severity and injury latency appear to have
substantial influence on these data, this pattern is once again considered preliminary. The influence
of lesion location is also noted as a potential mediator of clustering and switching proficiency here
(i.e., Troyer et al., 1997). As with the fluency data, analysis according to lesion location was not
statistically possible. However, should lesion location have been influential, the higher incidence of
temporal lobe lesions would primarily impair switching to semantic fluency, which was not the
case. This was also true of hemispheric lesion location. While left temporal injury has been
associated with the production of smaller clusters (Grossman 1981; Troyer et al., 1997), relatively
reduced cluster sizes do not appear to be driven by left hemispheric injury in this cohort, given the
predominance of right hemispheric injury. Moreover, the only case of left tempo-parietal injury
(i.e., #T07) demonstrated medium to large cluster sizes relative to the rest of his cohort.

Patients with psychosis were expected to show either a reduced number of clusters and
switches across categories (i.e., executive processes, but also interpreted as semantic in the
literature), or comparable clusters and switches with reduced mean words per cluster (i.e., semantic
processes). This hypothesis was supported by mental switching on both fluency tasks from PFTBI
patients; mental switches were statistically reduced relative to the healthy cohort alone for
phonological fluency, and relative to both healthy and TBIWP cohorts for semantic fluency.
However, patients with schizophrenia instead showed intermediate mental switching; their
performance was statistically matched with both reduced switching in PFTBI, and increased
switching from TBIWP and healthy participants. Neither hypothesis was supported with regard to
clustering by the psychotic cohorts. Instead, they were statistically matched to the comparison
groups on the number of clusters produced, and their size, for both tasks.

This result is generally inconsistent with the existing literature in schizophrenia. Patients
typically show a reduced number of total words, clusters, and switches (Henry & Crawford, 2005;
Landro & Ueland, 2008; Troyer et al., 1997), and/or fewer words per cluster (Bozikas et al., 2005;
Kosmidis et al., 2005; van Beilen et al., 2004). The former is considered evidence of impairments
in both executive and semantic processes, where the cognitive strategies generally employed during
clustering and switching are deficient, and the semantic store supporting the generation of clusters
is also either disorganised, unable to be sufficiently accessed, or both (Henry & Crawford, 2005;
Rossell & David, 2006). The latter argues that patients may utilise comparable cognitive strategies,
but are deficient according to the disorganisation of their semantic store (Bozikas et al., 2005;
Kosmidis et al., 2005; van Beilen et al., 2004). Thus, in keeping with the existing interpretations,
patients with schizophrenia in this research appear to have intact executive function and semantic organisation, access, and retrieval, with possible negligible executive impairment on the semantic task (i.e., as indicated by significantly reduced number of switches). However, as identified in the preceding discussions regarding the RBANS Language index and verbal fluency results, various other influences are suspected to have mediated these results; (i) insufficient statistical power, (ii) semantic fluency category-type, and (iii) minimal negative psychopathology. As such, this statistical outcome, and the following discussion on descriptive trends, is once again presented tentatively.

The psychotic cohorts demonstrated a similar pattern of outcomes on clustering and switching measures, with both steadily producing scores below the healthy participants on all but their semantic cluster size. However, the actual differences are diminutive. The increase in semantic cluster size from the schizophrenia cohort, which is in opposition to the existing literature, is generated by less than one additional word. Bearing in mind that both psychotic cohorts were marginally reduced on semantic fluency overall, and this difference did not reach statistical significance, this finding is not considered evidence of an enhanced proficiency for semantic clustering in schizophrenia. Furthermore, because these data reflected trends from the fluency analyses, in this instance, the analysis of clustering and switching is not considered to have provided additional insight into the subtle impairments underlying semantic deficiency, as has been considered elsewhere (Bozikas et al., 2005; Henry & Crawford, 2005; Landro & Ueland, 2008; Troyer, Moscovitch, & Winocur, 1997).

Clustering analysis did, however, identify impairments in the primary cohort of interest. Novel evidence for a concise deficit in executive function was obtained from patients with PFTBI, who were unable to efficiently move to a new cluster subcategory once the present cluster was exhausted. Although results again mirror the verbal fluency data, in identifying this distinct aspect of executive dysfunction in PFTBI the utility of clustering and switching subcomponent analyses is demonstrated. Interestingly, PFTBI clustering behaviour was more like TBIWP patients during phonological fluency, yet more like patients with schizophrenia during semantic fluency, in support of existing executive/semantic impairment in the relevant patient groups (Henry & Crawford, 2005; Kave et al., 2011; Stuss et al., 1998). Lesion location is not considered influential here, given that the PFTBI cohort had a matched number of injuries involving the frontal and temporal lobes ($N=4$), and the majority of these occurred in the right hemisphere ($N=10$, versus $N=4$ injuries to the left hemisphere). Finally, and most imperative, patients with PFTBI once again showed the poorest, or
equal poorest, performance on clustering and switching behaviour. While this was not illustrated statistically on all comparisons, these data represent important preliminary work.

7.6.3 Memory.

7.6.3.1 RBANS immediate and delayed memory indices.

All groups showed poorer delayed memory relative to immediate memory on the RBANS as hypothesised. However, statistical significance was reached for all but the schizophrenia cohort, suggesting comparable immediate and delayed memory capacity in schizophrenia. Both immediate and delayed memory scores from the three patient groups were descriptively reduced relative to healthy scores as hypothesised. Yet, once again, only selected contrasts were statistically significant; TBIWP performed comparably to the healthy cohort on immediate memory, and TBIWP, schizophrenia, and healthy cohorts were matched on delayed memory performance.

These data effectively suggest intact memory performance in the TBIWP patients. In fact, all TBIWP patients performed within one standard deviation of the RBANS norms. This is inconsistent with the literature documenting substantial deficits across degrees of injury severity (Ariza et al., 2006; Bennett-Levy, 1984; Carlesimo et al., 1998; Lezak, 1979; Owen et al., 1990; Perri et al., 2000; Tate et al., 1991; Vakil, 2005). However, these findings may be explained by locus of injury in this cohort. The RBANS immediate and delayed memory tasks use an assessment of verbal memory ability to gauge memory capacity. Lateralised functionality has been demonstrated previously in memory impairment post TBI, where focal left temporal lesions in particular have been associated with deficits in verbal memory (Ariza et al., 2006). Only two TBIWP patients sustained injuries in this region (#T02 and #T07), and, true to the literature, these patients demonstrated the lowest scores on the Delayed Memory index, and the equal lowest scores on the Immediate Memory index, respectively.

Reduced immediate memory was demonstrated in schizophrenia, while delayed memory performance was matched with the healthy and TBIWP cohorts. Patients with schizophrenia also uniquely illustrated comparable immediate and delayed memory ability, driven by their selective immediate memory deficit. Memory impairment is generally considered a persistent and heritable neuropsychological trait in schizophrenia, irrespective of symptom profile (Bartholomeusz et al., 2011; Broome et al., 2010; Cannon et al., 2005; Nieto & Castellanos, 2011; Pukrop et al., 2007). While scores showed some variability, this does not explain the lack of statistical differences on the Delayed Memory index, given that similar variability has been shown elsewhere on these indices where reliable group differences have been found (e.g., Gogos et al., 2010). Once again, greater
participant numbers may be required to account for patient heterogeneity when using the RBANS for memory assessment. However, inconsistencies in the outcome of memory measurements across studies are not unusual, and are often considered to reflect the aforementioned heterogeneity of the disease (Kalkstein et al., 2010; Palmer et al., 2010). It is noted that reduced performance on the Delayed Memory index was shown by all cohorts. Thus, while descriptively reduced in schizophrenia, delayed memory may not be deficient enough to warrant statistically significant impairment, especially relative to other patient groups. Furthermore, there remains contention in the literature as to which aspects of memory are the most impaired in schizophrenia (Kalkstein et al., 2010; Palmer et al., 2010). These data support a specialised deficit in immediate memory, and in doing so are aligned with research illustrating that deficits are especially prominent at the stage of information encoding (Dias et al., 2011; Zierhut et al., 2010).

Importantly, the PFTBI cohort showed significantly reduced performance across both memory tasks. The mean score of the group fell two standard deviations below the norms for immediate memory, and three standard deviations below the norms for delayed memory (although, individually, patients performed up to four standard deviations below norms on both indices, \(N = 4\)). Even to the List Recognition subtest, where the majority of individuals from the comparison cohorts performed at ceiling, a number of PFTBI patients illustrated marked difficulty. This result supports the majority of prior studies emphasising memory impairments in PFTBI (e.g., Fujii & Ahmed, 2002; Fujii et al., 2004; Sachdev et al., 2001). Although, true to the established heterogeneity in psychosis, intact memory has also been noted (e.g., Bamrah & Johnson, 1991).

Finally, recognition is considered less impaired than recall in schizophrenia (Beatty et al., 1993; Kalkstein et al., 2010). This is because recognition is facilitated by memory cues, and is thus less demanding on memory processing. The ceiling performance demonstrated by all but the PFTBI cohort on the List Recognition subtest meant that recognition versus recall assessments could not be performed. Nonetheless, ceiling performance by the majority of participants on this task, not shown to the unaided List Recall subtest, is itself preliminary evidence of enhanced abilities in recognition.

### 7.6.3.2 Semantic priming.

The semantic priming results did not reflect hypothesises; no significant group-wise differences were shown to any of the priming data. Moreover, the descriptive response patterns demonstrated by all four cohorts did not conform to hypothesised trends predicted from the existing literature. First, it was hypothesised that TBIWP patients would show reduced priming at the short SOA, but that long SOA priming would be comparable to healthy performance. This was because
the speed of the lexical decision task at the short SOA was expected to introduce additional cognitive load that TBIWP patients would find difficult to integrate given their executive dysfunction. Instead, the TBIWP cohort showed the greatest accuracy priming of all groups at both SOAs (while the healthy cohort showed the least). TBIWP patients also demonstrated the second greatest RT priming effect at the short SOA (once again with the healthy cohort showing the least). However, at the long SOA they showed the second least amount of RT priming, and demonstrated hypopriming as did healthy controls. That is, both TBIWP and healthy cohorts demonstrated faster responses to *unrelated*, than related, pairs at the long SOA. While this result provides evidence for comparable priming from the TBIWP and healthy cohorts at the long SOA in line with hypotheses, the response pattern, including hypopriming, is effectively the inverse to that hypothesised.

Thus overall, TBIWP patients were generally slower and more accurate in their responses during the lexical decision task. Accordingly, although not strictly reflecting hypothesised trends, these results align with the existing semantic processing literature in TBIWP (Hinchliffe et al., 1998; McWilliams & Schmitter-Edgecombe, 2008; Perri et al., 2000; Schmitter-Edgecombe et al., 1993). In brief, the semantic store is considered intact following TBI, with recorded deficits deemed an access problem, and/or the inefficient execution of semantic information (Haut et al., 1991b; McWilliams & Schmitter-Edgecombe, 2008; Perri et al., 2000). Importantly, this is typically demonstrated by slower RTs, but comparable response patterns from TBI participants (McWilliams & Schmitter-Edgecombe, 2008; Perri et al., 2000), as was shown here.

Given that the TBIWP patients demonstrated superior accuracy (though not significantly so), their reduced RTs may further be explained by a speed-accuracy trade-off, perhaps consciously applied to counteract known deficits. Research has demonstrated that insight into post injury deficits correlates highly with measures of executive function, whereby poorer insight is related to poorer executive function, and vice versa (Bogod, Mateer, & Macdonald, 2002). With reference to the relatively intact performance of the TBIWP patients on measures of executive function (discussed in Section: 7.6.5: Executive Function), it follows that they may have had reasonable insight into their (albeit minor) impairments post injury, and exercised greater caution during task engagement as a result. This behaviour would explain both their enhanced accuracy priming (at both SOAs), and their RT performance. Thus, although comparable response speed at the short SOA was likely dictated by the speed of the task itself, long SOA responses, where controlled processing is engaged, were probably consciously slowed to allow for additional response caution.
Next, patients with schizophrenia were expected to show reduced priming at both the short and long SOAs, with PFTBI patients illustrating a comparable pattern with a greater deficit. However, at both SOAs, the schizophrenia cohort instead illustrated the opposite; the greatest degree of RT priming, and the second greatest degree of accuracy priming. Moreover, the PFTBI cohort did not demonstrate priming patterns comparable to their psychosis counterparts as expected. Although their priming was generally reduced, they showed a slightly greater degree of priming relative to healthy participants, who showed the least. Theoretically, the PFTBI and healthy cohorts should instead represent opposite ends of the performance spectrum. An exception was shown for RT priming at the long SOA, where, consistent with hypothesised trends, PFTBI patients performed more like schizophrenia patients. However, in this case, the psychotic cohorts showed the greatest degrees of priming, which was again inconsistent with expected performance.

Semantic memory impairments are well established in psychosis (Chen et al., 1994; Rossell & David, 2006; Rossell et al., 1998; Rossell et al., 1999), with substantial evidence drawn from priming experiments (Manschreck et al., 1988; Rossell et al., 2000). However, normal and increased semantic priming has been shown by patients in the past, especially at a short SOA (Minzenberg et al., 2002; Surguladze et al., 2002). Short SOA priming is taken to reflect automatic processing, and the diversity in findings is believed to indicate heterogeneity in the spreading activation of semantic memory networks in patients (Minzenberg et al., 2002). This aligns again with the heterogeneity in schizophrenia generally, especially with regard to diversity in symptom severity and medication history. Despite being inconsistent with hypothesised trends, priming at the short SOA from the psychotic cohorts is, thus, in line with previous accounts of increased priming, and provides support for a sub-group of psychotic patients with relatively organised and efficient semantic networks.

On the other hand, priming at a long SOA (controlled semantic processing), has typically demonstrated consistent impairment (Henik, Priel, & Umansky, 1992; Minzenberg et al., 2002; Ober, Venogradov, & Shenaut, 1995; Ober et al., 1997), although there are some exceptions (e.g., affective categories, Rossell, 2004). Impaired priming at a long SOA is taken to mark a breakdown in controlled cognition, including cognitive strategy and sustained attention (Minzenberg et al., 2002; Ober et al., 1997). Thus, controlled processing at the long SOA is more likely to be effected by current symptoms and chronicity (i.e., cognition and attention are more

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7This research is not directly comparable given the affective stimuli, however, this study provides important evidence of negative results in the semantic priming literature in schizophrenia.
likely to be influenced by state, rather than trait, factors). The current findings do not reflect this established literature. In fact, both psychotic cohorts demonstrated relatively efficient priming at the long SOA, despite providing evidence for statistically impaired attention on the RBANS, and deficits in executive function as measured by the Stroop (discussed in Section: 7.6.5: Executive Function).

With reference to decreased priming from the healthy cohort, the semantic word pairs created for the lexical decision task may be responsible for the patterns of priming recorded here. Prime-target pairs can share various meaning-based relationships; purely semantic, purely associative, and jointly semantic and associative. In consideration for the potential confounds introduced by task design (see Rossell & Stefanovic, 2007), purely semantically-related pairs were carefully created, rated, and matched, for this research (see Section 7.3.2.4). This was to reduce the number of variables with the potential to complicate the priming data, and thereby isolate semantic priming from the cohorts. However, the semantic relationship between word pairs may have inadvertently become too pure to capture priming adequately. For instance, the pair cow-lion are semantically related because they share categorical and/or functional features; both are animals and have four legs (Rhodes & Donaldson, 2008). The pair chalk-cheese are associatively related because, while they do not share a semantic relationship, they are frequently used together in language, and thus linked in memory (Lucas, 2000; Rhodes & Donaldson, 2008). Doctor-nurse, on the other hand, share both a semantic and associative relationship given that they are both professions in the medical field (functional semantic relationship) and are often used together in language (associative relationship; Nestor et al., 2006). The latter two pairs, especially the doctor-nurse pair, demonstrate greater potency in meaning (this is known as the associative-boost, where the presence of the associative relationship ‘boosts’ the relatedness of the paired words; Moss, Ostrin, Tyler, & Marslen-Wilson, 1995). Thus, although the pair cow-lion is highly semantically related, it does not necessarily resemble semantic connections in the network, or thereby, the propagation of activated nodes in response to the prime ‘cow’. That is, when asked to list words that come to mind in response to the word ‘cow’ it would be unusual to list the word ‘lion’. Other associatively-, or semantic and associatively-related words, including super- and sub-ordinate categories are more typical, such as calf, bull, horns, grass, or other farm-based animals such as chicken, horse etc. By contrast, there are likely to be many semantic connections between the pair

As such, it is surprising that semantic priming in patients at a long SOA is not more inconsistent. Rossell (2004) highlighted that negative results are integral to the accurate picture of semantic processing abilities in psychosis. The general absence of these in the literature may explain why aspects of the semantic priming literature are so unclear.

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8As such, it is surprising that semantic priming in patients at a long SOA is not more inconsistent. Rossell (2004) highlighted that negative results are integral to the accurate picture of semantic processing abilities in psychosis. The general absence of these in the literature may explain why aspects of the semantic priming literature are so unclear.
cow-horse (or indeed doctor-nurse), because they are semantically related in more ways (i.e.,
greater semantic links) than cow-lion. According to spreading activation theory, the greater the
semantic connections between concepts, the greater the power of the prime to facilitate prime-
target responses (McNamara, 2005; Nestor et al., 2006). Indeed, this has been demonstrated in both
the healthy (Chiarello, Burgess, Richards, & Pollock, 1990) and schizophrenia (Nestor et al., 2006)
populations. Nestor et al. (2006) reported that both their healthy and psychotic participants were
primed least by semantic-only word pairs, relative to associative-only and dual semantic-associative
pairs. Accordingly, the semantic-only prime-target pairs used in this research are considered to have
had the greatest influence over the priming data recorded here from all four cohorts.

Reaction time hypopriming demonstrated at the long SOA by the healthy and TBIWP
cohorts, although negligible (i.e., .28ms and .33ms respectively), may also be explained by the use
of semantic-only pairs. Data from the healthy and TBIWP groups suggest that they found the
presentation of an unrelated word readily identifiable as distinct from primed concepts, in turn
facilitating faster RT’s. Related word pairs under controlled processing conditions (i.e., at the long
SOA), appear to have registered as a semantic match, as was evident by sufficient accuracy rates.
However, faster RTs were not facilitated in this condition, suggesting that additional cognition was
engaged. Priming behaviour of this kind would be demonstrated in response to word pairs that are
semantically related, but have few meaning-based links in the network (i.e., semantic-only
relationships). Consequently, as was illustrated, hypopriming would result; faster RTs to unrelated
versus related concepts.

Enhanced priming from the psychotic cohorts in response to these pairs may constitute
behavioural evidence of “hyperconnectivity” in the semantic network. This has been posited by
theories of wider and less discriminate spreading of activation to concepts within the network in
response to the prime (see Mathalon, Faustman, & Ford, 2002; Niznikiewicz et al., 1997;
Niznikiewicz et al., 2004; Salisbury, 2009). PFTBI accuracy hypopriming, however, appears to
have occurred independent of hypothesised facilitation effects afforded by network activation.
Some minor difficulty was shown in identifying semantically related, relative to unrelated, pairs by
the PFTBI patients. However, given that (i) they showed hypopriming to accuracy only, and not to
RTs, (ii) they demonstrated acceptable accuracy rates overall (>85% per condition), and (iii) the
actual differences between accuracy rates for related and unrelated pairs was negligible (i.e., 0.46%
at the short SOA, and 1.39% at the long SOA), this result does not implicate semantic memory
structure. Moreover, because this response pattern was not statistically significant (including in the
group x word relationship interaction following alpha reduction), this trend is probably an artefact
of poor attention, working memory (the target word was only on screen for 200ms), and executive
dysfunction. Thus, PFTBI patients may have experienced added difficulty with the general
demands of the task given the cumulative effect of their executive deficits.

Further potential confounds, as highlighted by the literature, are considered as a matter of
course in the following discussion. Speculations have been made about the effect of slowed patient
RTs, and the subsequent miscalculation of relative semantic priming. However, analyses were
conducted on calculations of proportional priming in this research to avoid the potential for this
miscalculation. Furthermore, although the healthy cohort showed the fastest RTs overall, RTs from
the psychotic cohorts were statistically comparable with these, suggesting that slowed patient RTs
are not a confound in this analysis. In fact, the TBIWP patients were slowest to respond (albeit, not
statistically), even relative to dually-diagnosed PFTBI patients who have shown the greatest degree
of morbidity on various other assessments administered in this battery. Therefore, given matched
injury severity, the presence of psychosis in PFTBI may have actually facilitated the speed of their
responses relative to TBIWP, offering further evidence of hyperconnectivity.

Looking more closely at relatedness proportion (RP), substantial empirical evidence has
shown that lexical priming tasks using 25% or less related pairs typically show equivalent, or
decreased, priming in psychosis relative to controls (Chapin, McGown, Vann, Kenny, & Youssef,
1992; Ober et al., 1997; Rossell, 2004; Rossell & Stefanovic, 2007; Vinogradov, Ober, & Stenaut,
1992). Statistically comparable priming at the short SOA (i.e., 25% RP) may thus have been
influenced by RP. However, given similar results at the long SOA, where the RP was at 75%, it is
clear that these findings were not driven by RP alone. Greater percentages of RP are typically
associated with greater priming in schizophrenia (Henik et al., 1995; Spitzer, Braun, Maier, Hulme,
& Maher, 1993; Surguladze et al., 2002). Accuracy priming from the psychotic cohorts was aligned
with this literature, albeit indicated by descriptive trends alone, and in the form of hypopriming in
PFTBI. Yet, their RT priming demonstrated the opposite by showing greater priming at the short
SOA where the RP was at 25%. Given that short SOA priming is taken to mark automatic
processing, this result provides further support for the theory of hyperconnectivity in psychosis.

Significantly greater degrees of priming have also been illustrated from schizophrenia
patients as a function of thought disorder (Manschreck et al., 1988). Disparate priming from the
psychotic cohorts may accordingly be explained by symptom profile. Although the groups were
statistically matched on ratings from the Global TLC measure, the mean score for the schizophrenia
cohort was considered “severe”, whereas assessments of thought disorder were in the “mild” range
for the PFTBI cohort. Thus, elevated priming from the schizophrenia cohort may partially reflect elevated levels of thought disorder, relative to PFTBI.

Finally, although the absence of statistical significance in this analysis is consistent with a subset of findings in the literature showing matched priming between healthy and psychotic cohorts, the potential for insufficient statistical power must also be explored. *A priori* power calculations were not possible for the PFTBI and TBIWP cohorts because similar studies using these cohorts have not been reported to date. Group sizes indicated by power analysis for the healthy and schizophrenia participants were taken from studies where group comparisons were performed for two groups on various cognitive neuropsychological measures, rather than four. In addition, a number of participants from both the healthy and schizophrenia groups were removed from analysis because of violations to the normality assumption, which reduced the total group size to below the number determined for these groups in *a priori* analysis (i.e., a minimum of 19 per group). Although significant group differences in priming have been demonstrated using groups of similar (e.g., Henik et al., 1995; Kwapil, Hegley, Chapman, & Chapman, 1990), and smaller sizes (e.g., Manschreck et al., 1988), these analyses were again performed on two-group, rather than four-group, comparisons. Group means, especially with regard to accuracy from the PFTBI cohort at the long SOA, indicate group differences that may have reached significance given greater statistical power. Moreover, while there is some overlap in standard error, the data show quite typical within-group variance, even in PFTBI where the variance was relatively elevated (e.g., Morgan et al., 2006; Rossell & Nobre, 2004). Taken together, this unfortunately suggests insufficient group sizes to power this analysis. However, the trends from this work indicate some important preliminary evidence for hyperconnectivity from the psychotic cohorts, which may be behaviourally isolated and observable by using semantic-only prime-target pairs. Post hoc power analysis was not conducted to confirm this speculation given that such analysis is logically flawed and misleading (see Hoenig & Heisey, 2001 for discussion).

### 7.6.4 Reasoning.

#### 7.6.4.1 Group-wise comparisons.

Due to existing reasoning deficits in the literature and the potential for executive dysfunction post injury, the TBIWP patients were expected to demonstrate reduced performance on the initial prediction index of the probabilistic reasoning task. They were not expected to demonstrate JTC behaviour. This hypothesis was supported only to the extent that the TBIWP cohort did not show JTC behaviour in either of the conditions. Patients with TBIWP demonstrated
the lowest, and equal lowest JTC behaviour for conditions one and two respectively. However, in conflict with hypothesised performance, their initial prediction data was very accurate; they were most accurate for the first condition, and equal most accurate for the second condition.

Impairment has been documented in a number of reasoning abilities following TBI and these are believed to arise as a result of executive dysfunction post injury (Bibby & McDonald, 2005; Geraci & Cantagallo, 2011; Goverover, 2004; Krawczyk et al., 2010; Morrison et al., 2004). Mild executive impairment was demonstrated by the cohort, although few significant contrasts were found between the TBIWP and healthy cohorts on the executive function tasks (discussed in the following Section: 7.6.5: Executive Function). Thus, executive dysfunction in the current TBIWP sample may not have been pronounced enough to impair probabilistic reasoning on the beads task. Furthermore, Osherson et al. (1998) has shown the laterality of reasoning, especially the dominance of left hemispheric regions during probabilistic reasoning. Relative to PFTBI, the TBIWP cohort had two additional patients with injuries to their left hemisphere, elevating the likelihood of probabilistic reasoning deficits in this cohort. As such, intact reasoning from TBIWP patients may partially reflect the inadequacy of the task as well (discussed later in this section).

Self-rated confidence from TBIWP patients was quite reasonable for both conditions (~80-90%), and this cohort showed the least amount of within group variability on both prediction and confidence indices.

The findings in schizophrenia have been especially inconsistent to date and, therefore, a response pattern for patients with schizophrenia was not hypothesised. In line with much of the existing literature (e.g., Huq et al. [1988] and McKay et al. [2007]), patients with schizophrenia did not show a significant JTC bias. The percentage of patients who made a decision by the first or second bead (i.e., JTC bias) exceeded that of the comparison cohorts descriptively; however, this amounted to only one additional patient compared with the healthy cohort for both conditions. For the first condition, the mean draws-to-decision from the schizophrenia patients was actually the most conservative of all cohorts. That is, during the first condition they waited the longest on average to make a decision. By contrast, they made the earliest judgement during the second and more difficult condition (i.e., ratio 60:40), however, this was still considered a conservative number of draws-to-decision (i.e., between 15-16 bead draws). It was clear that patient’s felt some uncertainty about the task objective during the first condition, and this may account for their greater draws-to-decision. The task was explained in the same way to all participants using the jars of beads as an illustration, and instructions were repeated upon request, however, patients generally appeared more comfortable with the task by the second condition (i.e., once they had effectively
completed a practice). This was noticeable over and above any comparable uncertainty felt by the other cohorts, and would account for the reduced mean draws-to-decision illustrated in the second condition, despite the more difficult probabilistic ratio.

The initial predictions of likelihood from the schizophrenia cohort were slightly below accuracy in the first condition, although substantial variability was shown from the group. Yet, their predictions for the second and more difficult condition were more accurate and less variable than the healthy cohort. This too may be an indication of initial task uncertainty; more than any other cohort schizophrenia patients tended to overthink the question of percentage likelihood during the first condition, with more than one requesting pen and paper to try and determine the answer mathematically. Importantly though, their accurate responses to this question by the second condition provides evidence of intact probabilistic reasoning. Patients also illustrated self-rated confidence that was comparable to the healthy participants on both conditions. However, they showed slightly larger group variability for the confidence level associated with their decision in the second condition, likely to reflect the more difficult ratio.

Patients with PFTBI were expected to show the largest degree of impairment, however, no prediction was made as to whether their response pattern would most closely reflect TBIWP or schizophrenia. An enhanced JTC style was not demonstrated by the PFTBI cohort. In fact, their data on this index was comparable to healthy performance. On average, PFTBI draws-to-decision most closely resembled the schizophrenia cohort; they made a decision approximately one bead earlier and one bead later than the schizophrenia cohort on the first and second conditions respectively. It appears, then, that cognition underlying the task performance on this index may be driven by the psychosis in PFTBI, rather than direct changes in cognitive processing arising as a result of their injury.

The prediction of likelihood data registered by the PFTBI patients was the furthest away from the correct response for both conditions, and thus in line with hypotheses. Despite this, however, their prediction on the second condition was still comparable to the one made by the healthy cohort. Given the poorest average predictions to both conditions, these data may suggest a negligible reduction in probabilistic reasoning in the PFTBI cohort, remembering, however, that these contrasts were not statistically significant. On the other hand, their prediction on the first condition, and draws-to-decision behaviour on both conditions, most closely reflected that of the schizophrenia cohort. Given that the schizophrenia patients illustrated intact probabilistic reasoning on this task, the performance in PFTBI may instead arise from generally deficient cognitive
processing. Relative to any other group, the PFTBI patients also demonstrated the largest variability in their initial predictions, yet, the greatest confidence in their decisions for both conditions, and this may offer further evidence that these results are underpinned by a general deficit in cognition.

Two important trends are noted here. First, the psychotic cohorts demonstrated the largest within group variability across all measures for this task. Once again, this is consistent with the large literature indicating the heterogeneity of psychosis (Badcock et al., 2005; Mercado, Johannesen, & Bell, 2011; Palmer et al., 1997; 2010). Second, self-rated confidence tended to be greater from the TBI cohorts. Bearing in mind that this was not demonstrated statistically, this behaviour may reflect poor insight as has been documented post TBI (O’Keeffe, Dockree, & Robertson, 2004; O’Callaghan, McAllister, & Wilson, 2012). This is not necessarily inconsistent with speculation that increased insight may have mediated TBIWP performance on the computerised semantic priming task. It is reasonable that patients post TBI may have insight into impairments in their physical abilities (i.e., speeded button presses for the priming task), whereas these may not be so obvious for aspects of complex cognition, such as reasoning. The incorrect appraisal of their existing cognitive impairment, while only mild in the case of TBIWP, may underlie this trend toward enhanced self-rated confidence from the injured cohorts. Moreover, Kennedy (2001) reported that when TBI patients were uncertain about the accuracy of an answer they responded with over-confidence, whereas healthy comparisons tended to be under-confident. These data are therefore consistent with Kennedy’s (2001) findings, and together provide evidence for a general over-confidence in decision making post TBI.

The probabilistic reasoning deficit purported to exist in psychosis, and underpin a general JTC style bias, was not captured by the beads task modified from Huq et al. (1988). Rather than a bias associated with psychosis, the findings from this work suggest that JTC behaviour may exist in a minority of individuals when a task outcome is considered predictable (i.e., condition one), irrespective of diagnosis. During this first, and easier, condition approximately 20-25% of participants evenly distributed across the cohorts demonstrated a JTC bias (with the exception of TBIWP patients where this number was only 10%). Under circumstances where the predictability of the outcome was less likely (i.e., in the second and more difficult condition, ratio 60:40), JTC behaviour was no longer evident (with the exception of one schizophrenia patient). Importantly, where descriptive group differences were noted in JTC behaviour these did not reach statistical significance. Moreover, the mean draws-to-decision from the psychotic cohorts did not approach the JTC bias cut-off, and accordingly, these data are in support of literature indicating that a JTC bias in psychosis may be inaccurate (i.e., Averbeck et al., 2012; Huq et al., 1988; Maher, 1992;
McKay et al., 2007; Moritz et al., 2007; 2009). Earlier responses from the psychotic cohorts on condition two may support arguments for a general data gathering bias, or “lowered threshold”, during decision making in psychosis (e.g., Averbeck et al., 2010; Moritz et al., 2007; 2009). However, the current findings alone do not provide sufficient evidence for a decision making style of this nature.

Adaptations of Huq et al.’s (1988) beads task are widely used in the schizophrenia research (Garety & Freeman, 1999; Langdon et al., 2010; Peters et al., 1997). However, the current results suggest that the validity of the beads task as a measurement of probabilistic reasoning, and/or the JTC bias, may need to be reviewed. This is especially true regarding the data obtained from the TBIWP cohort who, theoretically, should have demonstrated elevated deficits in reasoning. It was apparent during administration that the task may instead be capturing an individual’s propensity to gamble, and a number of participant comments reflected this view. This is made further likely given that the task was initially conceived using poker chips (Phillips & Edwards, 1966), and may also offer additional explanation for the absence of statistically significant contrasts. Should the task continue to be used to measure probabilistic reasoning, the incorporation of the initial prediction question, and reporting of these data, is recommended. Although these predictions were not statistically significant across cohorts, they offered valuable insight into the reasoning capacity of the participant, as well as the participant’s comprehension of the task, and this has proved valuable in understanding the trends in this dataset. Finally, given that there were obvious problems with task comprehension, especially from the schizophrenia cohort, it may be worth incorporating an initial practice task in future administrations.

7.6.4.2 Presence/absence of delusions.

A significantly enhanced JTC bias was not shown by patients with delusions relative to those without. These data are inconsistent with both the hypothesised trends and findings originally published by Huq et al. (1988). Deluded patients showed a higher propensity to make a decision within their first or second bead draw (i.e., JTC bias); however, the largest difference was approximately six per cent and not statistically significant. During condition one, deluded patients were also more conservative in their draws-to-decision than non-deluded patients, and although they decided sooner during condition two, their responses remained conservative, and far from the JTC cut-off (i.e., 15-16 bead draws). Initial predictions and self-rated confidence from the two groups were very closely matched across trials, with slightly higher variability for the group with
delusions on the second trial. Matched self-rated confidence is further inconsistent with the hypothesis established from the findings of Huq et al. (1988).

It is clear that these results mirror the data acquired from the schizophrenia and healthy cohort comparisons. All but two patients diagnosed with schizophrenia were included in the deluded group, along with all of the PFTBI patients. Thus, the majority of the non-deluded sample consisted of healthy controls (i.e., 92%), who were originally included in the non-deluded sample to ensure statistical power. As such, these contrasts are not considered adequate in the investigation of probabilistic reasoning ability in deluded versus non-deluded psychosis, and no further interpretation is provided. Non-deluded patients diagnosed with psychosis must constitute the non-deluded cohort in future research desiring to make this contrast.

7.6.5 Executive function.

All three patient cohorts were expected to show executive dysfunction in the form of poor mental inhibition and switching, processing speed, and attention deficits, relative to healthy control performance. These will be discussed in turn.

7.6.5.1 Mental inhibition and switching.

The measures of inhibition and switching included the Stroop inhibition and switching trials, as well as the Stroop derived interference and switching-interference scores, the TMT Form B, and the TMT derived difference score. Data followed the same pattern across all measures; superior performance was shown by the healthy cohort, followed by TBIWP, schizophrenia, and PFTBI patients who performed most poorly. Although this pattern supports hypothesised reductions in performance from the patient cohorts, not all contrasts were statistically significant in post hoc analyses.

Reduced inhibition and switching performance from the TBIWP cohort was intermediate between healthy and schizophrenia performance. On measures of mental inhibition, the TBIWP cohort performed both comparably and statistically worse than the healthy comparison, and both comparably and statistically better than patients with schizophrenia. This finding supports the few studies that have correctly calculated a Stroop derived interference score and documented impaired inhibition post TBI (Ponsford & Kinsella, 1992; Rios et al., 2004; Stuss et al., 1985). However, much of this work has reported that inhibition deficits may no longer exist once the effects of slowed processing speed are removed by analysis. Given the statistical inappropriateness of similar analysis in the current dataset (see Chapter Eight), it is unclear whether deficits illustrated here
reflect true impairment in mental inhibition alone, or were mediated by other executive dysfunction, especially poor processing speed. Although, it is noted that the TBIWP cohort in the current research did not demonstrate especially poor processing speed (discussed later in this section).

Statistically comparable mental switching from the TBIWP cohort (i.e., matched with the healthy and schizophrenia cohorts on all four indices), is inconsistent with indications of impaired cognitive flexibility post severe TBI on a modified version of the Stroop switching task (Perlstein et al., 2006; Seigourel et al., 2005), and on the Trail Making Task (Rios et al., 2004). Within group variability may explain the absence of statistically significant group distinctions in cognitive flexibility, given that impairment was shown descriptively. It is unlikely that this result is driven by insufficient statistical power due to the TBIWP sample size; both the healthy and schizophrenia cohorts were also statistically matched on all measures of mental switching, yet were more robust in sample size. Importantly, the TMT assessment of mental switching accounts for the effects of processing speed when applying the difference score, and thus, slowed processing speed can also be disregarded as influential. The effect of injury severity, however, could not be determined given insufficient statistical power for this analysis. The undue influence of severity was, however, hoped to be balanced by a representative sample across mild, moderate, and severe injury. Even so, the two poorest performers from the TBIWP cohort had sustained a severe head injury. While this may suggest that greater deficits in mental inhibition and switching follow severe TBI, the two remaining patients with a severe injury conversely demonstrated scores that were superior to the rest of the TBIWP cohort. Thus, descriptively at least, these results tend to support evidence that cognitive inhibition and switching may be unmediated by injury severity (Dimoska-Di Marco et al., 2011; Stuss et al., 1985).

Patients with schizophrenia showed intermediate inhibition and switching performance; on all measures they performed descriptively below TBIWP, and above PFTBI patients. However, statistical analyses indicated a deficit in mental inhibition only. This finding reflects substantial research indicating cognitive impairment on the Stroop from patients, and in delusion proneness (Barch et al., 2004; Brenton et al., 2011; Ferchiou et al., 2010; Orem & Bedwell, 2010). Facilitation as measured by Barch et al. (2004) was not computed given that the word and colour control conditions produce a derived interference score, that is effectively comparable to computed facilitation. As such, these data are contrary to reports from Barch et al. (2004) of equivalent inhibition interference effects in schizophrenia and healthy participants administered the Stroop. However, in finding this result using the traditional format of the task (e.g., as opposed to the single card version), these data demonstrate that the Stroop itself is not responsible for reports of
equivalent interference, contrary to suggestions from Henik and Salo (2004). Instead, as argued by Perlstein et al. (1998), these findings support the use of the traditional Stroop task in the assessment of cognitive inhibition in schizophrenia. Notably, this result is aligned more generally with the established executive dysfunction in patients.

Conversely, the robust evidence for deficient task switching abilities in schizophrenia was not demonstrated by this dataset (Hermens et al., 2010; Ravizza et al., 2010; Smith et al., 1998; Wylie et al., 2010). In particular, both Hermens et al. (2010) and Smith et al. (1998) reported poor mental switching on the TMT using schizophrenia samples of a smaller, and comparable size, respectively. Most notable, however, is the larger variability of the schizophrenia cohort in the current research, compared with previous work. However, both of these studies compared the schizophrenia cohort with a healthy sample only. Thus, these comparisons may have been underpowered, driven by the considerable heterogeneity of mental switching capabilities in the schizophrenia sample, and the four cohort design of the current study.

The greatest impairments in both mental inhibition and switching were again illustrated by the PFTBI cohort, who performed statistically below the comparison cohorts as hypothesised. Interestingly, although their deficits were much worse on each of these measures, the PFTBI patient data illustrated a pattern reflective of the one shown by the schizophrenia data; mental switching determined by the Stroop task appeared to be relatively better than the more substantial mental inhibition impairment (see Figure 7.14; Results). Yet, it is clear from both the Stroop and TMT data in PFTBI that mental switching is substantially impaired, even when isolated from the effects of reduced processing speed (i.e., significant differences were shown on the TMT difference score for the PFTBI group). This was also true despite the largest, and sizable, variability demonstrated by the PFTBI cohort across all cognitive inhibition and switching indices. Furthermore, the TMT ratio score for the PFTBI cohort approached the proposed threshold for substantial set-switching dysfunction (Arbuthnott & Frank, 2000). Accordingly, these data present novel evidence of considerably poor cognitive inhibition and switching in dually diagnosed PFTBI patients, both relative to health, and beyond the impairment of their brain-injured, and psychotic, counterparts.

7.6.5.2 Processing speed.

Processing speed was measured by the Stroop colour and word trials, and the TMT Form A. The same graded pattern of reduced performance was shown as to the abovementioned inhibition and switching measures. That is, superior performance was illustrated by healthy participants, followed by the TBIWP, schizophrenia, and PFTBI patients who recorded the slowest processing
speeds. Analysis of errors on the Stroop trials further indicated that group-wise differences were not mediated by a speed-accuracy trade-off in the traditional sense. Once again, however, not all comparisons were significant. On the Stroop, TBIWP patients again performed both comparably and statistically worse than the healthy comparison, and both comparably and statistically better than patients with schizophrenia. On the TMT, these cohorts were instead statistically matched.

Slowed information processing is one of the most consistently reported findings post brain injury, and in patients diagnosed with schizophrenia (Ben-David et al., 2011; Brebion et al., 1998; Clement & Kennedy, 2003; Ojeda et al., 2008; Ponsford, Draper, et al., 2008; Rios et al., 2004; Spikman et al., 2004). The current findings support established processing speed deficits in these cohorts; yet, this is the first study to statistically compare TBI and schizophrenia patients on these measures. This unique comparison has demonstrated that, akin to inhibition and switching ability, information processing post TBI is impaired relative to healthy individuals, although it may not be as impaired as in schizophrenia. Once again, the heterogeneity of cognitive processing is apparent given that each of these cohorts showed both statistically different, and statistically matched, performance with the cohort closest to them performance-wise on the Stroop measures. Large variability was also shown on the TMT (Form A). Given that Form A is a basic counting and visual search task, it may not be an especially sensitive measure of processing speed, and this would account for the statistically matched performance from the healthy, TBIWP, and schizophrenia cohorts, despite graded performance having been demonstrated descriptively.

Importantly, PFTBI performance was the most significantly impaired on all measures of processing speed as hypothesised. It is noted that this difference was only found relative to the healthy cohort comparison on the TMT, however, this is considered to reflect the reduced sensitivity of this measure as already mentioned. Evidence for processing speed deficits in a PFTBI sample is in support of work from Fujii et al. (2004), who suggested the same using retrospective chart review, and comparisons with healthy data drawn from their existing work. These findings thus provide valuable and novel evidence of slowed information processing in PFTBI patients using standardised measures, and matched group-wise hypothesis testing.

7.6.5.3 RBANS attention index.

Data from the RBANS Attention index reflected an identical pattern to the executive functions discussed in this section; superior attention was illustrated by healthy participants, followed by the TBIWP, schizophrenia, and PFTBI patients. This is unsurprising given that the executive functions, including attention, are considered inextricably linked frontal lobe processes.
The TBIWP cohort once again showed both comparable and statistically reduced attention relative to the healthy cohort, and both comparable and statistically superior attention relative to schizophrenia patients. Again, and imperative to this work, PFTBI patients illustrated statistically inferior attention as hypothesised.

These data are consistent with robust evidence of attentional impairment post traumatic brain injury (Oddy et al., 1985; Ponsford, Draper, et al., 2008; Spikman et al., 2000; Zino & Ponsford, 2006), and as a core cognitive feature in schizophrenia (Benton et al., 2011; Bleuler, 1911; Diwadkar et al., 2011; Kumar et al., 2010; Mitchie et al., 2000; Weiss et al., 2007). They further provide another important and novel finding in PFTBI given that the existing literature has conversely suggested a relatively minor impairment in attention (i.e., in 11.76% of cases; Fujii & Ahmed, 2002). Note, however, that this rate was drawn from a single study assessing chart review information against the available norms (Fujii & Ahmed, 2002). The substantial impairment in PFTBI found in the current research thus has additional credence according to its standardised and empirical design, and alignment with the prominent attentional deficits already established post TBI, and in schizophrenia.

7.6.6 Intelligence quotient.

7.6.6.1 Premorbid IQ.

Given that an elevated risk for psychosis has been associated with reduced premorbid IQ (Cannon et al., 1999; Crawford et al., 1992), it was hypothesised that psychotic patients would show reduced scores on the NART relative to healthy and TBIWP comparisons. Instead, the four cohorts were matched on premorbid (NART) IQ, with the lowest mean score shown by the TBIWP cohort (however, they also demonstrated the largest within group variability). NART scores from all cohorts fell within the “average” range for premorbid IQ. As such, although hypothesised premorbid IQ in TBIWP was supported, this result is negated by the same in the psychotic cohorts. This is the first time the standardised measurement of premorbid IQ has been reported in a cohort of PFTBI patients. It is unlikely that average range premorbid IQ in the current samples is indicative of “higher-functioning” psychosis subgroups as has been proposed in the literature (e.g., Badcock et al., 2005; MacCabe et al., 2012). Such cases typically show the preservation of intelligence (Badcock et al., 2005; Mercado et al., 2011; Palmer et al., 1997), not demonstrated by current IQ scores from the psychotic cohorts in this research (discussion following).

Despite not supporting hypothesised group differences in psychosis, matched average premorbid intelligence is a favourable outcome, given that it provides evidence of a well matched
total sample of average intelligence prior to injury and/or illness onset. Importantly, this indicates that pre-existing intellectual impairment has not depressed current intelligence, and thus, performance on the neuropsychological battery overall. Furthermore, this finding is aligned with emerging evidence refuting the link between reduced premorbid intelligence and psychosis (Carter et al., 2010, Szoke et al., 2008). This is the first known report of premorbid IQ in a PFTBI sample, and while substantial replication is necessary, these data advocate for psychosis proneness unrelated to reduced intellectual ability.

7.6.6.2 Current IQ.

By contrast, significant group differences were illustrated on the overall measure of current intelligence (WAIS IQ), and to the component parts of the WAIS (Weschler, 1955); visuo-spatial (Matrix Reasoning) and verbal (Vocabulary). Group-wise differences followed the same pattern on overall WASI IQ and verbal IQ; the poorest scores were demonstrated by patients with PFTBI, followed by statistically matched IQ from the schizophrenia and TBIWP cohorts, and superior IQ from the healthy cohort. Visuo-spatial IQ instead showed statistically matched scores from the psychotic cohorts, and these were reduced relative to the TBIWP and healthy cohorts who were also statistically matched.

While it was expected that TBIWP patients would demonstrate reduced current IQ, it was explicitly predicted that the verbal aspects of IQ would remain intact in this cohort. This was because it is well established that vocabulary represents a stable aspect of intelligence, independent of symptomatology (e.g., Szoke et al., 2008). However, TBIWP patients illustrated verbal IQ that was statistically below that of both the healthy and schizophrenia comparisons. Despite not supporting hypothesised TBIWP performance, this result is aligned with the premorbid IQ assessment in TBIWP (also a language-based measure). Thus, the consistent nature of verbal IQ pre- and post-traumatic brain injury was demonstrated by these data, and explains why current verbal IQ in TBIWP was not comparable with the healthy participants as hypothesised.

Superior visuo-spatial (Matrix Reasoning) IQ from the TBIWP patients was also inconsistent with hypothesised performance. Striking deficits in visuo-spatial IQ have been shown elsewhere post TBI (Chadwick et al., 1981; Clement & Kennedy, 2003; Donders, 1997). Further, these are typically more pronounced than verbal IQ impairment (Ferri et al., 2004), opposite to the result illustrated here. A number of potential influences are worth consideration in light of this result. First, slowed processing speed often constrains the measurement of visuo-spatial IQ (e.g., Ferri et al., 2004). However, the TBIWP cohort were proficient in processing speed (see previous
discussion), and the WASI Matrix Reasoning task is not performed under time pressure. Thus, visuo-spatial IQ should not have been mediated by processing speed constraints, should they exist. Next, indications that greater impairments in IQ are associated with greater injury severity (e.g., Curtis et al., 2009; Donders & Janke, 2008; Ferri et al., 2004; Rohling et al., 2011) do not appear to explain TBIWP visuo-spatial performance either. Injury severity was matched across brain injured cohorts according to LOC, PTA, and the percentage of patients classified as severely injured (40% in both). Therefore, had injury severity been driving this result, patients with TBIWP should illustrate visuo-spatial IQ deficits, similar to that of their injured counterparts (i.e., PFTBI patients).

Finally, the lateralisation of verbal and visuo-spatial aspects of intelligence has been established, where right hemispheric lesions are likely to reduce visuo-spatial IQ (e.g., Nass et al., 1989). Eighty per cent of patients from the TBIWP cohort had sustained an injury to the right hemisphere, relative to 100% of the PFTBI cohort. This may account for some of the better performance from TBIWP patients, however it is unlikely that hemispheric lesion location alone explains, (i) why visuo-spatial IQ from the TBIWP cohort was not poorer given the previous literature, and indeed, their reduced verbal IQ, and (ii) the size of the difference in performance IQ between the two brain-injured cohorts.

Hypothesised reductions in IQ (Full Scale and subscale measurement) in schizophrenia patients were supported relative to healthy performance. This result is consistent with substantial evidence of intellectual deficits in schizophrenia (Bilder et al., 1992; Caspi et al., 2003; Hoff et al., 2005; Jespen et al., 2010; Kalkstein et al., 2010; Seidman et al., 2006; Xiang et al., 2010b). Interestingly, of the three patient cohorts, schizophrenia patients had the most consistent scores across WASI Full Scale and component IQ measures (see Figure 7.15; Results). Deficits in verbal intelligence were most comparable to those shown by the TBIWP cohort (reflected in Full Scale IQ), whereas schizophrenia visuo-spatial IQ deficits were more like PFTBI impairment. However, this pattern is likely due to the abovementioned unusually poor verbal proficiency demonstrated by the TBIWP cohort.

Finally, patients with PFTBI again illustrated the poorest scores as hypothesised; however, this was supported statistically on Full Scale and verbal IQ, yet only descriptively on visuo-spatial IQ, where PFTBI poor performance was statistically matched with schizophrenia patients. Estimates of current IQ in PFTBI have been inconsistent and confined to single case reports to date. Nonetheless, these data support retrospective chart review findings published by Fujii et al. (2004) and Sachdev et al. (2004) who reported reduced IQ, but not a case study from Bamrah and Johnson (1991), who reported normal range IQ. The similar patterns across IQ subcomponents from the
TBIWP and PFTBI cohorts, not demonstrated by patients with schizophrenia, suggest that the profile of impairment in PFTBI IQ may be most influenced by deficits arising from the injury, while the dual diagnosis may be responsible for the relative degree of impairment. However, given the unexpected degree of verbal IQ impairment in TBIWP patients in this research, IQ profiles post injury in patients with, and without, subsequent psychosis, and their comparisons, require further replication.

7.6.7 Summary of the PFTBI cognitive neuropsychological profile.

The cognitive neuropsychological profile in PFTBI was overwhelmingly impaired relative to comparison cohorts. It appears that, overall, patients with PFTBI experience greater neuropsychological deficits than their single diagnosis counterparts. As noted, on tasks where significant differences were shown, PFTBI patients demonstrated significantly isolated inferior performance 63.33% of the time. This includes especially impaired immediate and delayed memory, attention, processing speed, mental inhibition and switching across various measures (including category switching during phonological fluency), current Full Scale and verbal intelligence, and importantly, overall neuropsychological function as measured by the RBANS Total Scale Score. On measures where group-wise differences were not significant, mean scores from the PFTBI cohort generally remained the poorest. These included assessments of visuo-spatial and Gestalt processing, language, phonological and semantic fluency (including the majority of cluster and switching measures), lexical decision task accuracy rates, predictions on the probabilistic reasoning trials (alongside the highest self-rated confidence), and visuo-spatial (Matrix Reasoning) intelligence.

Illustrated by the plots of standardised group means contained throughout this chapter, a similar pattern of incremental performance was demonstrated on the majority of assessments. This graded performance is a key finding, whereby the healthy cohort was generally identified as superior, followed by TBIWP, schizophrenia, and dually-diagnosed PFTBI patients. On a handful of assessments where significant group-wise differences were identified, the poor performance from PFTBI patients was statistically matched with another patient group. Statistical comparability was identified with schizophrenia patient performance on measures of immediate memory (Story Memory subscale), attention (Coding subscale), semantic fluency switches, and visuo-spatial intelligence. Conversely, statistical comparability with TBIWP patient performance was shown on phonological fluency (subcomponent ‘a’) only. It appears, then, that the effects of psychosis in PFTBI may be more influential on cognitive neuropsychological abilities than the effects of the
TBI. It is suspected, however, that the TBIWP patients were relatively well recovered and high functioning, given contrasts with deficits reported in the TBI literature. Therefore, they may not be a particularly representative sample.

In light of the previous, and limited, literature in PFTBI, this research has provided a clear indication that cognitive neuropsychological deficits are more thoroughly elucidated by comparisons made with matched cohorts, rather than available norms. This work is the first to make these comparisons using injury and clinically matched patients on a variety of recognised scales. It is also the first research to administer a full neuropsychological battery comprised of standardised measures, and driven by hypothesis testing. These data thus represent a novel contribution to the literature, indicating that dual brain injury and psychosis have a profound effect on overall cognitive neuropsychological function.
Chapter 8: Mediators of Cognitive Neuropsychological Performance

8.1 Introduction

As highlighted in Chapter Five (Section 5.1.7-5.1.9), the literature has indicated that a number of injury and illness-related variables are likely to influence cognitive neuropsychological performance. Analysis of covariance (ANCOVA) is typically applied in research of this nature, in an attempt to statistically account for these influences where group-wise comparisons are made. However, the correct application of this statistical test relies on key assumptions about the data. Preliminary analyses revealed that selected statistical assumptions were violated in the current dataset (see Appendix S for discussion). Thus, the ANCOVA technique was deemed statistically inappropriate. Instead, correlational analyses were performed to provide an indication of the likely mediators of performance for each participant group. Injury and illness-related factors identified as influential in the TBI and schizophrenia literature are contained in Table 8.1.

8.2 Hypotheses

Significant relationships were expected between injury/illness variables and cognitive neuropsychological variables in accordance with the existing literature. Mediating variables identified by the TBI and schizophrenia literature were, at minimum, expected to demonstrate comparable relationships in PFTBI performance. The hypothesised directionality of correlations are indicated in Table 8.2. No specific hypotheses were made regarding the time since injury, psychosis onset latency, or antipsychotic dosage, given that the effect of these variables on neurocognition is particularly unclear in the existing research.

8.3 Method

8.3.1 Participants.

The participant cohorts were detailed in Chapter Six. Reduced group sizes for tasks relevant to these analyses were as follows; (i) the Stroop task (schizophrenia group, \( n =22 \)), and (ii) current IQ (healthy control, \( n =22 \)) (see Chapter Six for details).

8.3.2 Experimental measures and procedure.

Injury and illness-related variables of interest were defined as measures that (i) have been identified in the existing literature as potential mediators of cognitive neuropsychological performance, (ii) were continuous in nature, and (iii) normally distributed. Although dichotomous categorical variables can be subjected to correlational analysis, the only relevant dichotomous
Table 8.1
Injury/Illness-Related Mediators on Cognitive Neuropsychological Performance according to the TBIWP and Schizophrenia Literature

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Hypothesised Mediators</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBIWP</td>
<td>Age of injury acquisition</td>
<td>Beauchamp et al., 2011; MacNeill Horton Jr. et al., 2010; Senathi-Raja et al., 2010.</td>
</tr>
<tr>
<td></td>
<td>Injury type (closed-head versus penetrating)</td>
<td>Hiscock et al., 2002.</td>
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<tr>
<td></td>
<td>Lesion location (hemisphere)</td>
<td>Nass et al., 1989.</td>
</tr>
<tr>
<td></td>
<td>Lesion location (lobe)</td>
<td>Anderson et al., 1995; Beauchamp et al., 2011; Berryhill et al., 1995; Krawczyk et al., 2010.</td>
</tr>
<tr>
<td></td>
<td>Time since injury</td>
<td>Dimoska-Di Marco et al., 2011; Senathi-Raja et al., 2010.</td>
</tr>
<tr>
<td></td>
<td>Processing speed</td>
<td>Dimoska-Di Marco et al., 2011; Ponsford &amp; Kinsella, 1992; Rios et al., 2004; Stuss et al., 1985.</td>
</tr>
<tr>
<td></td>
<td>Attention</td>
<td>Beauchamp et al., 2011; Perri et al., 2000.</td>
</tr>
<tr>
<td></td>
<td>Premorbid IQ</td>
<td>Morris et al., 2005.</td>
</tr>
<tr>
<td></td>
<td>Education</td>
<td>Leblanc et al., 2006.</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>Age of illness onset</td>
<td>Landro &amp; Ueland, 2008; Phillips et al., 2004; Sumiyoshi et al., 2001.</td>
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<tr>
<td></td>
<td>Positive symptoms (generally)</td>
<td>Averbeck et al., 2010; Menon et al., 2006; Moritz et al., 2007; Woodward et al., 2009.</td>
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<td></td>
<td>Positive symptoms (delusions)</td>
<td>Colbert &amp; Peters, 2002; Linney et al., 1998; Warman et al., 2007.</td>
</tr>
<tr>
<td></td>
<td>Negative symptoms</td>
<td>Bowie et al., 2004; Woodward et al., 2009.</td>
</tr>
<tr>
<td></td>
<td>Disorganised symptoms</td>
<td>Knight &amp; Silverstein, 1998; Silverstein et al., 2000; Uhlhaas et al., 2005; Uhlhaas et al., 2006.</td>
</tr>
<tr>
<td></td>
<td>Current IQ</td>
<td>Knowles et al., 2010; Lincoln et al., 2010.</td>
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<tr>
<td></td>
<td>Processing speed</td>
<td>Ojeda et al., 2008; Vinogradov et al., 2002.</td>
</tr>
<tr>
<td></td>
<td>Attention</td>
<td>Wilk et al., 2005.</td>
</tr>
<tr>
<td></td>
<td>Medication</td>
<td>Knowles et al., 2010.</td>
</tr>
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</table>

variable, injury type (i.e., closed head versus penetrating), was excluded given that 100% of participants had sustained a closed head injury. The remaining categorical variables, containing information on lesion location, were also excluded because they had greater than two categories; hemisphere (i.e., left, right, and both), and lobe.
In addition to variables listed in Table 8.1, correlations were also explored between cognitive neuropsychological variables and: (i) HADS anxiety scores, given statistically significant differences on HADS anxiety classifications (Chapter Six), and with reference to the reported effects of anxiety on neurocognition (see Byrne & Eysenck, 1995; Castaneda, Tuulio-Henriksson, Marttunen, Suvisaari, & Lonnqvist, 2008; O’Toole & Pedersen, 2011; Rinck, Becker, Kellermann, & Roth, 2003), and (ii) psychosis onset latency in the PFTBI group, given the novel nature of this research, and because the duration between the injury and subsequent development of illness may theoretically share a relationship with neuropsychological profile (e.g., a shorter illness onset latency may be related to poorer performance on the test battery).

Hypothesised mediating variables were subjected to Pearson Product-Moment correlational analyses using IBM® SPSS® software, Version 19 (IBM Corporation, New York, USA). Data from the TMT Form A and RBANS Attention Index were used as measures of processing speed and attention, respectively. Data cleaning and assessments of normality for the cognitive neuropsychological variables were contained in Chapter Seven. Normality for all Stroop and TMT items was corrected by transformation (detailed in Chapter Seven), and the four RBANS subtests unable to be corrected by transformation were omitted from this analysis; Figure Copy, Line Orientation, Picture Naming, and List Recognition. Bonferonni alpha correction was deemed too conservative to account for multiple comparisons in this analysis (i.e., 0.05/650, \( p < 0.0001 \)). Instead, alpha was set at \( p < 0.01 \), and these findings were interpreted with appropriate caution. Correlations significant at \( p < 0.05 \) were highlighted in tabulated results to indicate the potential for further relationship trends between variables. These are discussed in Appendix T.

---

9 Although it was suspected that the TMT Form A may have reduced sensitivity in identifying group-wise differences in processing speed (discussed in Chapter Seven results), this measure was deemed adequate in the exploration of linear relationships.
Table 8.2

Hypothesised Directionality of Correlations between Potential Mediators and Cognitive Neuropsychological Variables

<table>
<thead>
<tr>
<th>Potential Mediator</th>
<th>RBANS Immediate Memory</th>
<th>RBANS Visuo-Spatial</th>
<th>RBANS Attention</th>
<th>RBANS Delayed Memory</th>
<th>RBANS TOTAL</th>
<th>RBANS List Learning</th>
<th>RBANS Story Memory</th>
<th>RBANS Digit Span</th>
<th>RBANS Coding</th>
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<th>RBANS Figure Recall</th>
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**Note.** + = positive relationship hypothesised; - = negative relationship hypothesised; ? = relationship uncertain, exploratory correlational analysis.
Table 8.2

Hypothesised Directionality of Correlations between Potential Mediators and Cognitive Neuropsychological Variables (Continued)

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<th>Potential Mediator</th>
<th>Phonological Fluency (a)</th>
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<th>Stroop Colour Trial</th>
<th>Stroop Word Trial</th>
<th>Stroop Inhibition Trial</th>
<th>Stroop Switching Trial</th>
<th>Stroop Derived Interference</th>
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<th>TMT Form A</th>
<th>TMT Form B</th>
<th>TMT Difference Score</th>
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</table>

Note. + = positive relationship hypothesised; - = negative relationship hypothesised; ? = relationship uncertain, exploratory correlational analysis.
8.4 Results

The descriptive statistics for each cohort were presented in Chapters Six (injury/illness demographics) and Seven (cognitive neuropsychological task performance). The sections following present the results of the correlational analyses for each cohort in turn.

8.4.1 Healthy cohort.

Correlation coefficients for the healthy cohort are contained in Table 8.3. The data indicated that slower processing speed on the TMT Form A was related to reduced Coding, and processing speed, mental inhibition and switching, according to all Stroop trials and the TMT Form B. Better Attention was related to better Total RBANS, Digit Span, Coding, and mental switching (Stroop only). Increased “premorbid” IQ was associated with better phonological fluency (total), and better current IQ (WASI). However, increased current IQ was related to better Visuo-spatial processing and Story Recall.
Table 8.3
Correlation Coefficients for Potential Mediators and Cognitive Neuropsychological Variables in Healthy Controls

<table>
<thead>
<tr>
<th>Potential Mediator</th>
<th>RBANS Immediate Memory</th>
<th>RBANS Visuo-Spatial</th>
<th>RBANS Attention</th>
<th>RBANS Delayed Memory</th>
<th>RBANS TOTAL</th>
<th>RBANS List Learning</th>
<th>RBANS Story Memory</th>
<th>RBANS Digit Span</th>
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<td>-.01</td>
<td>-.69***</td>
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<td>.17</td>
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<td>-.15</td>
<td>.09</td>
<td>.51**</td>
<td>-.09</td>
</tr>
<tr>
<td>Total education (yrs)</td>
<td>.14</td>
<td>-.11</td>
<td>.23</td>
<td>.14</td>
<td>.19</td>
<td>-.07</td>
<td>.19</td>
<td>.16</td>
<td>.20</td>
<td>.17</td>
<td>.31</td>
<td>.35</td>
</tr>
</tbody>
</table>

*p < .05, **p < .01, ***p < .001

(continued)

Table 8.3
Correlation Coefficients for Potential Mediators and Cognitive Neuropsychological Variables in Healthy Controls (Continued)

<table>
<thead>
<tr>
<th>Potential Mediator</th>
<th>Phonological Fluency (a)</th>
<th>Phonological Fluency Total</th>
<th>Stroop Colour Trial</th>
<th>Stroop Word Trial</th>
<th>Stroop Inhibition Trial</th>
<th>Stroop Switching Trial</th>
<th>Stroop Derived Interference</th>
<th>Stroop Derived Switching Interference</th>
<th>TMT Form A</th>
<th>TMT Form B</th>
<th>TMT Difference Score</th>
<th>WASI Full Scale IQ</th>
<th>WASI Matrix Reasoning</th>
<th>WASI Vocabulary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Processing Speed (TMT A)</td>
<td>-.35</td>
<td>-.45*</td>
<td>.82***</td>
<td>.80***</td>
<td>.80***</td>
<td>.64***</td>
<td>.72***</td>
<td>.57***</td>
<td>-</td>
<td>.78***</td>
<td>.14</td>
<td>.14</td>
<td>.10</td>
<td>.06</td>
</tr>
<tr>
<td>Attention (RBANS Index)</td>
<td>.31</td>
<td>.24</td>
<td>-.41</td>
<td>-.32</td>
<td>-.51*</td>
<td>-.55**</td>
<td>-.50*</td>
<td>-.55**</td>
<td>-.37</td>
<td>-.32</td>
<td>-.07</td>
<td>.32</td>
<td>.12</td>
<td>.12</td>
</tr>
<tr>
<td>HADS anxiety</td>
<td>-.13</td>
<td>.03</td>
<td>.19</td>
<td>.25</td>
<td>.20</td>
<td>.22</td>
<td>.18</td>
<td>.21</td>
<td>.20</td>
<td>.30</td>
<td>.31</td>
<td>.22</td>
<td>-.04</td>
<td>.15</td>
</tr>
<tr>
<td>Premorbid (NART) IQ</td>
<td>.22</td>
<td>.51**</td>
<td>-.24</td>
<td>-.04</td>
<td>-.20</td>
<td>-.20</td>
<td>-.30</td>
<td>-.22</td>
<td>-.27</td>
<td>-.10</td>
<td>.21</td>
<td>.62**</td>
<td>.31</td>
<td>.23</td>
</tr>
<tr>
<td>WASI Full Scale IQ</td>
<td>.36</td>
<td>.46*</td>
<td>.15</td>
<td>.32</td>
<td>.17</td>
<td>-.08</td>
<td>.13</td>
<td>-.13</td>
<td>.14</td>
<td>.29</td>
<td>.22</td>
<td>-</td>
<td>.40</td>
<td>.51*</td>
</tr>
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<td>.02</td>
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<td>-.11</td>
<td>.14</td>
<td>-.12</td>
<td>.06</td>
<td>-.01</td>
<td>-.18</td>
<td>.29</td>
<td>-.05</td>
<td>.32</td>
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</table>

*p < .05, **p < .01, ***p < .001
8.4.2 Traumatic brain injury without psychosis (TBIWP).

Correlation coefficients for the TBIWP patient cohort are presented in Table 8.4. Longer duration (i.e., years) since injury was related to more impaired mental switching on the Stroop (switching trial, and derived switching interference). Slower processing speed was related to reduced List Recall, but better mental switching on the TMT (Form B), while better attention was related to better total performance on the RBANS, and higher Full Scale IQ. Increased premorbid IQ correlated with better Immediate Memory and phonological fluency (a) word production. However, increased current IQ was related to better Attention, and the WASI subscale scores (as would be expected).
Table 8.4
Correlation Coefficients for Potential Mediators and Cognitive Neuropsychological Variables in TBIWPI

<table>
<thead>
<tr>
<th>Potential Mediator</th>
<th>RBANS Immediate Memory</th>
<th>RBANS Visuospatial</th>
<th>RBANS Attention</th>
<th>RBANS Delayed Memory</th>
<th>RBANS TOTAL</th>
<th>RBANS List Learning</th>
<th>RBANS Story Memory</th>
<th>RBANS Digit Span</th>
<th>RBANS Coding</th>
<th>RBANS List Recall</th>
<th>RBANS Story Recall</th>
<th>RBANS Figure Recall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of injury (yrs)</td>
<td>.07</td>
<td>.42</td>
<td>.50</td>
<td>.30</td>
<td>.36</td>
<td>-.29</td>
<td>-1.15</td>
<td>.06</td>
<td>.09</td>
<td>.10</td>
<td>-1.6</td>
<td>.15</td>
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<tr>
<td>Injury severity (LOC) (min)</td>
<td>-.21</td>
<td>-.13</td>
<td>.08</td>
<td>-.56</td>
<td>-.28</td>
<td>-.54</td>
<td>-1.12</td>
<td>.09</td>
<td>-.25</td>
<td>-.69*</td>
<td>-.65*</td>
<td>-.52</td>
</tr>
<tr>
<td>Injury severity (PTA) (min)</td>
<td>-.67*</td>
<td>.39</td>
<td>-.19</td>
<td>-.24</td>
<td>-.30</td>
<td>-.46</td>
<td>-.73*</td>
<td>-.44</td>
<td>.09</td>
<td>-.11</td>
<td>-.12</td>
<td>-.60</td>
</tr>
<tr>
<td>Time since injury (yrs)</td>
<td>-.23</td>
<td>-.35</td>
<td>-.12</td>
<td>-.59</td>
<td>-.36</td>
<td>-.56</td>
<td>.03</td>
<td>-.20</td>
<td>-.12</td>
<td>-.64*</td>
<td>-.65*</td>
<td>-.65*</td>
</tr>
<tr>
<td>Processing Speed (TMT A)</td>
<td>-.21</td>
<td>-.15</td>
<td>.07</td>
<td>-.38</td>
<td>-.22</td>
<td>-.62</td>
<td>-.26</td>
<td>.10</td>
<td>-.52</td>
<td>-.83**</td>
<td>-.51</td>
<td>-.34</td>
</tr>
<tr>
<td>Attention (RBANS Index)</td>
<td>.54</td>
<td>.60</td>
<td>-.24</td>
<td>-.61</td>
<td>-.35</td>
<td>-.33</td>
<td>.05</td>
<td>-.12</td>
<td>-.14</td>
<td>-.37</td>
<td>-.44</td>
<td>-.65</td>
</tr>
<tr>
<td>HADS anxiety</td>
<td>-.14</td>
<td>-.50</td>
<td>-.24</td>
<td>-.61</td>
<td>-.35</td>
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<td>.05</td>
<td>-.12</td>
<td>-.14</td>
<td>-.37</td>
<td>-.44</td>
<td>-.65</td>
</tr>
<tr>
<td>Premorbid (NART) IQ</td>
<td>.76**</td>
<td>-.28</td>
<td>.42</td>
<td>.16</td>
<td>.46</td>
<td>.29</td>
<td>.68*</td>
<td>.69*</td>
<td>-.12</td>
<td>-.15</td>
<td>.07</td>
<td>.45</td>
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<tr>
<td>WASI Full Scale IQ</td>
<td>.31</td>
<td>.27</td>
<td>.79**</td>
<td>.08</td>
<td>.53</td>
<td>-.02</td>
<td>.15</td>
<td>.37</td>
<td>.51</td>
<td>.12</td>
<td>-.44</td>
<td>.35</td>
</tr>
<tr>
<td>Total education (yrs)</td>
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<td>.40</td>
<td>.03</td>
<td>.38</td>
<td>.33</td>
<td>.20</td>
<td>.02</td>
<td>-.33</td>
<td>.47</td>
<td>.63*</td>
<td>-.34</td>
<td>-.10</td>
</tr>
</tbody>
</table>

*p < .05, **p < .01, ***p < .001

(continued)

Table 8.4
Correlation Coefficients for Potential Mediators and Cognitive Neuropsychological Variables in TBIWPI (Continued)

<table>
<thead>
<tr>
<th>Potential Mediator</th>
<th>Phonological Fluency (a)</th>
<th>Phonological Fluency Total</th>
<th>Stroop Colour Trial</th>
<th>Stroop Word Trial</th>
<th>Stroop Inhibition Trial</th>
<th>Stroop Switching Trial</th>
<th>Stroop Derived Interference</th>
<th>Stroop Derived Switching Interference</th>
<th>TMT Form A</th>
<th>TMT Form B</th>
<th>TMT Difference Score</th>
<th>WASI Full Scale IQ</th>
<th>WASI Matrix Reasoning</th>
<th>WASI Vocabulary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of injury (yrs)</td>
<td>-.18</td>
<td>-.23</td>
<td>.03</td>
<td>-.23</td>
<td>.02</td>
<td>-.29</td>
<td>.05</td>
<td>-.28</td>
<td>-.29</td>
<td>.52</td>
<td>.71*</td>
<td>.45</td>
<td>.48</td>
<td>.27</td>
</tr>
<tr>
<td>Injury severity (LOC) (min)</td>
<td>-.06</td>
<td>-.07</td>
<td>-.26</td>
<td>.15</td>
<td>.17</td>
<td>-.70*</td>
<td>.20</td>
<td>.69*</td>
<td>.43</td>
<td>-.10</td>
<td>.10</td>
<td>.08</td>
<td>.06</td>
<td>.05</td>
</tr>
<tr>
<td>Injury severity (PTA) (min)</td>
<td>-.66*</td>
<td>-.36</td>
<td>.54</td>
<td>.50</td>
<td>.31</td>
<td>.12</td>
<td>.29</td>
<td>.10</td>
<td>-.03</td>
<td>-.25</td>
<td>-.30</td>
<td>-.30</td>
<td>-.04</td>
<td>-.41</td>
</tr>
<tr>
<td>Time since injury (yrs)</td>
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<td>.09</td>
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<td>.25</td>
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<td>.78**</td>
<td>.47</td>
<td>.77**</td>
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<td>-.51</td>
<td>.05</td>
<td>.12</td>
<td>.08</td>
<td>.12</td>
</tr>
<tr>
<td>Processing Speed (TMT A)</td>
<td>-.13</td>
<td>-.17</td>
<td>.02</td>
<td>.35</td>
<td>.28</td>
<td>.64*</td>
<td>.30</td>
<td>.63</td>
<td>-</td>
<td>.86**</td>
<td>.39</td>
<td>.12</td>
<td>.05</td>
<td>.18</td>
</tr>
<tr>
<td>Attention (RBANS Index)</td>
<td>.44</td>
<td>.37</td>
<td>-.47</td>
<td>-.66*</td>
<td>-.60</td>
<td>-.37</td>
<td>-.57</td>
<td>-.35</td>
<td>-.07</td>
<td>.69*</td>
<td>.71*</td>
<td>.79**</td>
<td>.66*</td>
<td>.65*</td>
</tr>
<tr>
<td>HADS anxiety</td>
<td>.05</td>
<td>.07</td>
<td>.08</td>
<td>.34</td>
<td>.59</td>
<td>.54</td>
<td>.51</td>
<td>.51</td>
<td>-.11</td>
<td>-.19</td>
<td>-.14</td>
<td>.03</td>
<td>-.21</td>
<td>.25</td>
</tr>
<tr>
<td>Premorbid (NART) IQ</td>
<td>.76**</td>
<td>.53</td>
<td>-.40</td>
<td>-.37</td>
<td>-.33</td>
<td>-.03</td>
<td>-.31</td>
<td>-.02</td>
<td>-.31</td>
<td>.15</td>
<td>.32</td>
<td>.29</td>
<td>-.11</td>
<td>.55</td>
</tr>
<tr>
<td>WASI Full Scale IQ</td>
<td>.35</td>
<td>.26</td>
<td>-.47</td>
<td>-.65*</td>
<td>-.18</td>
<td>-.20</td>
<td>-.13</td>
<td>-.19</td>
<td>.12</td>
<td>.63</td>
<td>.65</td>
<td>-</td>
<td>.83**</td>
<td>.85**</td>
</tr>
<tr>
<td>Total education (yrs)</td>
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<td>.17</td>
<td>.35</td>
<td>.19</td>
<td>-.04</td>
<td>-.47</td>
<td>-.07</td>
<td>-.49</td>
<td>.59</td>
<td>.39</td>
<td>.01</td>
<td>.04</td>
<td>.05</td>
<td>.06</td>
</tr>
</tbody>
</table>

*p < .05, **p < .01, ***p < .001,
8.4.3 Schizophrenia.

Correlation coefficients for schizophrenia patients are presented in Table 8.5. In schizophrenia, a longer duration of illness was related to reduced performance on Story Recall, whereas increased thought disorder was related to reduced Figure Recall. Processing speed was related to half of the RBANS scales in schizophrenia; slower processing correlated with poorer Attention, Delayed Memory, Coding, Story Recall, Figure Recall, and the Total RBANS score. Slower processing speed was also related to reduced phonological fluency (both ‘a’ and total trials), and all Stroop measures (except for the word trial), as well as being highly positively correlated with the related TMT scales (Form B and difference score, as would be expected). Better attention was related to better Digit Span, Coding, Figure Recall, Stroop colour, and processing speed and mental switching on the TMT scales. Finally, better premorbid IQ was related to better current Full Scale IQ, while increased current IQ was related to better Figure Recall, as well as showing large correlations with the related WASI subscales.
**Table 8.5**  
**Correlation Coefficients for Potential Mediators and Cognitive Neuropsychological Variables in Schizophrenia**

<table>
<thead>
<tr>
<th>Potential Mediator</th>
<th>RBANS Immediate Memory</th>
<th>RBANS Visuo-Spatial</th>
<th>RBANS Attention</th>
<th>RBANS Delayed Memory</th>
<th>RBANS TOTAL</th>
<th>RBANS List Learning</th>
<th>RBANS Story Memory</th>
<th>RBANS Digit Span</th>
<th>RBANS Coding</th>
<th>RBANS List Recall</th>
<th>RBANS Story Recall</th>
<th>RBANS Figure Recall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of Illness Onset (yrs)</td>
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<td>.39</td>
<td>.25</td>
<td>.38</td>
<td>.30</td>
<td>-.36</td>
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<td>.10</td>
<td>.05</td>
<td>-.30</td>
<td>.17</td>
<td>.36</td>
</tr>
<tr>
<td>Illness Duration (yrs)</td>
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<td>-.25</td>
<td>-.12</td>
<td>-.26</td>
<td>-.04</td>
<td>-.46*</td>
<td>-.31</td>
<td>-.48*</td>
<td>-.11</td>
<td>-.53**</td>
<td>-.35</td>
</tr>
<tr>
<td>PANSS Delusions</td>
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<td>.06</td>
<td>.36</td>
<td>.16</td>
<td>.11</td>
<td>.19</td>
<td>.12</td>
<td>.23</td>
<td>.39</td>
<td>.41*</td>
<td>.22</td>
<td>-.08</td>
</tr>
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<td>PANSS Positive Scale</td>
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<td>.15</td>
<td>.09</td>
<td>-.08</td>
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<td>.09</td>
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<td>.13</td>
<td>-.26</td>
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<td>-.18</td>
<td>-.18</td>
<td>-.08</td>
<td>-.01</td>
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<td>.10</td>
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<td>-.18</td>
<td>-.27</td>
<td>-.08</td>
<td>-.19</td>
<td>-.03</td>
<td>.03</td>
<td>.07</td>
<td>-.15</td>
<td>-.38</td>
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<td>PANSS Total</td>
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<td>.10</td>
<td>-.09</td>
<td>-.23</td>
<td>-.07</td>
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<td>.02</td>
<td>.08</td>
<td>.16</td>
<td>-.01</td>
<td>-.41*</td>
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<td>-.04</td>
<td>.03</td>
<td>-.13</td>
<td>.03</td>
<td>.07</td>
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<td>.10</td>
<td>.27</td>
<td>-.30</td>
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<tr>
<td>SAPS lifetime hallucinations</td>
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<td>-.20</td>
<td>-.08</td>
<td>.10</td>
<td>.04</td>
<td>.16</td>
<td>.10</td>
<td>-.06</td>
<td>.13</td>
<td>.20</td>
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<td>-.15</td>
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<tr>
<td>SAPS current delusions</td>
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<td>.02</td>
<td>.25</td>
<td>.08</td>
<td>.02</td>
<td>.20</td>
<td>.12</td>
<td>.22</td>
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<td>.40</td>
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<td>.09</td>
<td>.16</td>
<td>.07</td>
<td>.24</td>
<td>.16</td>
<td>.03</td>
<td>.24</td>
<td>.36</td>
<td>.12</td>
<td>-.01</td>
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<td>TLC Total Score</td>
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<td>-.25</td>
<td>-.28</td>
<td>-.15</td>
<td>-.35</td>
<td>-.19</td>
<td>-.13</td>
<td>-.24</td>
<td>-.38</td>
<td>-.03</td>
<td>-.15</td>
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<td>.18</td>
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<td>.02</td>
<td>.25</td>
<td>.25</td>
<td>.02</td>
<td>.01</td>
</tr>
<tr>
<td>Processing Speed (TMT A)</td>
<td>-.37</td>
<td>-.52*</td>
<td>-.71***</td>
<td>-.56**</td>
<td>-.76***</td>
<td>-.28</td>
<td>-.43*</td>
<td>-.44*</td>
<td>-.70***</td>
<td>-.40</td>
<td>-.66***</td>
<td>-.56**</td>
</tr>
<tr>
<td>Attention (RBANS Index)</td>
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<td>.31</td>
<td>-</td>
<td>.35</td>
<td>.52</td>
<td>-.15</td>
<td>.02</td>
<td>.74***</td>
<td>.56***</td>
<td>.13</td>
<td>.23</td>
<td>.55**</td>
</tr>
<tr>
<td>HADS anxiety</td>
<td>.14</td>
<td>-.20</td>
<td>-.13</td>
<td>-.27</td>
<td>.04</td>
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<td>-.08</td>
<td>-.12</td>
<td>.10</td>
<td>-.22</td>
<td>-.29</td>
<td>-.05</td>
</tr>
<tr>
<td>Premorbid (NART) IQ</td>
<td>.15</td>
<td>.26</td>
<td>.20</td>
<td>.14</td>
<td>.28</td>
<td>-.10</td>
<td>.41*</td>
<td>.31</td>
<td>-.05</td>
<td>-.13</td>
<td>.33</td>
<td>.26</td>
</tr>
<tr>
<td>WASI Full Scale IQ</td>
<td>.27</td>
<td>.54**</td>
<td>.36</td>
<td>.26</td>
<td>.44*</td>
<td>.18</td>
<td>.42*</td>
<td>.28</td>
<td>.38</td>
<td>-.03</td>
<td>.35</td>
<td>.58**</td>
</tr>
<tr>
<td>Total education (yrs)</td>
<td>-.03</td>
<td>-.02</td>
<td>-.14</td>
<td>.31</td>
<td>.04</td>
<td>.06</td>
<td>-.18</td>
<td>.11</td>
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*p < .05, **p < .01, ***p < .001 (continued)
**Table 8.5**

**Correlation Coefficients for Potential Mediators and Cognitive Neuropsychological Variables in Schizophrenia (Continued)**

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<th>Stroop Derived Interference</th>
<th>Stroop Derived Switching Interference</th>
<th>TMT Form A</th>
<th>TMT Form B</th>
<th>TMT Difference Score</th>
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<th>WASI Matrix Reasoning</th>
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*p < .05, **p < .01, ***p < .001
8.4.4 Psychosis following traumatic brain injury (PFTBI).

Correlation coefficients for the PFTBI patients are contained in Table 8.6. Greater injury severity as defined by duration of LOC was related to reduced Story Memory and Story Recall performance. However, greater injury severity as defined by duration of PTA was related to reduced Story Memory, Coding, List Recall, Story Recall, and mental switching on the Stroop (both the switching and derived switching scores). Psychotic symptoms demonstrated no relationships with measures of cognitive neuropsychological performance once the conservative alpha was applied ($p < .05$). Slower processing was related to poorer Story Memory, Coding, List Recall, Story Recall, Stroop word and inhibition trials, and mental switching (Stroop switching and derived switching). The TMT Form A score was also highly correlated with Form B scores as would be expected, but not with the TMT difference score. Better attention was related to better Digit Span, Coding, phonological fluency (both subtest ‘a’ and total), processing speed, and mental inhibition and switching (according to all Stroop measures and Form A and B of the TMT). Interestingly, higher scores on the HADS anxiety scale (i.e., greater anxiety) were related to higher current IQ (Full Scale and Matrix Reasoning subscale). Greater premorbid IQ was related to the greatest number of measures in the PFTBI cohort, including; better Attention, Digit Span, Coding, and the RBANS Total, as well as better performance on both phonological fluency measures, and all Stroop and TMT measures of processing speed, mental inhibition and switching (except for the TMT difference score). However, current IQ correlated highly with the visuo-spatial IQ subscale only (i.e., Matrix Reasoning).
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<th>RBANS Delayed Memory</th>
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*p < .05, **p < .01, *** p < .001

(continued)
Table 8.6
Correlation Coefficients for Potential Mediators and Cognitive Neuropsychological Variables in PFTBI (Continued)

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<td>-.52</td>
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<td>.73*</td>
<td>.63*</td>
<td>.80**</td>
<td>.60</td>
<td>.79**</td>
<td>.73*</td>
<td>.72*</td>
<td>.44</td>
<td>-.12</td>
<td>.01</td>
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<td>-.13</td>
<td>.19</td>
<td>.12</td>
<td>.28</td>
<td>.09</td>
<td>.28</td>
<td>.08</td>
<td>.24</td>
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<td>.49</td>
<td>.34</td>
<td>.28</td>
<td>.02</td>
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<td>Age of Illness Onset (yrs)</td>
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<td>.48</td>
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<td>.09</td>
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<td>Illness Onset Latency (mths)</td>
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<td>-.17</td>
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<td>-.14</td>
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<td>Antipsychotic Medication % Maximum Dosage</td>
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<td>.66*</td>
<td>-.55</td>
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<td>-.33</td>
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<td>-.29</td>
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<td>PANSS Delusions</td>
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<td>-.54</td>
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<td>-.39</td>
<td>-.42</td>
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<td>-.49</td>
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<td>-.35</td>
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<td>PANSS.Negative Scale</td>
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<td>-.57</td>
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<td>.03</td>
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<td>-.25</td>
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<td>-.57</td>
<td>.69*</td>
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<td>-.17</td>
<td>-.20</td>
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<td>-.04</td>
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<tr>
<td>SAPS lifetime hallucinations</td>
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<td>-.28</td>
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<td>-.34</td>
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<td>-.45</td>
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<td>-.21</td>
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<tr>
<td>TLC Total Score</td>
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<td>.07</td>
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<td>.44</td>
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<tr>
<td>TLC Global Score</td>
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<td>-.13</td>
<td>.03</td>
<td>-.14</td>
<td>.03</td>
<td>.18</td>
<td>-.16</td>
<td>-.46</td>
<td>.34</td>
<td>.30</td>
<td>.32</td>
</tr>
<tr>
<td>Processing Speed (TMT A)</td>
<td>-.68*</td>
<td>-.61</td>
<td>.63*</td>
<td>.80**</td>
<td>.73**</td>
<td>.82**</td>
<td>.71*</td>
<td>.82**</td>
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<td>.39</td>
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<td>-.16</td>
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<tr>
<td>Attention (RBANS Index)</td>
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<td>.78**</td>
<td>-.84**</td>
<td>-.88**</td>
<td>-.80**</td>
<td>-.89**</td>
<td>-.77**</td>
<td>-.88**</td>
<td>-.84**</td>
<td>-.76**</td>
<td>-.40</td>
<td>.40</td>
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<td>.48</td>
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<td>-.35</td>
<td>-.25</td>
<td>-.35</td>
<td>-.41</td>
<td>-.41</td>
<td>-.15</td>
<td>.74**</td>
<td>.75**</td>
<td>.57</td>
</tr>
<tr>
<td>Premorbid (NART) IQ</td>
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<td>.82**</td>
<td>-.79**</td>
<td>-.87**</td>
<td>-.94**</td>
<td>-.85**</td>
<td>-.92**</td>
<td>-.84**</td>
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<td>-.88**</td>
<td>-.67*</td>
<td>.54</td>
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<td>.63*</td>
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<td>WASI Full Scale IQ</td>
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<td>.31</td>
<td>-.05</td>
<td>-.49</td>
<td>-.47</td>
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<td>-.34</td>
<td>-.45</td>
<td>-.36</td>
<td>-.92***</td>
<td>.60</td>
<td></td>
</tr>
<tr>
<td>Total education (yrs)</td>
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<td>.43</td>
<td>-.01</td>
<td>-.42</td>
<td>-.23</td>
<td>-.22</td>
<td>-.22</td>
<td>-.22</td>
<td>-.18</td>
<td>-.27</td>
<td>-.08</td>
<td>.67*</td>
<td>.71</td>
<td>.64*</td>
</tr>
</tbody>
</table>

*p < .05, **p < .01, ***p < .001
8.4.5 Summary of statistically significant relationships.

To help summarise the data and aid comparisons across cohorts, mediating variables that demonstrated relationships with cognitive neuropsychological performance in more than one cohort have been tallied and presented graphically in Figures 8.1 to 8.4. Overall, executive function (i.e., processing speed and attention) demonstrated the greatest number of relationships with cognitive neuropsychological task performance (Figures 8.1 and 8.2). For the healthy cohort, these were shown mostly on tasks where performance was timed, and thus there was an emphasis on speed. However, patient performance, especially from the psychotic cohorts, appeared to be more widely influenced by executive function; relationships were identified with processing speed on more than 50% of tasks for schizophrenia patients, whereas this was similar for attention in PFTBI (i.e., 46.15%). Yet, the greatest influence over PFTBI neurocognitive performance appeared to be premorbid IQ, where relationships were identified with 53.85% of measures. Interestingly, this was unique to PFTBI, with the comparison cohorts showing very few relationships with premorbid IQ (Figure 8.3). By contrast, current IQ demonstrated a small number of relationships for all cohorts, with the smallest number shown by PFTBI patients (3.85%), and the greatest number shown by schizophrenia patients on 15.38% of tasks (Figure 8.4).

Injury variables appeared to be less influential over task performance from TBIWP, relative to PFTBI, patients. However, this was not demonstrated for the illness/clinical variables, with only two relationships shown following the application of alpha correction, and these were specific to the schizophrenia cohort; longer duration of illness and increased thought disorder were associated with aspects of delayed memory (reduced Story Recall and Figure Recall, respectively). However, it is noted that a number of relationships were demonstrated for both illness demographics and symptom profiles at trend level ($p < .05$), and these were shown for both psychotic cohorts (see Appendix T). Finally, the PFTBI cohort demonstrated the greatest number of relationships relative to any other cohort overall (even when this tally was confined to demographic variables relevant to all four cohorts), and the largest coefficients, with the majority between $r = .70$ and $r = .90$. 


Figure 8.1. Percentage of significant correlations between cognitive neuropsychological tasks and processing speed (TMT Form A) for each cohort.

Figure 8.2. Percentage of significant correlations between cognitive neuropsychological tasks and attention (RBANS subscale) for each cohort.
Figure 8.3. Percentage of significant correlations between cognitive neuropsychological tasks and premorbid (NART) IQ for each cohort.

Figure 8.4. Percentage of significant correlations between cognitive neuropsychological tasks and current (WASI) IQ for each cohort.
8.5 Discussion

This chapter aimed to explore the relationships between potential mediators (i.e., injury, illness, and executive function variables) and the cognitive neuropsychological task performance from each of the four cohorts. It was hoped that the identification of significant correlations between these variables would provide an indication of their influence over the task performance reported for each cohort in the previous chapter (Chapter Seven). These analyses were completed in lieu of ANCOVA in Chapter Seven, given the statistical inappropriateness of this test with the current dataset.

Overwhelmingly, the executive functions (processing speed and attention), demonstrated the greatest number of relationships with neurocognitive task performance, and these were also the greatest in strength. These relationships were in the hypothesised direction for each of the cohorts, where faster processing speed and better attention were related to better performance on all tasks. Interestingly, the executive functions appeared to have more of an influence as neurocognition became more impaired across the groups, the result being that processing speed and attention exerted the greatest influence over performance from the psychotic cohorts (i.e., on 84.62% and 80.77% of measures from the schizophrenia and PFTBI cohorts, respectively).

Injury variables demonstrated relatively few relationships with performance. This result was unexpected given the extensive TBI literature that has highlighted the mediating influence of injury-specific demographics on neurocognition (e.g., Leblanc et al., 2006; Moran & Gillon, 2004; Sullivan & Riccio, 2010). However, as discussed in Chapter Five (Section 5.1.7), although the existing literature has commented on these influences, a clear picture of their relationship with neurocognition has not been established. For the PFTBI cohort, the greatest influence appeared to be injury severity, measured by both the duration of LOC, and of PTA. These were aligned with hypotheses, where greater injury severity was related to poorer performance. Interestingly, these relationships were isolated to PFTBI performance, despite the TBI groups having been matched on injury severity. Although, at least in part, this is probably reflective of the greater range of LOC and PTA in the PFTBI cohort (see Chapter Six).

Furthermore, the duration between their injury and assessment was the only injury variable that influenced TBIWP performance, not shown in PFTBI. This is a noted outcome because it was one of the few demographics for which the TBI cohorts were unmatched. Relative to PFTBI, the TBIWP patients had acquired their injury closer to the time of
assessment (see Chapter Six). As such, this is aligned with findings that cognitive function generally shows the most transient over the first two years post injury, with more stable impairments being typical after this time (Schretlen & Shapiro, 2003). Still, this interpretation is offered with due consideration given that a relationship was only shown for two of 26 measures. Moreover, no relationships were demonstrated between the age of injury acquisition and neuropsychological performance for either TBI group. This was surprising, especially in the PFTBI sample where four patients had acquired their injury during childhood/adolescence. It has been reported that childhood TBI may leave the child at greater risk because damage disrupts the developing brain (Beauchamp et al., 2011a). On the other hand, increased neuroplasticity in children may allow for neurocognitive recovery, offering one possible explanation for the absence of relationships in this dataset.

Illness demographics, including symptom profile, demonstrated very little relationship with task performance. However, although relationships were hypothesised to be greater in number in accordance with suggestions made in the literature (e.g., Henry & Crawford, 2005; Rossell, 2006; Rossell et al., 1999), no particular characteristic of illness has been consistently identified as influential across studies. The duration of illness was related to neurocognition in the hypothesised direction; that is, a longer duration of illness was related to poorer performance. Yet, this was demonstrated only in schizophrenia, with illness duration appearing to have no influence over performance for the PFTBI patients. Again, although the psychotic cohorts were matched on illness duration, these results probably reflect the greater range from the schizophrenia cohort. Similarly, thought disorder related only to reduced Figure Recall in the schizophrenia cohort. This aligns with literature highlighting the influence of thought disorder on memory systems (e.g., in semantic memory, Gouzoulis-Mayfrank et al., 2003), and with hypotheses. Yet, a greater number of relationships were expected, especially from the schizophrenia cohort who had a mean thought disorder score in the ‘severe’ range. Low (mild) scores of thought disorder from the PFTBI cohort possibly explain the absence of relationships from this group.

Greater antipsychotic dosage did not demonstrate a relationship with task outcome. It is imperative to note that this does not reflect that medication in the schizophrenia and PFTBI cohorts was unrelated to neurocognitive task performance, but that differences in the maximum dosage (once again matched across cohorts) was not especially associated with performance. Furthermore, as reflected by the exploratory hypothesis, the specific effects of antipsychotics on neurocognition are unclear. On one hand, larger doses may effectively
reduce positive symptoms and thereby indirectly improve cognition, yet, on the other hand, larger doses may be associated with greater side effects, including decreased processing speeds and attention. This dual effect on cognitive neuropsychological performance has already been illustrated for Clozapine (Pallanti, Quercioli, & Pazzagli, 1999; Rajji et al., 2010), and would be further variable from patient to patient. Thus, the absence of relationships here is not surprising.

In PFTBI patients, greater anxiety as measured by the HADS anxiety scale was related to higher IQ. While anxiety was predicted to reduce cognitive neuropsychological performance, as has been demonstrated by the literature (Byrne & Eysenck, 1995; Castaneda et al., 2008; O’Toole & Pedersen, 2011; Rinck et al., 2003), there were no other relationships identified with scores on the HADS anxiety scale. However, there is evidence for a link between higher IQ and anxiety in patients with generalised anxiety disorder (GAD), which has been associated with the depletion of choline and related compounds in subcortical white matter in these patients (Coplan et al., 2011). It stands to reason that brain tissue choline levels in PFTBI may also be mediating the relationship between anxiety and IQ, especially given that; (i) PFTBI patients showed the greatest degree of anxiety on the HADS (albeit not significantly so), (ii) choline tissue levels and have been linked to TBI as an early marker of trauma (Scremin, Li, Roch, Booth, & Jenden, 2006), and (iii) choline treatment has demonstrated efficacy in enhancing recovery post TBI (Guseva, Hopkins, Scheff, & Pauly, 2008; Scremin et al., 2006), including measurable improvements in neurocognition (Calatayud Maldonado, Calatayud Perez, & Aso Escario, 1991; Guseva et al., 2008). On the other hand, this relationship was not shown in the TBIWP cohort. However, TBIWP patients also demonstrated the lowest level of anxiety as measured by the HADS, which may account for this result.

Interestingly, premorbid IQ correlated with current IQ in all but the TBI cohorts. Given the relatively poor performance from the TBIWP cohort on both on the NART (premorbid IQ) and the verbal scale of the WASI (Chapter Seven), TBIWP would be predicted to show the strongest relationship here. Similarly, as already noted, relative to any other potential mediator, premorbid IQ exerted the most influence over neuropsychological performance from the PFTBI patients (see Figure 8.3), with current IQ being one of the only exceptions (although, a relationship was shown at trend level). Thus, in this case, the smaller sample sizes of the TBI cohorts may have caused this relationship to go undetected. Still, the number of relationships demonstrated between premorbid IQ and the PFTBI data suggests
that intelligence prior to injury, and subsequent illness, is particularly influential over the cognitive neuropsychological profile post diagnosis. Thus, the potential for a predictive relationship is highlighted, similar to the one demonstrated in other syndromes (e.g., Brill et al., 2009).

Conversely, current Full Scale IQ (WASI) illustrated minimal influence over neurocognition, ranging from 3.85% to 15.38% (see Figure 8.4). This was inconsistent with hypotheses, given existing work that has shown the link between intelligence and neurocognition, especially in schizophrenia (Knowles et al., 2010; Lincoln et al., 2010). As discussed in Chapter Three, however, evidence has accrued more recently to suggest the autonomy of IQ and neurocognition (Badcock et al., 2005; Wilk et al., 2005), and these data may offer further support for this hypothesis, both in schizophrenia and other cohorts.

Given that the pattern of neuropsychological deficits in PFTBI suggest that the psychotic aspects of their illness are driving the majority of deficits, it is surprising that neurocognitive performance was not related to the latency of symptom onset in this group. This was further expected due to the range of onset latency demonstrated by the group; from two months to 12 years (with a mean of approximately 4.97 years). It is also likely that some of the injury localisation data unable to be investigated in these analyses had some influence on the neurocognitive results from the TBI cohorts. The literature is often specific about certain injury demographics and resultant effects, for example, where visual Gestalt processing is reduced in patients with right hemispheric lesions relative to those with left-sided lesions (Delis et al., 1986; Robertson & Lamb, 1991). Ideally, much larger cohorts separating the TBI and PFTBI samples into subgroups specific to locus of injury should be investigated in group-wise analyses.

These data have demonstrated that selected injury and illness-related factors are associated with neurocognition. It is likely that these behave as mediators of poor performance given the prior literature in TBI and schizophrenia. However, it is noted that a number of relationships, or absence of relationships, remain unexplained here. Due to small sample sizes, limited statistical correction was able to be applied for multiple comparisons. This is a substantial limitation of this analysis, and means that it is highly likely that some of these findings are spurious. As such, the relationships demonstrated here are acknowledged cautiously, and further investigation of these potential mediators is considered vital. Moreover, although the greater number of relationships identified in the psychotic cohorts suggests that certain mediators may be more influential where neurocognition is more
impaired, it is likely that some of the stronger relationships (i.e., larger coefficients) shown for the PFTBI cohort reflect the larger range of this group on particular variables. Thus, the larger coefficients demonstrated for this group should not necessarily be taken as an indication of the greater influence of these variables. Larger group sizes are required to determine the representativeness of this sample, and thereby the accuracy of these findings.
Chapter 9: Discriminant Function Analysis: Prediction of PFTBI from Neuropsychological Profile

9.1 Introduction

Discriminant function analysis (DFA) was conducted to determine whether performance on the cognitive neuropsychological battery could correctly classify PFTBI group membership, as distinct from healthy, TBIWP, and schizophrenia control cohorts. The discriminant model was then cross-validated to investigate how well the classification procedure may correctly predict cognitive neuropsychological scores in a new sample.

9.2 Hypotheses

Group distinctions according to neuropsychological profile were expected to be shown by DFA. At a minimum, these were expected to distinguish between the PFTBI and healthy cohorts, following their anticipated performance as the poorest, and best, scorers respectively. Thus, a distinction was expected between the hypothesised opposite ends of the neuropsychological performance spectrum. No further hypotheses were made beyond this.

9.3 Method

9.3.1 Participants.

The participant cohorts were detailed in Chapter Six. It is noted that the schizophrenia cohort was reduced in size on the Stroop task (n = 22) (see Chapter Six for details).

9.3.2 Experimental measures and procedure.

All variables from the cognitive neuropsychological battery were considered for DFA analysis. Measures were excluded as predictor variables where; (i) no group differences were shown by group-wise comparisons detailed in Chapter Seven, (ii) one variable contributed to another; in this case, the total score was taken except where these represented derived scores. For example, the TMT difference and ratio scores were omitted in favour of TMT Trial A and TMT Trial B. Remaining variables were only included in analysis if they complied with the normality assumption (according to skewness and kurtosis coefficients where non-normal distributions are defined by coefficients exceeding 2 x +/- the standard error; Groeveveld & Meeden, 1984). This left the RBANS Total index score and the Stroop Colour trial score. These were not too highly correlated (r = -.48, p < .001) and thus deemed appropriate for DFA analysis (Chan, 2005). Statistical analyses were conducted using IBM® SPSS® software, Version 19 (IBM Corporation, New York, USA). Data cleaning results, including
assessments of normality for all cognitive neuropsychological variables were detailed in Chapter Seven.

9.4 Results

9.4.1 Discriminant function.

The descriptive statistics for the RBANS total and Stroop Colour trial were detailed in Chapter Seven, however, these are restated in Table 9.1 for convenience. The linear combination of predictors significantly differentiated the four cohorts; Wilks’s Λ = .49, χ² (6, N = 65⁹) = 43.42, p < .001. An eigenvalue of .95 indicated that 95.2% of the variance was explained by the discriminant function. The function showed a large positive coefficient (both standardised function and structure [within-group] coefficients) with the RBANS Total index score alongside a negative coefficient with Stroop Colour trial performance (see Table 9.2). This indicates a linear discriminant function capturing general neurocognition, where higher scores on the RBANS Total index (better performance on immediate and delayed memory, visuo-spatial, language, and attention tasks), were associated with lower scores on the Stroop Colour trial (reduced and superior processing speed). This interpretation was consistent with the descriptive and inferential statistics for these variables already discussed at length (Section 7.5 Results), and with the discriminant function group means. Group centroids for the discriminant function showed that healthy controls were the highest performers, followed by TBIWP, schizophrenia, and finally PFTBI patients who show the poorest performance; discriminant function group means 1.00, .39, -.46, and -1.68, respectively (see Figure 9.1).

Table 9.1
Mean (SD) Performance on the RBANS Total and Stroop Colour Trial by Cohort

<table>
<thead>
<tr>
<th>Measure</th>
<th>HC (n = 23)</th>
<th>TBIWP (n = 10)</th>
<th>SCZ (n = 23)*</th>
<th>PFTBI (n = 10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBANS Total</td>
<td>110.57 (10.79)</td>
<td>100.80 (13.11)</td>
<td>88.52 (16.56)</td>
<td>74.90 (16.84)</td>
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<tr>
<td>Stroop Colour Trial</td>
<td>25.52 (4.95)</td>
<td>28.10 (5.02)</td>
<td>34.45 (9.44)</td>
<td>48.10 (22.22)</td>
</tr>
</tbody>
</table>

* n=22 for Stroop Colour trial due to colour blindness in one patient.

⁹ As per the MANOVA analyses n = 22 for the schizophrenia group Stroop task data, this case was thus excluded from all discriminant function combinations.
Table 9.2

*Standardised Canonical and Correlation Coefficients of Predictor Variables with the Discriminant Function*

<table>
<thead>
<tr>
<th></th>
<th>Standardized Canonical Coefficients</th>
<th>Within-group Correlation Coefficients</th>
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</thead>
<tbody>
<tr>
<td>RBANS Total</td>
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<td>.94*</td>
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<td>Stroop Colour</td>
<td>-.38</td>
<td>-.74*</td>
</tr>
</tbody>
</table>

*largest absolute correlation between each variable and any discriminant function

9.4.2 Group classification.

Table 9.3 provides the group classification results. The discriminant function correctly classified 52.3% of individuals in the sample; 69.6% of healthy controls, 40% of TBIWP, 40.9% of patients with schizophrenia, and 50% of the dual-diagnosis (PFTBI) group. Misclassified healthy control cases were predominantly (i.e., 26.1%) mistaken for TBIWP patients; and this was similarly shown for misclassified TBIWP cases, where 30% were mistaken for healthy group membership. Interestingly, no TBIWP cases were misclassified as PFTBI cases. Likewise, misclassified schizophrenia cases were predominantly mistaken for dual-diagnosis PFTBI cases (27.3%), and PFTBI cases were predominantly (40%) mistaken for schizophrenia cases, with only 10% (n = 1) mistakenly allocated to TBIWP group membership. Importantly, no healthy cases were mistaken for PFTBI membership and no PFTBI cases were mistaken for healthy membership. The kappa coefficient was computed and ruled out chance agreement; coefficient greater than zero, $\kappa = .35$, $p < .001$. Finally, the leave-one-out technique was employed for cross validation, and indicated that the classification procedure would correctly classify 47.7% of the cases in a new sample.

Table 9.3

*Classification Matrix Based on the Neuropsychological Linear Discriminant Function*

<table>
<thead>
<tr>
<th>Cohort</th>
<th>% Correct</th>
<th>Predicted Group Membership</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Healthy Control</td>
<td>TBIWP</td>
</tr>
<tr>
<td>Healthy Control</td>
<td>69.6%</td>
<td>16</td>
</tr>
<tr>
<td>TBIWP</td>
<td>40.0%</td>
<td>3</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>40.9%</td>
<td>3</td>
</tr>
<tr>
<td>PFTBI</td>
<td>50.0%</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>52.3%</td>
<td>22</td>
</tr>
</tbody>
</table>

9.5 Discussion

Discriminant function analysis (DFA) was completed to investigate whether PFTBI group membership could be determined by cognitive neuropsychological profile, as distinct from healthy, TBIWP, and schizophrenia control cohorts. The significant
Figure 9.1. Group centroids on two discriminant functions derived from RBANS Total (neurocognition) and Stroop Colour trial (processing speed) scores. Discriminant function one was significant. Group centroids (x-axis) illustrate the superior performance of healthy controls, followed by TBIWP, schizophrenia, and finally PFTBI according to the linear combination of neurocognition and processing speed.

discriminant function explained 95.2% of the variance from the total sample, and demonstrated an inverse relationship between total scores on the RBANS and scores on the Stroop colour trial. That is, superior general neurocognition (including immediate and delayed memory, visuo-spatial, language, and attention) accompanied faster processing speed. This pattern was true for all four cohorts and appears appropriate given that it is (i) consistent with the descriptive and group-wise results on these measures (detailed in Chapter Seven), and (ii) theoretically plausible that faster processing speeds are associated with
superior neurocognition. The group centroids for the discriminant function also reflected the pattern of poor performance demonstrated by the existing group-wise comparison data (Chapter Seven); the best performance was shown by the healthy cohort, followed by TBIWP, schizophrenia, and finally PFTBI. As such, healthy and PFTBI cohorts represented opposite, and significantly distinct, extremes of the performance spectrum as hypothesised.

Nonetheless, correct classification by the discriminant function was just above chance for the entire sample (52.3%), with the greatest rates of incorrect classifications shown for patients from the TBIWP and schizophrenia cohorts (40% and 40.9% respectively). Given that these groups were designed to represent TBI and psychosis counterparts of the PFTBI patients, and thus, share comparable neuropsychological deficits to some degree, these misclassifications are reasonable. Patients with TBIWP were misclassified as both healthy and schizophrenia participants, whereas patients with schizophrenia were misclassified as belonging to all three alternative cohorts. In both cases, this at least partially reflects the heterogeneity in neuropsychological profile according to severity of injury in TBI (e.g., Haut et al., 1991a; Perlstein et al., 2006; Seignourel et al., 2005), and the typical heterogeneity already established in schizophrenia (e.g., Passerieux et al., 1997).

The pattern of misclassifications of the TBIWP patients, however, is probably driven by an additional bias in the TBIWP sample. In particular, the three patients misclassified as healthy cases suggests cognitive neuropsychological ability that is inconsistent with the existing literature reporting substantial deficits post TBI in both neurocognition (Kave et al., 2011; McKenna et al., 2006; Oddy et al., 1985; Perri et al., 2000; Zino & Ponsford, 2006) and processing speed (Ben-David et al., 2011; Ponsford et al., 2008; Rios et al., 2004; Spikman et al., 2004). Despite having been statistically matched on injury severity with the PFTBI cohort, there is evidently a greater rate of return to healthy functioning than would be predicted from existing studies. This bias is made all the more likely given the considerably small size of the TBIWP cohort, and further accounts for the majority of healthy case misclassifications as TBIWP. The three TBIWP patients misclassified as patients with schizophrenia provide evidence for deficits closer to those suggested by the existing research. It would be expected that a larger TBIWP cohort eliminating this bias would also demonstrate a minority of misclassifications as PFTBI cases.

As noted, a critical finding was that no healthy cases were mistaken for PFTBI membership and no PFTBI cases were mistaken for healthy membership. Thus, it appears that the combined measurement of general neurocognition and processing speed consistently
distinguishes between healthy and PFTBI cases, and is likely to remain consistent in comparisons made in a new sample (i.e., kappa coefficient). Accordingly, these novel data indicate that cognitive neuropsychological status is a moderate predictor of PFTBI, as distinct from both healthy and TBIWP individuals, yet only just above chance when compared with schizophrenia patients (i.e., 50-60%). Thus, this analysis has indicated that the nature of general cognitive neuropsychological deficits in PFTBI may be more greatly influenced by the psychotic aspects of their dual diagnosis than the effects of the TBI itself. However, this impression may be inaccurate given the potential bias of the TBIWP cohort.
Chapter 10: General Discussion and Conclusions

10.1 Introduction

This chapter summarises the key empirical findings and major conclusions of this thesis. These are discussed within the context of their theoretical, diagnostic, treatment, and research implications. The chapter concludes with reference to the unique contribution made by this research and subsequent insight into the cognitive neuropsychological profile of the cohort central to this investigation; PFTBI.

10.2 Key Empirical Findings: A Summary

Dually-diagnosed PFTBI is associated with substantial deficits in cognitive neuropsychological function. PFTBI assessments indicated a profile that is most similar to the one demonstrated by schizophrenia patients, although significantly marked in degree of impairment. This was further supported by DFA analysis, where the greatest misclassification of the PFTBI cohort was as a schizophrenia patient, and vice versa. Moderate prediction of patient group membership was indicated by this analysis using scores from two prominent features of the neuropsychological battery (i.e., RBANS Total [overall neurocognition] and Stroop Colour Trial [processing speed]). In addition, language-specific deficits were uniquely shared by the brain injured cohorts, partially driven by the laterality of language processing.

The additive nature of deficits in PFTBI was apparent. This manifested as a consistently greater degree of impairment, even where group-wise differences were not significant. Moreover, in presentation, the PFTBI cohort appeared considerably more unwell, some too unwell to undertake even the most basic of cognitive assessment, despite matched injury severity and clinical symptomatology. In some cases this was demonstrated by considerable physical impairment, including wheelchair confinement and substantially restricted movement, especially reduced control of the head and limbs (i.e., arms, hands, and digits). Executive dysfunction was also quite pronounced, especially the reduced capacity for attention and concentration, and in some cases reduced motivation as well.

Imperative to this work was the statistical match of injury and illness demographics from the PFTBI and patient comparison groups. This has established that reduced neurocognition in PFTBI does not appear to be specifically attributable to mediating characteristics of either the illness or injury. However, these factors were associated with neurocognition for all patient groups, and the executive functions may become more critical to cognitive neuropsychological performance as impairment increases.
10.3 Methodological Strengths of this Research

Substantial discussion throughout this thesis was devoted to the methodological limitations of the existing literature, and the resulting ambiguity of findings. These shortcomings were thoroughly considered during the design of this research protocol, and every effort was made to incorporate a methodology that overcame the common limitations where possible. Primarily, this meant the recruitment of PFTBI patients for one on one assessment, rather than relying on piecemeal chart information where the accuracy of data is often undetermined. This allowed for wideranging recruitment sites to achieve the best representation of PFTBI patients in Melbourne, instead of recruitment confined, for instance, to hospital inpatients, which may be unrepresentative of the PFTBI population.

Control over a number of additional variables was also afforded by this procedure. Chief among these was the confinement of recruitment to cases where the traumatic brain injury preceded the development of psychotic symptoms. The verification of this, and of vital injury/illness information, was extensively sought from the relevant clinic and/or hospital files, and in one case further confirmation was pursued from a first degree relative. This procedure also allowed for family history data to be systematically recorded, which was important given the existing theoretical literature pertaining to heredity.

Paramount to this work was the systematic assessment of both the cognitive neuropsychological profile and clinical symptoms of patients. First, this allowed for the standardised measurement of neurocognition, but also for the implementation of a comprehensive neurocognitive battery informed by the existing, and substantial, literature in TBI and schizophrenia. Next, it was imperative that the clinical diagnosis of each patient was confirmed, and the features of the psychosis were defined, according to an established diagnostic interview and standardised measures administered by trained clinicians. Together these achievements set this work above the existing PFTBI data in clarity and completeness of the features of this dual diagnosis.

Moreover, comparisons of PFTBI with patient controls in this way is novel. Previous work that has attempted this has utilised existing databases (Fujii et al., 2004), chart information (Fujii & Ahmed, 2002; Sachdev et al., 2001), or norms (Bamrah & Johnson, 1991; Fujii et al., 2002; 2004). This meant that all participants were taken through an identical protocol, which was another important aspect of statistical control. The statistical matching of a substantial number of injury and illness demographics was also novel, and essential, given
the high likelihood that these behave influentially over the neurocognitive outcomes of interest. Patient cohorts were matched extremely well on all but three clinical/injury variables; reduced negative symptoms, an increased latency between injury and assessment, and lower incidence of induced coma in PFTBI. However, it is unlikely that these underpinned the reduced performance in PFTBI, given that reduced negative symptoms, and a longer latency between injury and assessment, are both associated with better cognition in other cohorts (Che et al., 2012; Dimoska-Di Marco et al., 2011; Hammer, Katsanis, & Iacono, 1995; Martino, Bucay, Butman & Allegri, 2007; Senath-Raja et al., 2010).

Coma induced directly post injury was considerably imbalanced across the TBI groups; one of the PFTBI patients versus seven of the TBIWP patients. Importantly, this treatment disparity does not implicate greater injury severity in the TBIWP cohort as the groups were statistically matched on LOC/PTA injury severity measures. While induced coma may be predictive of better long-term neurocognitive outcome, this did not appear to be the case; the three TBIWP cases who did not experience induced coma post injury did not demonstrate reduced performance relative to the rest of the TBIWP cohort. Although the sample is small, this suggests that induced coma does not interact with neurocognitive performance directly. Thus, the lower incidence of coma in the PFTBI cohort also does not appear to account for their impaired performance.

Finally, adherence to the statistical appropriateness of analyses was viewed as critical, especially given the common misuse of ANCOVA to achieve control over group differences on potential covariates (Miller & Chapman, 2001, see Appendix S). Partialing out the influence of a wide range of patient-related and executive function-based influences over neurocognition, although appealing, generally remains an unobtainable goal. The executive functions in particular are inextricably linked to other aspects of neurocognition, causing difficulties in isolating specific deficits. Moreover, common impairments in aspects of cognition, such as processing speed and attention, are unavoidably implicated in many of the paradigms used to measure neurocognition elsewhere (e.g., semantic priming, working memory). Although the measurement of known influences is essential, at best, the investigation of group-wise differences on these influences, and their relationships with outcomes of interest, can only be highlighted. Accordingly, the close matching of cohorts on as many influential variables as possible may remain the best procedure for control of these influences.
10.4 Theoretical Implications

Given matched demographics from the brain injured cohorts, it does not appear that a specific type, or location, of injury is behaving pathogenically in PFTBI with regard to the development of psychosis. Moreover, as demonstrated by the comparable profile patterns in schizophrenia, deficits in neurocognition appear to be largely driven by the psychosis. Thus, these data do not support a distinct organic syndrome in PFTBI, but favour instead psychosis as conceptualised on a spectrum, which accounts nicely for heterogeneity and overlap into other syndromes (Badcock & Dragovic, 2006; Heckers, 2009; Landro & Ueland, 2008; Verdoux & van Os, 2002).

The aetiology of PFTBI, then, appears to align conceptually with an existing model of schizophrenia. The two-hit hypothesis proposes prenatal genetic or environmental occurrences that effect brain development in a way that increases vulnerability to psychosis (i.e., the first ‘hit’). A second, or multiple, stressor(s) later in life then triggers disease onset (i.e., ‘hit’ two; Bayer, Falkai, & Maier, 1999; MacDonald & Schulz, 2009; Maynard, Sikich, Lieberman, & LaMantia, 2001). Importantly, the first hit is not confined to genetic defects that arise due to heritability. This is vital because, as discussed in Chapter Two, the existing PFTBI literature has documented cases of PFTBI both with and without a family history of psychosis (AbdelMalik et al., 2003; Fujii & Ahmed, 2001). Thus, for example, severe maternal stress might constitute a first hit conferring congenital vulnerability to psychosis. Established examples of the second hit were ordered according to influence by Macdonald and Shultz (2009, p.496), and include; “migrant status, older fathers, Toxoplasmosis gondii antibodies, prenatal famine, lifetime cannabis use, obstetrical complications, urban rearing, winter or spring birth”, and perhaps, traumatic brain injury.

The group-wise difference in early injury treatment may further offer preliminary evidence for the hypothesis that coma operates protectively against PFTBI. It may be that by slowing the brain’s reactionary response to areas of damage and swelling, and thus enabling mechanisms of healing to infiltrate damaged cells, the sprouting and reconnection of new neuronal fibres in the reorganisation of brain tissue has some bearing on the prospective development of psychotic symptoms. There is much evidence for reduced network connectivity in schizophrenia (Kyriakopoulos et al., 2012; Liemburg et al., 2012; Repovs & Barch, 2012; Yu et al., 2011), with the absence of specific connections having been proposed as candidate psychosis endophenotypes (Meda et al., 2012). The breakdown of key network
connections post injury may thus contribute to the aetiology of post injury psychosis in selected cases.

10.5 Diagnostic Implications

First, clinically, PFTBI is not especially unique, although the “absence” of negative symptoms in this cohort may be a feature worth further investigation. The potential for negative symptoms as a diagnostic distinction has been raised previously by Fujii and Ahmed (2002), however, as discussed in Chapter Two, evidence for negative symptoms in PFTBI has also been reported (e.g., Buckley et al., 1993; Sachdev et al., 2001). Given low levels of negative symptoms in the schizophrenia group as well, this may have resulted instead from a recruitment bias. Patients with negative symptoms are less likely to volunteer for participation involving multiple hours of cognitive testing. Of the 25 PFTBI patients approached for participation only 40% agreed, and amotivation associated with negative symptoms could be one explanation for this success rate. Following-up with the PFTBI patients who declined to participate, and gauging their willingness to undertake a brief clinical interview, may help to ascertain whether negative symptoms and poor motivation were involved in their decision. Nonetheless, negative symptoms as a clinical distinction is certainly worth further investigation given the statistical difference shown on the PANSS total negative scale for psychotic cohorts.

The majority of PFTBI cases in this research had, at least by the time of assessment, been diagnosed with schizophrenia/schizophreniform psychosis (i.e., as detailed in Chapter Six; six of the ten received this as their first diagnosis, whereas three received it as a subsequent diagnosis, and one had a diagnosis of paranoid psychosis). This has further theoretical bearing on the clinical profile in PFTBI, including the various features of the psychosis in its initial likeness to diagnostically-defined schizophrenia, and/or the development of symptoms over the trajectory of PFTBI. Of course, given the exceptional paucity of this literature it is unclear how accurately the present sample reflects the PFTBI population.

Next, as already noted, the cognitive neuropsychological profile in PFTBI was strikingly similar to schizophrenia in its pattern of deficits on the majority of measures, albeit significantly greater in degree. Evidence of a language-driven likeness with TBIWP was illustrated on phonological fluency, which encompassed the switching and clusters of phonological fluency as well as total output, and WASI Vocabulary. Furthermore, although
PFTBI was more like schizophrenia in the degree of IQ impairment, especially on visuo-spatial impairment, their pattern of deficits across the WASI subscales reflected the pattern in TBIWP. Again, this appears to be driven by scores on the WASI Vocabulary subscale, providing further evidence for a language-specific deficit in TBI. While group-wise analysis for lesion location in the TBI cohorts was not statistically feasible, the raw data suggest that this reduced performance may reflect the laterality of language processing skills.

Schizophrenia manifests as common clinical and neurocognitive features, with great diversity in its aetiology and presentation from patient to patient (MacDonald & Schulz, 2009; Nasrallah, Tandon, & Keshavan, 2011; Tandon, Keshavan, & Nasrallah, 2008a; 2008b; 2009; 2010; Keshavan, Nasrallah, & Tandon, 2011; Keshavan, Tandon, Boutros, & Nasrallah, 2008). The diversity in schizophrenia is so extreme that it has been considered a feature of the disease (Nasrallah et al., 2011). The data from both psychotic cohorts were true to the existing literature in this respect. Given such extreme diversity, and thereby considerable overlap, it would be difficult to identify a poorly functioning schizophrenia patient from a relatively high-functioning PFTBI patient, even with a known TBI history.

However, alongside the similarities, the findings from this research suggest that a handful of neuropsychological features may distinguish PFTBI patients from other cohorts. Tasks where the PFTBI cohort illustrated performance distinct from the other groups included, (i) delayed memory (mostly driven by the List Recognition and Story Memory subscales), (ii) RTs and accuracy on the lexical decision task (especially to related pairs at the long SOA where slower RTs and particularly reduced accuracy were shown), (iii) accuracy semantic priming (but not RT semantic priming), which is related to (ii), and (iv) a pattern of deficits on IQ where verbal IQ (Vocabulary subscale) is especially reduced relative to visuo-spatial IQ (Matrix Reasoning subscale). Thus, a cluster of specific deficits have emerged from these data centred on verbal learning and memory. These deficits may underpin the unique pattern of semantic priming to related word pairs in PFTBI.

Due to exacerbated neurocognitive deficits in PFTBI overall, and especially in executive function, cognitive neuropsychological assessment of patients with suspected PFTBI should be kept brief. In accordance with these findings, the essential features of a neurocognitive battery, where the aim is to identify the potential for PFTBI, should focus on assessments of verbal learning and memory. Most delayed memory assessments have a verbal memory component, and any incorporating list learning, or story memory, would be expected to capture the demonstrated PFTBI deficits well. By contrast, semantic priming
experiments, while valuable, take time to create and administer, and also require relatively proficient motor skills which are likely to be compromised post injury. Assessments such as the Rey Auditory Verbal Learning Test (Schmidt, 1996), subtests from the Wechsler Memory Scale (Weschler, 1997), including Logical Memory and Verbal Paired Associates, or the delayed memory component of the RBANS (Randolph, 1998) as used here would be recommended (although the RBANS requires 30 minutes between initial list/story presentation and recall). However, the California Verbal Learning Test-Second Edition (CVLT-II; Delis, Kaplan, Kramer, & Ober, 2000) possibly provides the most comprehensive assessment of verbal learning and memory and can be administered in 15 minutes by short form. Due to its comprehensive assessment, acquisition of semantic clustering, and demonstrated efficacy in TBI patients with frontal lesions (Baldo, Delis, Kramer, & Shimamura, 2002), as well as schizophrenia (Stone et al., 2011), this test would be most highly recommended following the results of this research.

10.6 Treatment: The Clinical Utility of Outcomes

PFTBI cases are clearly complex and have a range of treatment needs. These should be carefully considered when deciding on the best treatment option and schedule, and should be adaptable on a patient to patient basis. However, in general terms, treatment requiring substantial patient engagement (i.e., relying on executive function) would have little success unless it followed effective cognitive remediation. Cognitive Remediation Therapy (CRT) is a behavioural, skill-training intervention, that has demonstrated empirical efficacy in the lasting improvement of cognitive processes such as, attention, memory, executive function, problem solving, social cognition, and metacognition (Contreras et al., 2012; Medalia & Choi, 2009; Wykes, Huddy, Cellard, McGurk, & Czobor, 2011). CRT targets many of the profound deficits demonstrated by PFTBI patients in this research. Substantial evidence has shown improvements of moderate range effect sizes on cognitive test performance, and daily functioning, in response to CRT in patients with schizophrenia (Krabbendam & Aleman, 2003; McGurk et al., 2007; Kurtz, Moberg, Gur, & Gur, 2001), and traumatic brain injury (Ashley et al., 2012; Ben-Yishay & Diller, 1993; Cicerone, 2002; Galbiati et al., 2009; Gauggel & Niemann, 1996; Ownsworth & Mcfarland, 1999; Suzman, Morris, Morris, & Milan, 1997). It follows that CRT may be an efficacious intervention in PFTBI as well.

Improvements in cognition are also associated with better psychosocial, vocational, and overall long-term function (Bell, Tsang, Greig & Bryson, 2009; Contreras et al., 2012; Kurtz, Seltzer, Fujimoto, Shagan & Wexler, 2009; McGurk & Mueser, 2006; McGurk, Mueser,
Derosa, & Wolfe, 2009; Wykes, 1994). Thus, CRT targets the primary deficits in PFTBI, with potential ‘spill over’ effects into other areas of impairment. Further to these benefits, successful CRT may provide a platform for Cognitive Behaviour Therapy (CBT), given that substantially impaired executive function, attention, planning, and memory would otherwise provide a barrier to successful CBT engagement and outcome. CBT in schizophrenia has been efficacious in addressing the impact, such as the distress and disability, associated with positive and negative symptoms (Gould, Meuser, Bolton, Mays, & Goff, 2001; Thomas, Rossell, Farhall, Shawyer, & Castle, 2011; Trower et al., 2004; Wykes, Steel, Everitt, & Tarrier, 2008). Therefore, it may be a beneficial treatment for these symptoms in PFTBI, in conjunction with appropriate antipsychotics. Given evidence for the similarities in clinical profile, there is no basis for tailoring antipsychotics and/or other medication therapy beyond the usual best practice in schizophrenia. However, part of this process would be consideration for medication-based treatments that have shown to be better tolerated regarding side effects of reduced neurocognition and slowed processing speed. Although CBT efficacy has not been as widely researched in TBI, there is some literature to suggest that CBT is useful in the reduction of various psychological sequelae (Doering & Exner, 2011), and even sleep disturbance post injury (Quellet, & Morin, 2007). Furthermore, CBT is well tolerated, positively appraised by patients, and benefits gained from the sessions are generally sustained in the long term (Davis, Ringer, Strasburger, & Lysaker, 2008; Gould et al., 2001; Tai & Turkington, 2009). It may therefore be advantageous in the improvement of pathology arising from both the TBI and the psychosis in PFTBI.

Thus, adjunctive therapy is most appropriate in PFTBI to improve functioning and enhance quality of life for these patients. This should be inclusive of CRT to address cognitive deficits, CBT to manage clinical symptoms and other injury-based behavioural disturbances, and strategic additions focused on enhancing social skills, incorporating vocational training, and supporting sustained employment. Efficacy has already been established in psychosis for comprehensive rehabilitation programmes of this kind (Davis et al., 2008; McGurk, Mueser, Feldman, Wolfe, & Pascaris, 2007; McGurk, Mueser, & Pascaris, 2005; McGurk, Twamley et al., 2007; Wykes et al., 2011).

10.7 Limitations and Important Recommendations for Future Research

Noted throughout, the greatest limitation to this work was sample size, and the subsequent inadequacy of statistical power for certain analyses. While every effort was made to avoid this issue, the substantial heterogeneity in cognitive neuropsychological function
characteristic of psychosis, together with the inherent recruitment issues of patients with PFTBI, meant that recruitment only reached a sample size of ten during the period of this thesis. This reduced the size of the matched TBIWP cohort as well. Further, because a priori power analysis was determined using prior work investigating two groups, it is speculated that the indications of appropriate group sizes may not have been relatable to four-group analyses on some measures. The absence of statistically significant differences on some key neurocognitive variables, where notable differences in the mean were demonstrated descriptively, is therefore believed to reflect a power issue.

With reference to the discussion in Chapter Seven, it would also be advantageous to replace various tasks incorporated in the testing battery. The following alterations are noted: (i) the RBANS language scale should be supplemented by additional language measures given ceiling performance in the Picture Naming subtest, and the propensity for cognitive strategy using fruits/vegetable fluency in the Semantic Fluency subtest; (ii) an alternative to the GECIT task should be considered in the measurement of Gestalt processing given inconsistencies in the findings from this task relative to both the existing literature and the RBANS Visuo-spatial Index; (iii) semantic priming in PFTBI should be reassessed using pairs of dual semantic-associative relationships. It is hypothesised that the semantic-only pairs used in this research may have been too pure to capture priming. This work should also be replicated using subgroups of all three types of word pair relationships (i.e., semantic-only, associative-only, and semantic-associative) to determine the accuracy of this hypothesis; (iv) probabilistic reasoning should be comprehensively assessed using a range of tasks with well-established validity, and demonstrated outcome replication in psychosis.

With regard to the RBANS Language scale, a substitution for picture naming, such as the Boston Naming Test (BNT; Kaplan, Goodglass, & Weintraub, 2001), would be ideal given its incorporation of both high frequency and low frequency objects (del Toro et al., 2010; Nicholas, Brookshire, MacLennan, Schumacher, & Porrazzo, 1989), provided appropriate norms are utilised (Hawkins, Sledge, Orleans, Quinlan, Rakfeldt, & Huffman, 1993; Nicholas et al., 1989). Cognitive strategy is likely to be engaged for semantic fluency irrespective of the category used, although the incorporation of additional semantic fluency trials may prove advantageous in differentiating semantic impairments. For example, the addition of an “animal” and “body parts” trial along with the existing “fruits/vegetables” trial, to match the three-trial (FAS) phonological fluency task.

The literature has shown that rather than being unable to utilise Gestalt principles in
visual processing, patients with schizophrenia do so less readily (Chey & Holzman, 1997; Landgraf et al., 2011; Rief, 1991). An imbedded figure task may help to capture this impairment (Bower & Glass, 1976; Chey & Holzman, 1997), although the efficacy of this task may be especially sensitive to timing; when provided with enough time patients with schizophrenia may perform comparatively to controls by using bottom up processing instead (see John & Hemsley, 1992). Both the Navon figure (Delis et al., 1986) and the Rey Osterrieth Figure (Robertson & Lamb, 1991) have successfully demonstrated the laterality of global (Gestalt)/local processing in TBI (see Chapter Four). However, this task may not be sensitive enough to capture impairment in schizophrenia (Silverstein, Osborn, & Palumbo, 1998). The “report of numerosity” task (see Chapter Three) utilised by Schwartz-Place & Gilmore (1980) appears to capture this deficit well, without implicating short term/working memory processes, which may be a confound with the imbedded figure, Navon, and Rey Osterrieth tasks. Poor Gestalt processing on this task has been replicated in patients (Wells & Leventhal, 1984), and may thus offer an appropriate alternative to the GECIT task in PFTBI samples.

Future work should allow for an extensive period of recruitment to ensure both the increase in final PFTBI cohort size, and to allow for the better match of the unmatched injury demographics in this research. This would also allow for the statistical comparison of lesion location, which is predicted to have significant bearing over neurocognition in PFTBI, especially with regard to language-based faculties. While it is considered that the differences between TBI samples in latency from injury to assessment reflect a recruitment bias, this remains speculative until wider investigations have been completed. Further, it was surprising that neurocognitive performance was not related to the latency of symptom onset in PFTBI (Chapter Eight). This result should be replicated extensively before the influence of onset latency on functional outcome in PFTBI can be excluded. An appropriate avenue for investigation would be to follow brain injured patients at risk for psychosis (according to the best existing indications for psychosis proneness), over the trajectory of their recovery. Longitudinal investigations of this nature, especially with individuals identified as “ultra high risk” for symptom onset, have been lucrative in schizophrenia (e.g., Lin et al., 2011; Sun et al., 2009). The protective effects of induced coma post injury warrant extensive follow-up. No work to date has investigated this phenomenon in PFTBI, yet it may be a promising avenue for future investigation, with the potential to have a significant bearing on the development of PFTBI.
It is also imperative that the apparent absence of negative symptoms in PFTBI is investigated thoroughly. Findings from this research, and from Fujii and Ahmed (2002), have been constrained by methodological shortcomings; here, because of PFTBI sample size, and from Fujii and Ahmed (2002), due to incompatible retrospective chart review where assessment is not controlled or necessarily standardised. Ideally, this should be done (i) using multiple complementary standardised measurements of clinical symptoms, (ii) assessing patients as a stand alone measurement, rather than part of research that has recruited for participation in larger sized assessment batteries (this is critical in helping delineate the effects of amotivation from the existing data), and (iii) the eventual investigation into the relationship between negative symptoms and neurocognition in PFTBI.

10.8 Conclusion

Patients with PFTBI have substantially impaired neurocognition. Despite large overlap with schizophrenia, and some language-driven likeness to TBIWP, PFTBI was overwhelmingly associated with the greatest degree of deficit. In general, this suggests the additive effect of impairments associated with, first, the injury, and then, the psychosis. It is hypothesised that these may develop and evolve in a manner aligned with the two-hit theory of schizophrenia. Specific distinctions in clinical, injury, and cognitive neuropsychological profile worth follow-up include; (i) negative symptoms, (ii) lesion location, (iii) the latency of post injury assessments between groups, (iv) illness onset latency specific to PFTBI, (v) induced coma, (vi) delayed memory and semantic memory (i.e., priming), (vii) and visuo-spatial (Matrix Reasoning IQ) performance.

This research has provided the first systematic assessment of the cognitive neuropsychological profile in PFTBI using standardised neuropsychological measures, and a battery of this size. It has also uniquely compared the established profile with data obtained from three comparison cohorts; a healthy group, TBI patient group, and schizophrenia patient group. In doing so, it was necessary to determine the clinical and injury characteristics of the patient groups, also using psychometrically established measures, and statistically match these to isolate the cognitive neuropsychological profile in PFTBI from obvious mediators related to injury and illness. This endeavour was relatively successful, and as such, this work has provided a novel and valuable contribution to the limited PFTBI literature.

The recruitment and assessment of PFTBI is significantly constrained by the extent of morbidity in these patients. The result has been a paucity of published work, and these have
relied on retrospective chart review, case studies, and loosely defined, but crucial, injury variables. These first and preliminary empirical findings have demonstrated value in the face-to-face assessment of PFTBI cases, and suggest that replication of this work may be profitable. Subsequent investigations must be committed to substantial periods of recruitment, across international sites, with an aim to engage the maximum possible PFTBI cases. Such work has the potential to inform aetiology, diagnosis, and treatment, for a cohort who suffer significantly as a result of their injury and illness.
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Appendices
Appendix A: Traumatic Brain Injury (TBI) Severity Classification

Injury Severity is typically classified by the assessment of the following parameters where available; duration of loss of consciousness (LOC), duration of post-traumatic amnesia (PTA), and Glasgow Coma Scale (GCS) score. Structural imaging data and duration of alteration of consciousness (AOC) is also considered in some circumstances.

Score range and consequent severity classification for each of these parameters are detailed in Table A.1. Data included here is primarily taken from the Department of Defense and Department of Veterans Affairs (2008), and included with reference to the following publications; Helps et al. (2008), Mathias & Coats (1999); McAllister et al. (1999); McWilliams & Schmitter-Edgecombe (2008), and Ponsford, Draper, et al. (2008).

Table A.1

Traumatic Brain Injury (TBI) Parameters for Severity Classification

<table>
<thead>
<tr>
<th>Severity Classification</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOC</td>
<td>0-30min</td>
<td>&gt;30min and &lt;24hrs</td>
<td>&gt;24hrs</td>
</tr>
<tr>
<td>PTA</td>
<td>0-24hrs</td>
<td>&gt;1day and &lt;7days</td>
<td>&gt;7 days</td>
</tr>
<tr>
<td>GCS</td>
<td>12-15</td>
<td>9-11</td>
<td>3-8</td>
</tr>
<tr>
<td>AOC</td>
<td>24hrs or less</td>
<td>&gt;24hrs – severity determined by additional parameters</td>
<td></td>
</tr>
<tr>
<td>Imaging</td>
<td>Normal structural imaging</td>
<td>Normal or abnormal structural imaging</td>
<td></td>
</tr>
</tbody>
</table>

Note. LOC = Loss of Consciousness; PTA = Post Traumatic Amnesia; GCS = Glasgow Coma Scale; AOC = Alteration of Consciousness. Parameters do not apply to penetrating brain injuries where the dura matter is breached.
Appendix B: List of Publications included in PFTBI Review (Chapter Two)


model of delusions. European Archives of Psychiatry and Clinical Neuroscience, 260(8), 571-581.


Appendix C: Stroop Interference and Switching-Interference Derived Score Calculations

Stroop Interference and Switching-Interference derived score calculations were performed in accordance with the existing literature (e.g., Barch et al., [2004], Ben-David et al. [2011], and Rios et al., [2004]). The formula for these calculations is as follows;

Interference or Switching-Interference Score = I/S – CW

Where I/S = Stroop Inhibition or Inhibition-Switching Trial Score
CW = (Stroop Colour x Stroop Word Trial Scores) / (Stroop Colour + Stroop Word)
Appendix D: Trail Making Task (Reitan, 1955; 1958)
Appendix E: Ethical Approval

Human Research Ethics Committee (HREC) Certificates of Approval for this research are contained in this Appendix. Ethical approval was obtained from the following institutions; (i) RMIT University (#s3058809), (ii) Monash University (#CF09/0211-2009000081), (iii) Alfred Hospital (#301/08), (iv) Austin Health (#H2008/03325), and (v) Epworth Healthcare (#49610).
4 February 2009

Rachel Batty

Dear Rachel

Project: An examination of the risk factors, phenomenology and actiology of psychosis following traumatic brain injury with a focus on psychological treatment related factors

I am pleased to advise that this project was reviewed by the Human Research Ethics Committee at its meeting on 4 February 2009. It was noted by the committee that the project had been approved by the Austin Health Human Research Ethics Committee.

Responsibilities of primary investigator
It is important to emphasise that primary investigators are responsible for ensuring that the project proceeds according to the proposal approved by the Human Research Ethics Committee. The Committee’s approval of the project is not absolute. New and unforeseen ethical issues may arise. A researcher should continue to consider the ethical dimensions of the research as the project progresses.

Adverse events or unexpected outcomes
As the primary investigator you have a significant responsibility to monitor the research and to take prompt steps to deal with any unexpected outcomes. You must notify the Committee immediately of any serious or unexpected adverse effects on participants, or unforeseen events, which may affect the ethical acceptability of your project. Any complaints about the project received by the researcher must be referred immediately to the Ethics Officer.
Conflicts of interest
When reporting the research, the researcher should again disclose any actual or potential conflicts of interest, including any financial or other interest or affiliation that bears on the research. Conflicts of interest can arise after a project has been approved, and where they do they must be reported as soon as possible.

Amendments
If, as you proceed with your investigation you find reason to amend your research method, you should advise the Human Research Ethics Committee and seek approval for the proposed changes. If you decide to discontinue your research before its planned completion you must also advise the Committee of this and of the circumstances. Depending on the type of amendment — whether it is minor or major — will determine how long the review process for an amendment will take.

If you anticipate any problems in meeting this requirement please contact me to discuss an alternative secure data storage arrangement.

All reports or communication regarding this project is to be forwarded to the Ethics Officer.

On behalf of the Human Research Ethics Committee I wish you well with your research.

Yours sincerely

Peter Burke
Ethics Officer
RMIT Human Research Ethics Committee
Human Ethics Certificate of Approval

Date: 27 January 2009
Project Number: CF09/0211 - 2009000081
Project Title: An examination of the risk factors, phenomenology and aetiology of psychosis following traumatic brain injury with a focus on psychological treatment related factors
Chief Investigator: Assoc Prof Susan Rossell
Approved: From: 27 January 2009 to 27 January 2014

Terms of approval
1. The Chief Investigator is responsible for ensuring that permission letters are obtained and a copy forwarded to SCERH before any data collection can occur at the specified organisation. Failure to provide permission letters to SCERH before data collection commences is in breach of the National Statement on Ethical Conduct in Human Research and the Australian Code for the Responsible Conduct of Research.
2. Approval is only valid whilst you hold a position at Monash University.
3. It is the responsibility of the Chief Investigator to ensure that all investigators are aware of the terms of approval and to ensure the project is conducted as approved by SCERH.
4. You should notify SCERH immediately of any serious or unexpected adverse effects on participants or unforeseen events affecting the ethical acceptability of the project.
5. The Explanatory Statement must be on Monash University letterhead and the Monash University complaints clause must contain your project number.
6. Amendments to the approved project (including changes in personnel): Requires the submission of a Request for Amendment form to SCERH and must not begin without written approval from SCERH. Substantial variations may require a new application.
7. Future correspondence: Please quote the project number and project title above in any further correspondence.
8. Annual reports: Continued approval of this project is dependent on the submission of an Annual Report. This is determined by the date of your letter of approval.
9. Final report: A Final Report should be provided at the conclusion of the project. SCERH should be notified if the project is discontinued before the expected date of completion.
10. Monitoring: Projects may be subject to an audit or any other form of monitoring by SCERH at any time.
11. Retention and storage of data: The Chief Investigator is responsible for the storage and retention of original data pertaining to a project for a minimum period of five years.

Professor Ben Canny
Chair, SCERH

Cc: Assoc Prof Andrew Francis; Dr Neil Thomas; Dr Yitzchak Hollander; Assoc Prof Malcolm Hopwood; Rachel Batty

Postmasters: Monash University, Vic 3800, Australia
Building 3E, Room 111, Clayton Campus, Wellington Road, Clayton
Telephone +61 3 9905 5490 Facsimile +61 3 9905 1420
Email: scerrh@adm.monash.edu.au  www.monash.edu/health/research/ethics/human/index.html
ABN 12 377 614 012 CRICOS Provider #00008C
ETHICS COMMITTEE CERTIFICATE OF APPROVAL

This is to certify that

Project No: 301/08

Project Title: An examination of the risk factors, phenomenology and aetiology of psychosis following traumatic brain injury with a focus on psychological treatment related factors.

Principal Researcher: A/Professor Susan Rossell

Protocol No: dated: 12:00:00 AM

Participant Information and Consent Form version 1 dated: September, 2008 was considered by the Ethics Committee on 23-Oct-2008 and APPROVED on 13-Nov-2008

It is the Principal Researcher's responsibility to ensure that all researchers associated with this project are aware of the conditions of approval and which documents have been approved.

The Principal Researcher is required to notify the Secretary of the Ethics Committee, via amendment or progress report, of

- Any significant change to the project and the reason for that change, including an indication of ethical implications (if any);
- Serious adverse effects on participants and the action taken to address those effects;
- Any unforeseen events or unexpected developments that merit notification;
- The inability of the Principal Researcher to continue in that role, or any other change in research personnel involved in the project;
- Any expiry of the insurance coverage provided with respect to sponsored clinical trials and proof of re-insurance;
- A delay of more than 12 months in the commencement of the project; and,
- Termination or closure of the project.

Additionally, the Principal Researcher is required to submit

- A Progress Report on the anniversary of approval and on completion of the project (forms to be provided);

The Ethics Committee may conduct an audit at any time.

All research subject to the Alfred Hospital Ethics Committee review must be conducted in accordance with the National Statement on Ethical Conduct in Human Research (2007).

The Alfred Hospital Ethics Committee is a properly constituted Human Research Ethics Committee in accordance with the National Statement on Ethical Conduct in Human Research (2007).

SPECIAL CONDITIONS

None

SIGNED

Chair, Ethics Committee (or delegate)

Please quote Project No and Title in all correspondence.
TO:        A/Prof Susan Rossell  
Alfred Psychiatry Research Centre  
1st Floor Old Baker Building, Commercial Road  
PROJECT:  Melbourne Vic 3004  
PROTOCOL: An examination of the risk factors, phenomenology and aetiology  
of psychosis following traumatic brain injury with a focus on  
psychological treatment related factors  
PROJECT NO: H2008/03325  
FROM:      Jill Davis Research Ethics Unit Manager  
DATE:      17 November 2008  
Information and Consent Form – Patient (sessions 1&2)  
Version 4 dated November 2008, Participant Information and  
Consent Form (sessions 3&4) Version 4 dated November 2008,  
Participant Information and Consent Form (session 5)  
Version 4 dated November 2008, Participant Information and  
consent Form (session 6) Version 4 dated November 2008,  
Person Responsible Information and Consent Form (session  
1&2) Version 4 dated November 2008, Person Responsible  
Information and Consent Form (session 3&4) Version 4 dated  
November 2008, Person Responsible Information and  
Consent Form – CBR Component (session 6) Version 4 dated  
November 2008, Participant Demographic Information Form  
Version 2 dated June 2008, Screening Questionnaire Version  
2 dated June 2008  

Approval Period: 17 November 2008 – 17 November 2011  

Further to my letter dated 25 September 2008 concerning the above detailed project,  
I am writing to acknowledge that your response to the issues raised by the Human  
Research Ethics Committee at their meeting on 18 September 2008 is satisfactory.  
This project now has full ethical approval for a period of three years from the date of  
this letter.  

For trials involving radiation to volunteers, the research must be added to the Austin  
Health Research with Human Volunteer’s licence issued by the Department of
Human Services – Radiation Safety Section prior to commencement. The HREC must be notified when the research has been added to the licence.

It is now your responsibility to ensure that all people associated with this particular project are made aware of what has actually been approved. Any changes to the original application will require a submission of a protocol amendment to the Committee for consideration as this approval only relates to the original application as detailed above.

The Committee has requested me to make arrangement for progress reports to be submitted by the Investigator to the Committee at the end of twelve (12) months, or sooner if the project is completed within twelve (12) months. Should your study not commence twelve (12) months from the date of this letter this approval will lapse. A resubmission to the Human Research Ethics Committee would then be necessary before you could commence.

The Committee wishes to be informed immediately of any untoward effects experienced by any participant in the trial where those effects in degree or nature were not anticipated by the researchers.

DETAILS OF ETHICS COMMITTEE:

It is the policy of the Committee not to release personal details of its members. However I can confirm that at the meeting at which the above project was considered, the Committee fulfilled the requirements of the National Health and Medical Research Council in that it contained men and women encompassing different age groups and included people in the following categories:

Chairperson
Lay Man
Lay Woman
Minister of Religion
Lawyer
Person with Research Experience
Person with Counselling Experience

Additional members include:
- Nurse Administrator
- Surgeon
- Pharmacologist
- Pharmacist

I confirm that the Principal Investigator or Co-Investigators were not involved in the approval of this project. I further confirm that all relevant documentation relating to this study is kept on the premises of Austin Health for more than three years.

The Committee is organised and operates according to the Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95), annotated with TGA comments; and The National Statement on Ethical Conduct in Human Research (NHMRC The National Statement) and the applicable laws and regulations; and the Health Privacy Principles in The Health Records Act 2001. This hospital is registered under the United States DHHS Federal Wide Assurance number 00001363.
PLEASE NOTE: The Committee requests that the Research Ethics Unit (ethics@austin.org.au) is informed of the actual starting date of the study as soon as the study commences. A written notice (e-mail, fax or letter) is considered the appropriate format for notification.

Jill Davis
Human Research & Ethics Committee
Certificate of Approval

<table>
<thead>
<tr>
<th>Project Title:</th>
<th>An examination of the risk factors, phenomenology and aetiology of psychosis following traumatic brain injury</th>
</tr>
</thead>
<tbody>
<tr>
<td>Principal Investigator:</td>
<td>A/Prof Susan Rossell</td>
</tr>
<tr>
<td>Epworth study no:</td>
<td>49610</td>
</tr>
<tr>
<td>HREC Meeting date:</td>
<td>7 July 2010</td>
</tr>
<tr>
<td>Board of Management approval:</td>
<td>28 July 2010</td>
</tr>
<tr>
<td>Duration of Project:</td>
<td>31/07/2010 – 30/03/2011</td>
</tr>
</tbody>
</table>

Alan R. Kinkade
Group Chief Executive

Terms and conditions of approval:
The Principal Investigator is required to notify the Human Research Ethics Committee of the following;

All Projects:
2. Any proposed changes to the protocol or approved documentation or the addition of documents (including flyers, brochures, advertising materials etc) must be submitted to the Human Research Ethics Committee for approval prior to implementation
3. The Principal Investigator must notify HREC of
   a. Any serious adverse effects of the study on participants and steps taken to deal with them
   b. Any unforeseen events (e.g. protocol violations or complaints)
   c. Investigators withdrawing from or joining the project
4. A Progress Report must be submitted annually and at the conclusion of the project
5. Epworth HealthCare HREC approval must remain current for the entire duration of the project. If the project is not completed in the allocated time a renewal request must be submitted to the HREC. Investigators undertaking projects without current HREC approval risk their indemnity, funding and publication rights

Clinical Trials:
7. Must report all internal (occurring at Epworth HealthCare) Serious Adverse Events (SAE) to the sponsor and the HREC within 72 hours of occurrence
8. Must report all Suspected Unexpected Serious Adverse Reactions (SUSARS) to the Therapeutic Goods Administration (TGA). For sponsored studies, the sponsor may take this responsibility

I, ........................................................................................................... accept the terms and conditions set out above.

Signature of Researcher: ................................................. Date: ..........................
Appendix F: Research Pamphlet Distributed to Clinicians at CBDATS

Psychosis & Head Injury

ALFRED PSYCHIATRY RESEARCH CENTRE

The Alfred Psychiatry Research Centre is conducting research into the development of psychosis following a head injury

Suitable Participants:
General Inclusion Criteria
18-55 years of age
TBI prior to developing psychosis

General Exclusion Criteria
Pre-morbid psychosis/mania
Current delirium
Severe current morbidity
Current substance abuse

For more information contact Rachel Batty on or speak with Mal Hopwood
Appendix G: Plain Language Statement and Participant Consent

Participant Information and Consent Form – Patient (Sessions 1 & 2)
The Monash-Alfred Psychiatry Research Centre, Melbourne

Full Project Title: An examination of the risk factors, phenomenology and aetiology of psychosis following traumatic brain injury

Short Title: Psychosis following traumatic brain injury

Principal Researcher: A/Prof Susan Rossell

Associate Researchers: Miss Rachel Batty (PhD Candidate), A/Prof Andrew Francis, Dr Neil Thomas, Dr Yitzchak Hollander, A/Prof Mal Hopwood, Prof Jennie Ponsford & Simon Baker

1. Introduction
You are invited to take part in this research project. This is because you have either had a traumatic brain injury (TBI) or have been diagnosed with schizophrenia, or both. The research project aims to add to our knowledge on the possible causes behind some of the symptoms which occur following a serious brain injury.

This Participant Information and Consent Form tells you about the research project. It explains the procedures involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don’t understand or want to know more about. Before deciding whether or not to take part, you might want to talk about it with a relative, friend or healthcare worker.

Participation in this research is voluntary. If you don’t wish to take part, you don’t have to. You will receive the best possible care whether you take part or not.

If you decide you want to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

- understand what you have read;
- consent to take part in the research project;
- consent to participate in the research processes that are described;
- consent to the use of your personal and health information as described

You will be given a copy of this Participant Information and Consent Form to keep.

2. What is the purpose of this research project?
Occasionally after a traumatic brain injury, some people have some unusual and distressing experiences e.g. visual hallucinations, unusual thoughts, disturbed speech. To date, no research has investigated why brain injured patients have these experiences, or the range and severity of these symptoms. The purpose of this project is to further understand these unusual experiences in order to develop new treatments for people with a serious brain injury.
To do so, we will be comparing traumatic brain injury (TBI) patients with these unusual experiences, with TBI patients who have not reported such experiences and schizophrenia patients who have the unusual experiences but do not have a TBI. We hope to involve 40 people from each of these groups, from a number of different hospitals, including the Alfred Hospital and the Royal Talbot Hospital. Following a clinical screening session to make sure you’re eligible, we will be asking you to complete 1) a detailed clinical interview (not required if you have not had any unusual experiences following your TBI), 2) a cognitive assessment, and 3) an electroencephalogram (EEG) session.

This research has been initiated by the investigators named on page one, and has been funded by the Austin Hospital Medical Research Foundation and RMIT University.

Results of this research will be used by the researcher Miss Rachel Batty to obtain a Doctor of Philosophy (Psychology and Disability) Degree.

3. What does participation in this research project involve?

You will be asked to engage in three testing sessions of approximately two hours each. Sessions can be completed on the same day, with breaks, if you require and are not tired, or can be completed over a number of days, depending on your preference.

**Session 1 - Clinical Interview (schizophrenia & TBI with unusual experiences only)**

During the clinical interview the researcher will ask you a range of questions about yourself as we would like to know some background information about you and what signs and symptoms you have been experiencing since either your head injury or clinical diagnosis. In the interview you will be asked to talk to us in detail about your experiences. In the interview you will be asked to talk to us in detail about your experiences. These questions will be straightforward and there are no right or wrong answers – we are simply interested in your experiences, opinions and beliefs. We will request that this interview be recorded (audio only) because we want to make sure that we don’t miss any of the information you share. These tapes will be strictly confidential and only the principal researchers of this project will have access to them.

**Session 2 - Cognitive tasks**

This session involves a range of psychological and cognitive tasks which are designed to assess how you process information. Some of these tasks will assess your memory whilst others will assess your ability to process visual information, as well as your language ability. All of these will be word and/or picture tasks and will be assessed by the researcher using paper/pencil. Each task will be explained fully prior to completion.

**Session 3 - Electroencephalogram (EEG) recording**

You will be asked to have an electroencephalogram (EEG) recording while you are completing some basic computerised tasks. This requires a series of electrodes to be attached to your scalp to record brain activity. This is safe and will not hurt you. This will be held at the Alfred Hospital at your convenience. We can arrange transport for you if you need it.

You will not be paid for your participation in this research, but you will be reimbursed for your time ($25 for the clinical/cognitive sessions together and $25 for the EEG session).
4. **What are the possible benefits?**

You will receive no direct benefits as a result of participating in this research.

5. **What are the possible risks?**

Disclosure of personal information during the interview, questionnaires, or psychological tasks may potentially result in you becoming upset or distressed. If this should happen, the researcher is able to arrange for counselling or other appropriate support. Any counselling or support will be provided by staff who are not members of the research team. In addition, you may prefer to suspend or end your participation in the research if distress occurs. There may be additional risks that the researchers do not expect or do not know about. Tell a member of the research team immediately about any new or unusual symptoms that you get.

Except for a minor cold sensation as the EEG cap is filled with gel, there are no known adverse consequences or risks resulting from the EEG procedure. The EEG acquisition device (Neuroscan SynAmps2) complies with Australian standards AS2500 and AS3003, and the principal researcher of this study has over 10 years experience using EEG. You will be monitored regularly throughout the EEG acquisition to ensure that you are comfortable. If you feel uncomfortable at any time during the recording and wish to stop, you will be able to inform the researcher and recording will be stopped immediately.

6. **What if new information arises during this research project?**

During the research project, new information about the risks and benefits of the project may become known to the researchers. If this occurs, you will be told about this new information and the researcher will discuss whether this new information affects you.

7. **Can I have other treatments during this research project?**

It is important to tell your doctor and the research staff about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments. You should also tell your doctor about any changes to these during your participation in the research.

If you are a current patient of either A/Prof Malcolm Hopwood or Dr Yitz Hollander it is important that you know that neither of these doctors will have any access to specific information collected for the study. They will be able to view de-identified data only.

8. **Do I have to take part in this research project?**

Participation in any research project is voluntary. If you do not wish to take part you don’t have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage, and all unprocessed material relating to your participation will be destroyed. If this is the case, it is important for you to know that your decision to participate or not participate in this project will in no way effect your clinical treatment.

9. **What if I withdraw from this research project?**

If you decide to withdraw, please notify a member of the research team before you withdraw. If you do withdraw, all information about you will be disposed of in a confidential disposal process at the Monash Alfred Psychiatry Research Centre under the supervision of Prof Susan Rossell.
10. How will I be informed of the results of this research project?

We will send you a summary of the findings in plain English at the completion of the project. The results will be presented within the Monash Alfred Psychiatry Research Centre, Monash University and RMIT University. Additionally, we hope that the results will be presented at scientific meetings and in scientific journals. If this is the case we will give you details of how to access these publications.

11. What else do I need to know?

- What will happen to information about me?

All the information you give us will be treated in the strictest confidence to be used only for research purposes and this confidentiality will be maintained except where information is authorised or required by law. Any information obtained in connection with this research project that can identify you will remain confidential and will only be used for the purpose of this research project. Your name will not be used and a code number will identify all participants. The information will be kept in a locked cabinet and only researchers involved in the study will have access to the information. In addition, any computer files will be accessible by a password, known only by the Principal Investigator and Associate Researcher Miss Rachel Batty. The information will be retained for a minimum of seven years after which it will be disposed of by use of a confidential disposal process at the Alfred Psychiatry Research Centre under the supervision of Prof Susan Rossell. The results of the project will not present individuals’ data, but data collapsed into groups. In any publication, information will be provided in such a way that you cannot be identified. Information about you may be obtained from your health records held at this, and other, health services for the purposes of this research. Information about your participation in this research project may be recorded in your health records.

- How can I access my information?

In accordance with relevant Australian and/or Victorian privacy and other relevant laws, you have the right to access the information collected and stored by the researchers about you. You also have the right to request that any information, with which you disagree, be corrected. Please contact one of the researchers named at the end of this document if you would like to access your information.

- What happens if I am injured as a result of participating in this research project?

If you suffer an injury as a result of participating in this research project, hospital care and treatment will be provided by the public health service at no extra cost to you if you elect to be treated as a public patient.

- Is this research project approved?

The ethical aspects of this research project have been approved by the Human Research Ethics Committee of Austin Health, and by the Human Research Ethics Committee at the Alfred Hospital, Melbourne.

This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2007) produced by the National Health and Medical Research Council of Australia. This statement has been developed to protect the interests of people who agree to participate in human research studies.
Participant Consent Form – Patient (Sessions 1 & 2)
The Monash-Alfred Psychiatry Research Centre, Melbourne

**Full Project Title:** An examination of the risk factors, phenomenology and aetiology of psychosis following traumatic brain injury.

**Short Title:** Psychosis following traumatic brain injury

I have read, or have had read to me in a language that I understand, this document and I understand the purposes, procedures and risks of this research project as described within it.

I give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to the Monash Alfred Psychiatry Research Centre, Melbourne, concerning my disease and treatment that is needed for this project. I understand that such information will remain confidential.

**Tick Appropriate Box**

- [ ] I give permission for the session 1 interview to be recorded. I understand that this information will remain strictly confidential.

- [ ] I do not give permission for the session 1 interview to be recorded, but agree to participate in the research project without being recorded.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described.

I understand that I will be given a signed copy of this document to keep.

Participant’s name (printed) ..............................................................

Signature Date

Name of witness to participant’s signature (printed) ..........................

Signature Date

Declaration by researcher*: I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Researcher’s name (printed) ..............................................................

Signature Date

* A senior member of the research team must provide the explanation and provision of information concerning the research project. Note: All parties signing the consent section must date their own signature.
13. **Who can I contact?**

Who you may need to contact will depend on the nature of your query, therefore, please note the following:

**For further information or appointments:**

If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the principal researcher, A/Prof Susan Rossell on (03) 9076 8650 (In emergency: 0414 493 784) or any of the following people:

Name: Dr Neil Thomas                        Name: A/Prof Andrew Francis
Role: Senior Clinical Psychologist          Role: Senior Psychologist
Telephone: (03) 8541 6333                   Telephone: (03) 9925 7782

If you wish to contact someone, independent of the study, about ethical issues or your rights or to make a complaint, you may contact Ms Rowan Frew, Alfred Ethics Manager, Telephone 9076 3848, or Dr Andrew Crowden, Chairperson Austin Health Human Research Ethics Committee, Telephone 9496 2901.
Appendix H: Screening Questionnaire

Psychosis following Traumatic Brain Injury

Rachel Batty, A/Prof Susan Rossell, A/Prof Andrew Francis, Dr Neil Thomas, A/Prof Mal Hopwood, Dr Yitzchak Hollander, Prof Jennie Ponsford and Simon Baker

Screening Questionnaire

Participant Code: ____

All participants

1. Do you speak English? Yes  No

2. Have you ever had an operation on your eyes? Yes  No
   Details if yes __________________________
   (participant will be excluded if they are unable to use corrective eyewear (glasses or contact lens) to enable them ~20/20 vision). Remind participant to bring corrective eye wear to test sessions.

3. Have you ever had been diagnosed with any of the following?
   a) Stroke           Yes  No
   b) Multiple Sclerosis (MS) Yes  No
   c) Huntington's Disease Yes  No
   d) Parkinson's Disease Yes  No
   (a Yes answer will exclude them from the study)

TBI Only

4. Prior to your head injury did you have any significant learning or memory difficulties? Yes  No
   Details if yes __________________________
   (a Yes answer will exclude them from the study)
TBI w psychosis

5. Prior to your head injury did you have a mental illness that required you to see a psychiatrist?  Yes  No

Details if yes ________________________________________________________________

(a previous psychosis / mania exclude TBI participants from the study, other illnesses are not exclusion criteria and will be recorded)

TBI w/out psychosis

7. Has anyone in your family been diagnosed with a psychotic illness?

Yes  No

(a Yes answer will exclude them from the study)

AVAILABILITY

Day of week ____________________________  Time ____________________________
Appendix I: Participant Demographic Form

Psychosis following Traumatic Brain Injury

Rachel Batty, A/Prof Susan Rossell, A/Prof Andrew Francis, Dr Neil Thomas, A/Prof Mal Hopwood, Dr Yitzchak Hollander, Prof Jennie Ponsford and Simon Baker

Participant Demographic Information
To be completed in consultation with participants

Name: ____________________________________________

Address: _______________________________________

______________________________________________ Postcode: _________

Telephone number: ___________________________ Date of birth: ________
Psychosis following Traumatic Brain Injury

Rachel Batty, A/Prof Susan Rossell, A/Prof Andrew Francis, Dr Neil Thomas, A/Prof Mal Hopwood, Dr Yitzchak Hollander, Prof Jennie Ponsford and Simon Baker

Participant Demographic Information
To be completed in consultation with participants

Participant Code: __________________________________________

Referred By: _____________________________________________

Probable Patient Group: __________________________________

Gender:

☐ Male
☐ Female

Living Arrangements:
Is your living location classified as

☐ urban
☐ rural

TBI ONLY
When you had your TBI were you living

☐ urban
☐ rural

Relatives:
How many first degree relatives do you have?

☐ mother ☐ father

☐ brother ☐ sister

☐ son ☐ daughter

age _____ age _____
Education:

a) At what age did you begin your formal education? ________________

b) What education standard you have completed? (Circle as many as appropriate)

1. Commenced Secondary  
2. Completed Secondary
3. Commenced Tafe / diploma  
4. Completed Tafe / diploma
5. Commenced Trade Qualification  
6. Completed Trade Qualification
7. Commenced Tertiary degree  
8. Completed Tertiary degree
9. Currently Studying  
10. Other

Details: ____________________________________________________________

What is the total number of years you have spent in formal study? __________

Employment:

a) What is your current employment status?

1. Employed full time  
2. Employed part time
3. Casual employment  
4. Unemployed (but seeking work)
5. Home duties  
6. Student
7. Retired  
8. Disability pension

b) If currently working, what is your current occupation? ________________

c) If retired, what was your occupation? ________________________________

d) If student, what is the occupation of your i) mother ________ ii) father ________
FOR TBI groups only:
e) Prior to you head injury, what was your occupation? ____________________________

FOR SCHIZOPHRENIA group only:
f) Prior to the start of your illness, what was your occupation? ______________________

Brief medical details:

Any current medication: ____________________________

TBI and SCHIZOPHRENIA groups only:

Name of treating physician (psychiatrist or neurologist): ____________________________

Address: ____________________________

Telephone: ____________________________

Clinical injury variables:

To be completed in consultation with participants and their treating physicians, with access to medical records

1. How many head injuries have you had? ______________

2. What date did your most recent injury occur? __________ your age ____

3. What type of injury was it?
   □ penetrating
   □ closed

3. Location of the most recent brain lesion?
   
   Right hemisphere   Left hemisphere
   
   Frontal   Temporal   Parietal   Occipital
   
   Description: ____________________________

3. How long were you unconscious following your most recent head injury? __________

4. Did you experience amnesia following your most recent head injury? __________

   if yes, for how long _________
PREVIOUS HEAD INJURIES

Previous Head Injury #1
1. Date ____
2. Location_______
3. Type__________
4. LoC__________
5. PTA__________

Previous Head Injury #2
6. Date ____
7. Location_______
8. Type__________
9. LoC__________
10. PTA__________

Previous Head Injury #3
11. Date ____
12. Location_______
13. Type__________
14. LoC__________
15. PTA__________

TBI with psychosis participants
5. Has anyone in your family been diagnosed with a psychotic illness? Yes   No
Who ___________________________  What ___________________________

ALL PARTICIPANTS

6. Have you ever had/been diagnosed with any of the following?

<table>
<thead>
<tr>
<th></th>
<th>Obstructive complications (pre/post delivery)</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>Heart disease</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>b</td>
<td>Hypertension (elevated, esp. diastolic, blood pressure)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>c</td>
<td>Diabetes</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>
7. Rate current/prior exercise and dietary behaviour.

<table>
<thead>
<tr>
<th>Exercise</th>
<th>Current</th>
<th>Before Injury</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Mild</td>
<td>Mild</td>
</tr>
<tr>
<td></td>
<td>Occasional</td>
<td>Occasional</td>
</tr>
<tr>
<td></td>
<td>Regular</td>
<td>Regular</td>
</tr>
</tbody>
</table>

**Diet**

<table>
<thead>
<tr>
<th></th>
<th>Current</th>
<th>Before Injury</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salt intake</td>
<td>Low Mid High</td>
<td>Low Mid High</td>
</tr>
<tr>
<td>Fat intake</td>
<td>Low Mid High</td>
<td>Low Mid High</td>
</tr>
</tbody>
</table>
Appendix J: Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983), the LEEDS Dependence Questionnaire (Raistrick et al., 1994), and the Edinburgh Handedness Inventory (Oldfield, 1971)

### Hospital Anxiety and Depression Scale (HADS)

*Zigmond and Snaith (1983)*

Respondents are asked to choose one response from the four given for each interview. They should give an immediate response and be dissuaded from thinking too long about their answers. The questions relating to anxiety are marked "A", and to depression "D". The score for each answer is given in the right column. Instruct the patient to answer how it currently describes their feelings.

#### A I feel tense or 'wound up':
- Most of the time: 3
- A lot of the time: 2
- From time to time, occasionally: 1
- Not at all: 0

#### D I still enjoy the things I used to enjoy:
- Definitely as much: 0
- Not quite so much: 1
- Only a little: 2
- Hardly at all: 3

#### A I get a sort of frightened feeling as if something awful is about to happen:
- Very definitely and quite badly: 3
- Yes, but not too badly: 2
- A little, but it doesn't worry me: 1
- Not at all: 0
<table>
<thead>
<tr>
<th>D</th>
<th>I can laugh and see the funny side of things:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>As much as I always could</td>
</tr>
<tr>
<td></td>
<td>Not quite so much now</td>
</tr>
<tr>
<td></td>
<td>Definitely not so much now</td>
</tr>
<tr>
<td></td>
<td>Not at all</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>A</th>
<th>Worrying thoughts go through my mind:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>A great deal of the time</td>
</tr>
<tr>
<td></td>
<td>A lot of the time</td>
</tr>
<tr>
<td></td>
<td>From time to time, but not too often</td>
</tr>
<tr>
<td></td>
<td>Only occasionally</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>D</th>
<th>I feel cheerful:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Not at all</td>
</tr>
<tr>
<td></td>
<td>Not often</td>
</tr>
<tr>
<td></td>
<td>Sometimes</td>
</tr>
<tr>
<td></td>
<td>Most of the time</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>A</th>
<th>I can sit at ease and feel relaxed:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Definitely</td>
</tr>
<tr>
<td></td>
<td>Usually</td>
</tr>
<tr>
<td></td>
<td>Not Often</td>
</tr>
<tr>
<td></td>
<td>Not at all</td>
</tr>
</tbody>
</table>
### I feel as if I am slowed down:

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Nearly all the time</td>
<td>3</td>
</tr>
<tr>
<td>Very often</td>
<td>2</td>
</tr>
<tr>
<td>Sometimes</td>
<td>1</td>
</tr>
<tr>
<td>Not at all</td>
<td>0</td>
</tr>
</tbody>
</table>

### I get a sort of frightened feeling like 'butterflies' in the stomach:

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Not at all</td>
<td>0</td>
</tr>
<tr>
<td>Occasionally</td>
<td>1</td>
</tr>
<tr>
<td>Quite Often</td>
<td>2</td>
</tr>
<tr>
<td>Very Often</td>
<td>3</td>
</tr>
</tbody>
</table>

### I have lost interest in my appearance:

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Definitely</td>
<td>3</td>
</tr>
<tr>
<td>I don't take as much care as I should</td>
<td>2</td>
</tr>
<tr>
<td>I may not take quite as much care</td>
<td>1</td>
</tr>
<tr>
<td>I take just as much care as ever</td>
<td>0</td>
</tr>
</tbody>
</table>

### I feel restless as I have to be on the move:

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Very much indeed</td>
<td>3</td>
</tr>
<tr>
<td>Quite a lot</td>
<td>2</td>
</tr>
<tr>
<td>Not very much</td>
<td>1</td>
</tr>
<tr>
<td>Not at all</td>
<td>0</td>
</tr>
</tbody>
</table>
### I look forward with enjoyment to things:

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>As much as I ever</td>
<td>0</td>
</tr>
<tr>
<td>Rather less than I</td>
<td>1</td>
</tr>
<tr>
<td>Definitely less than</td>
<td>2</td>
</tr>
<tr>
<td>Hardly at all</td>
<td>3</td>
</tr>
</tbody>
</table>

### I get sudden feelings of panic:

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Very often</td>
<td>3</td>
</tr>
<tr>
<td>Quite often</td>
<td>2</td>
</tr>
<tr>
<td>Not very</td>
<td>1</td>
</tr>
<tr>
<td>Not at all</td>
<td>0</td>
</tr>
</tbody>
</table>

### I can enjoy a good book or radio or TV program:

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Often</td>
<td>0</td>
</tr>
<tr>
<td>Sometimes</td>
<td>1</td>
</tr>
<tr>
<td>Not often</td>
<td>2</td>
</tr>
<tr>
<td>Very seldom</td>
<td>3</td>
</tr>
</tbody>
</table>

### Scoring

(add the As = Anxiety. Add the Ds = Depression). The norms below will give you an idea of the level of Anxiety and Depression.

0-7 = Normal
8-10 = Borderline abnormal
11-21 = Abnormal
The Leeds Dependence Questionnaire

On this page there are questions about the importance of alcohol and/or other drugs in your life.

Think about your drinking/other drug use in the last week and answer each question ticking the closest answer to how you see yourself.

<table>
<thead>
<tr>
<th>Question</th>
<th>Never</th>
<th>Sometimes</th>
<th>Often</th>
<th>Nearly always</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Do you find yourself thinking about when you will next be able to have another drink or take more drugs?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Is drinking or taking drugs more important than anything else you might do during the day?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Do you feel that your need for drink or drugs is too strong to control?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Do you plan your days around getting and taking drink or drugs?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5. Do you drink or take drugs in a particular way in order to increase the effect it gives you?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Do you take drink or other drugs morning, afternoon and evening?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Do you feel you have to carry on drinking or taking drugs once you have started?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Is getting the effect you want more important than the particular drink or drug you use?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Do you want to take more drink or drugs when the effect starts to wear off?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. Do you find it difficult to cope with life without drink or drugs?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
EDINBURGH HANDEDNESS INVENTORY

<table>
<thead>
<tr>
<th>Surname</th>
<th>Given Names</th>
<th>Date of Birth</th>
<th>Sex</th>
</tr>
</thead>
</table>

Please indicate your preferences in the use of hands in the following activities by putting \(+\) in the appropriate column. Where the preference is so strong that you would never try to use the other hand unless absolutely forced to, put \(++\). If in any case you are really indifferent put \(+\) in both columns.

Some of the activities require both hands. In these cases the part of the task, or object, for which hand preference is wanted is indicated in brackets.

Please try to answer all the questions, and only leave a blank if you have no experience at all of the object or task.

<table>
<thead>
<tr>
<th></th>
<th>LEFT</th>
<th>RIGHT</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Writing</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Drawing</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Throwing</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Scissors</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Toothbrush</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Knife (without fork)</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Spoon</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Broom (upper hand)</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Striking Match (match)</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Opening box (lid)</td>
<td></td>
</tr>
<tr>
<td>i</td>
<td>Which foot do you prefer to kick with?</td>
<td></td>
</tr>
<tr>
<td>ii</td>
<td>Which eye do you use when using only one?</td>
<td></td>
</tr>
</tbody>
</table>

L.Q. Leave these spaces blank DECILE

MARCH 1970
Appendix K: Debriefing Statement

Debriefing Statement – Sessions One & Two
The Monash-Alfred Psychiatry Research Centre, Melbourne

**Full Project Title:** An examination of the risk factors, phenomenology and aetiology of psychosis following traumatic brain injury

**Principal Researcher:** A/Prof Susan Rossell

Your participation in this study required you to complete (1) an interview that asked you to share some of your experiences, opinions and beliefs, and (2) an electroencephalogram (EEG) recording while you completed a range of tasks that are designed to assess how you think about things (process information). This is because we are interested in whether the opinions and beliefs of people with psychosis, and the way information is processed, is different compared to those without psychosis. We are also interested to see whether brain activity is different for people with psychosis and people without psychosis during these tasks.

Importantly, there are no right or wrong answers associated with these questions and/or tasks, we are simply interested in your personal experiences and the way that you think about things.

The recording of your brain activity, which you have taken part in for this study, is both safe and harmless. The EEG acquisition device (Neuroscan SynAmps2) complies with Australian standards AS2500 and AS3003, and the principal investigator has over 10 years experience using EEG. Except for a minor cold sensation as the EEG cap is filled with gel, there are no known adverse consequences.

When all the data has been collected and analysed, the results from this research will be reported in a thesis, and possibly presented in publications or at conferences. No information will be presented that identifies you personally. A summary of the general findings, in the form of a newsletter, can be sent to you if you wish. The principal researcher will be pleased to tell you more about the research, or answer any questions you may have. If you have experienced any anxiety or distress during the study or afterwards, or if you would like to discuss any issues regarding the research, please do not hesitate to contact one of the researchers, whose details are provided below. They will be available to speak with you about any aspect of the study, or refer you to a health professional who could manage your specific concerns. Should you have any issues about the conduct of the study, you may contact Ms Rowan Frew, Ethics Manager, Research and Ethics Unit, via telephone on 03 9076 3848 or Dr Andrew Crowden, Chairperson Austin Health Human Research Ethics Committee, Telephone 9496 2901.

We appreciate you taking the time to participate in this research.

A/Prof Susan Rossell
Ph. 03 9076 8650
Email susan.rossell@monash.med.edu.au

Dr Neil Thomas
Ph. 03 8541 6333

A/Prof Andrew Francis
Ph. 03 9925 7782
Appendix L: Non-significant Categorical Group Comparisons
Figure L1. Percentage of participants at each level of education across the four participant groups. Percentage differences are not significant.
**Figure L2.** Percentage of participants qualifying for LEEDS Dependence Questionnaire categories across participant groups. Percentage differences are not significant.

**Figure L3.** Percentage of participants qualifying for HADS Depression Questionnaire categories across participant groups. Percentage differences are not significant.
Appendix M: Scale for the Assessment of Thought, Language, and Communication (TLC); TLC Disorder Global Rating Cutoffs (Andreasen, 1986)

0 = No TLC disorder; Occasional instances of the less pathological forms and no more than one instance of the more pathological (which is felt in context to be clinically insignificant).

1 = Mild TLC disorder; Occasional instances of TLC disorder which are felt in context to be mild but clinically significant.

2 = Moderate TLC disorder; Significant and unquestionable impaired verbal output which leads to a moderate disturbance in communication at least from time to time.

3 = Severe TLC disorder; Disorder significant enough to impair communication for a substantial part of the interview; many instances of the more pathological manifestations of TLC.

4 = Extreme TLC disorder; TLC disorder so severe that communication is difficult or impossible most of the time.
Appendix N: Clustering and Switching Analysis Procedure (Troyer et al., 1997, pp.145-6)

Appendix

Scoring Rules for Clustering and Switching

For each protocol, six scores were calculated, including the total number of correct words generated, mean cluster size, and number of switches for phonemic and semantic fluency, respectively. These scores are defined as follows:

Total number of correct words generated: This was calculated as the sum of all words produced, excluding errors and repetitions.

Mean cluster size: Cluster size was counted starting with the second word in a cluster. That is, a single word was given a cluster size of 0, two words had a cluster size of 1, three words had a cluster size of 2, and so forth. Errors and repetitions were included. The mean cluster size was computed for the three phonemic trials and for the one semantic trial.

Number of switches: This was calculated as the total number of transitions between clusters, including single words, for the three phonemic contexts, and for the one semantic trial. Errors and repetitions were included.

Phonemic Fluency

Clusters on phonemic fluency trials consisted of successively generated words that shared any of the following phonemic characteristics:

First letters: words beginning with the same first two letters, such as arm and art

Rhymes: words that rhyme, such as sand and stand

First and last sounds: words differing only by a vowel sound, regardless of the actual spelling, such as sit, seat, suit, sight, and sought

Homonyms: Words with two or more different spellings, such as some and sun, as indicated by the participant

Semantic Fluency (Animals)

Clusters on semantic fluency trials consisted of successively generated words belonging to the same subcategories, as specified here. Subcategories are organized by learning environment, human use, and zoological categories. Commonly generated examples are listed for each category, although listings are not exhaustive.

Living Environment

Africa: antelope, buffalo, camel, cheetah, chimp, cobra, elephant, gazelle, giraffe, gorilla, hippopotamus, hyena, impala, jackal, lemur, leopard, lion, manatee, mongoose, monkey, orangutan, panther, rhinoceros, tiger, wildebeest, warthog, zebra

Australia: eagle, kangaroo, kiwi, opossum, platypus, Tasmanian devil, wallaby, wombat

Arctic/Far North: auk, caribou, musk ox, penguin, polar bear, reindeer, seal

Farm: chicken, cow, donkey, ferret, goat, horse, male, pig, sheep, turkey

North America: alligator, auk, beaver, bobcat, caribou, chipmunk, cougar, deer, elk, fox, lynx, mountain lion, puma, rabbit, raccoon, skunk, squirrel, wolverine

Water: alligator, auk, beaver, crocodile, dolphin, fish, frog, lobster, manatee, muskrat, newt, octopus, otter, oyster, penguin, platypus, salamander, sea lion, seal, shark, toad, turtle, whale

Human Use

Beasts of burden: camel, donkey, horse, llama, ox

Food: bear, chinchilla, fox, mink, rabbit

Pets: budgie, canary, cat, dog, gerbil, golden retriever, guinea pig, hamster, parrot, rabbit

Zoological Categories

Bird: budgie, conor, eagle, finch, kiwi, macaw, parrot, parakeet, pelican, penguin, robin, toucan, woodpecker

Bovine: bison, buffalo, cow, musk ox, yak

Canine: coyote, dog, fox, hyena, jackal, wolf

Deer: antelope, caribou, elk, gazelle, gazelle, impala, moose, reindeer, wildebeest

Felidae: bobcat, cat, cheetah, cougar, jaguar, leopard, lion, lynx, mountain lion, ocelot, panther, puma, tiger

Fish: bass, guppy, salmon, trout

Insect: ant, beetle, cockroach, flea, fly, praying mantis

Invertebrates: starved, antaeus, hedgehog, mole, shrew

Clustering and Switching Analysis Procedure (Troyer et al., 1997, pp.145-6) (continued)

Primate: ape, baboon, chimpanzee, gibbon, gorilla, human, lemur, marsupial, monkey, orangutan, shrew

Rodent: beaver, chinchilla, chipmunk, gerbil, gopher, groundhog, guinea pig, hamster, hedgehog, hamster, mole, mouse, muskrat, porcupine, rat, squirrel, woodchuck

Waxen: badger, ferret, marten, mink, mongoose, otter, polecat, skunk

General Scoring Rules

In the case in which two categories overlapped, with some items belonging to both categories, some items belonging exclusively to the first category, and some items belonging exclusively to the second category, the overlapping items were assigned to both categories. For example, for dog, cat, tiger, lion, the first two items were scored as pets, and the last three items were scored as felines. Cat was included in both the pet category and the feline category.

In the case where smaller clusters were embedded within larger ones, or two categories overlapped, but all items could correctly be assigned to a single category, only the larger, common category was used. For example, for fly, sila, sila, sila all begin with sfl, but an additional cluster was not scored for the last two words, which differ only by a vowel sound.

Received January 17, 1996
Revision received May 28, 1996
Accepted May 31, 1996
### Appendix O: Prime-TARGET Stimuli (Semantic Priming Task)

**Table O1**

Full List of Prime-TARGET Semantic Pairs (Matched)

<table>
<thead>
<tr>
<th>Prime</th>
<th>Target</th>
<th>Prime</th>
<th>Target</th>
<th>Prime</th>
<th>Target</th>
<th>Prime</th>
<th>Target</th>
</tr>
</thead>
<tbody>
<tr>
<td>track-TRAIL</td>
<td>coat-JACKET</td>
<td>pull-DRAG</td>
<td>pause-HESITATE</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>smile-FROWN</td>
<td>street-AVENUEN</td>
<td>jerk-SHOVE</td>
<td>dinner-LUNCH</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hockey-RUGBY</td>
<td>house-FLAT</td>
<td>wipe-RUB</td>
<td>lake-RIVER</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mile-INCH</td>
<td>growth-INCREASE</td>
<td>physics-BIOLOGY</td>
<td>centimetre-MILLIMETRE</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>parcel-ENVELOPE</td>
<td>icon-SYMBOL</td>
<td>vegetable-CEREAL</td>
<td>carrot-CELERY</td>
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<td>damp-MOIST</td>
<td>guitar-CELLO</td>
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<td>road-PATH</td>
<td>thump-FIST</td>
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<td>palace-Castle</td>
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<td>morning-NIGHT</td>
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<td>jazz-DANCE</td>
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<td>blow-STORM</td>
<td>graph-CHART</td>
<td>ballet-OPERA</td>
<td>spice-HERB</td>
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<td>oil-GAS</td>
<td>bride-WIFE</td>
<td>solo-DUET</td>
<td>bounce-THROW</td>
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<td>mud-DIRT</td>
<td>thread-WIRE</td>
<td>screw-TWIST</td>
<td>sofa-LOUNGE</td>
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<td>bleach-MOP</td>
<td>wagon-CART</td>
<td>cow-GOAT</td>
<td>ankle-ELBOW</td>
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<td>oven-KITCHEN</td>
<td>wheat-FLOUR</td>
<td>mountain-VALLEY</td>
<td>advice-HELP</td>
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<td>lift-SHAFT</td>
<td>estate-MANOR</td>
<td>float-DRIFT</td>
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<td>snail-CRAB</td>
<td>effort-INITIATIVE</td>
<td>sheet-BLANKET</td>
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<td>lover-FRIEND</td>
<td>uniform-COSTUME</td>
<td>dawn-DUSK</td>
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<td>carry-DROP</td>
<td>hair-FACE</td>
<td>bucket-SPoon</td>
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<td>spouse-PARTNER</td>
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<td>pillow-CUSHION</td>
<td>garden-SUNSHINE</td>
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<td>junior-YOUTH</td>
<td>stereo-RADIO</td>
<td>talent-SKILL</td>
<td>breakfast-YOGHURT</td>
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Table O2

Full List of Prime-TARGET Semantic Pairs (Unmatched)

<table>
<thead>
<tr>
<th>Prime-TARGET Unmatched Pairs Allocated to Each Set</th>
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</thead>
<tbody>
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<td><strong>Set A</strong></td>
</tr>
<tr>
<td>Track-GAS</td>
</tr>
<tr>
<td>Smile-TRAIL</td>
</tr>
<tr>
<td>Hockey-SMIRK</td>
</tr>
<tr>
<td>Mile-ENVELOPE</td>
</tr>
<tr>
<td>Parcel-STORM</td>
</tr>
<tr>
<td>Earth-WHEEL</td>
</tr>
<tr>
<td>Football-PARTNER</td>
</tr>
<tr>
<td>Road-GOLF</td>
</tr>
<tr>
<td>Jumper-MOP</td>
</tr>
<tr>
<td>Rain-HEAVEN</td>
</tr>
<tr>
<td>Bacon-DIRT</td>
</tr>
<tr>
<td>Morning-FEAR</td>
</tr>
<tr>
<td>Fly-KITCHEN</td>
</tr>
<tr>
<td>Blow-VEST</td>
</tr>
<tr>
<td>Oil-FOG</td>
</tr>
<tr>
<td>Mud-PORK</td>
</tr>
<tr>
<td>Bleach-YOUTH</td>
</tr>
<tr>
<td>oven-RUGBY</td>
</tr>
<tr>
<td>Grin-INCH</td>
</tr>
<tr>
<td>Pedal-FROWN</td>
</tr>
<tr>
<td>Anger-SAUCE</td>
</tr>
<tr>
<td>Gravy-PATH</td>
</tr>
<tr>
<td>Spouse-NIGHT</td>
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<tr>
<td>Junior-GLIDE</td>
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### Table O3

#### Full List of Prime-TARGET Filler Pairs

<table>
<thead>
<tr>
<th>Prime-TARGET Matched/Unmatched Filler Pairs Allocated to Each Set</th>
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</thead>
<tbody>
<tr>
<td><strong>Set E (Matched)</strong></td>
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<tr>
<td>Cigar-CIGARETTE</td>
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<tr>
<td>Type-CATEGORY</td>
</tr>
<tr>
<td>Sitting-ROOM</td>
</tr>
<tr>
<td>Example-ILLUSTRATION</td>
</tr>
<tr>
<td>Chalk-MARBLE</td>
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<tr>
<td>Office-DEPARTMENT</td>
</tr>
<tr>
<td>Belief-ASSUMPTION</td>
</tr>
<tr>
<td>Worm-CATERPILLAR</td>
</tr>
<tr>
<td>Text-PAPER</td>
</tr>
<tr>
<td>Milk-WATER</td>
</tr>
<tr>
<td>Sink-BATH</td>
</tr>
<tr>
<td>Drive-SPEED</td>
</tr>
<tr>
<td>Hook-PIN</td>
</tr>
<tr>
<td>Fight-WIN</td>
</tr>
<tr>
<td>Degree-LEVEL</td>
</tr>
<tr>
<td>Wrist-CLOCK</td>
</tr>
<tr>
<td>Book-COMIC</td>
</tr>
<tr>
<td>Wild-CREATURE</td>
</tr>
<tr>
<td>Hero-LEGEND</td>
</tr>
<tr>
<td>Pit-DITCH</td>
</tr>
<tr>
<td>Barn-SHED</td>
</tr>
<tr>
<td>Plaster-CEMENT</td>
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<td>Towel-COMB</td>
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<td>Column-PARAGRAPH</td>
</tr>
<tr>
<td>News-REPORT</td>
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<tr>
<td>Cake-ICING</td>
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<td>Shape-CUBE</td>
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<td>Copper-BRONZE</td>
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<td>Tan-SHINE</td>
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<tr>
<td>Cherry-CHRISTMAS</td>
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<tr>
<td>Button-SHIRT</td>
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<td>Pear-ORANGE</td>
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<td>Wing-TAIL</td>
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<tr>
<td>Telescope-STAR</td>
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<td>Hamster-RABBIT</td>
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(continued)
Table O3

Full List of Prime-TARGET Filler Pairs (continued)

<table>
<thead>
<tr>
<th>Prime-TARGET Matched/Unmatched Filler Pairs Allocated to Each Set</th>
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</thead>
<tbody>
<tr>
<td><strong>Set E (Matched)</strong></td>
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<tr>
<td>----------------------</td>
</tr>
<tr>
<td>Soda-COKE</td>
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<tr>
<td>Tease-MOCK</td>
</tr>
<tr>
<td>Canal-pond</td>
</tr>
<tr>
<td>Bike-HELMET</td>
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<tr>
<td>Suck-STRAW</td>
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<tr>
<td>Powder-SMOKE</td>
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<tr>
<td>Clue-HINT</td>
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<tr>
<td>Turtle-TORTOISE</td>
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<tr>
<td>Gauze-BANDAGE</td>
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<td>Cotton-NEEDLE</td>
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<tr>
<td>Fern-PINE</td>
</tr>
<tr>
<td>Jockey-RIDER</td>
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<tr>
<td>Heart-LUNG</td>
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<tr>
<td>Set G</td>
</tr>
<tr>
<td>---------------</td>
</tr>
<tr>
<td>Beam-MURT</td>
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<td>Pasta-PHAIR</td>
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<td>Opal-DEILS</td>
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<td>Lorry-AMBOW</td>
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<td>Whisk-HUDE</td>
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<td>Canary-PSOUDES</td>
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<td>Gutter-YAL</td>
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<tr>
<td>Liquid-RURP</td>
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<td>Walnut-CAK</td>
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<tr>
<td>Leaflet-OUNTE</td>
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<td>Flow-STEEVED</td>
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<td>Scarf-FALD</td>
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<td>Verse-VADE</td>
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<td>Spoke-STRAUDS</td>
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<td>Scene-DRARFED</td>
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<td>Erode-PHUGS</td>
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<td>Spike-SNOXT</td>
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<td>Disk-SAMS</td>
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<td>Hospital-YECS</td>
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<tr>
<td>Farm-SWOG</td>
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<tr>
<td>Entrance-GWIG</td>
</tr>
<tr>
<td>Waltz-DURS</td>
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<tr>
<td>Stable-CIVE</td>
</tr>
<tr>
<td>Minister-LISSED</td>
</tr>
<tr>
<td>Beef-GWIND</td>
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<tr>
<td>Club-SPIES</td>
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<tr>
<td>Ear-WRIPPED</td>
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<tr>
<td>Porch-KLISPS</td>
</tr>
<tr>
<td>Theory-ZABS</td>
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<tr>
<td>Cabbage-ZETH</td>
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<td>Double-KED</td>
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<td>Coral-NAL</td>
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<td>Event-SOOO</td>
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<tr>
<td>Deer-BYNE</td>
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<tr>
<td>Boss-QUOIGNEED</td>
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(continued)
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<th>Set G (Continued)</th>
<th>Set H</th>
<th>Set H (Continued)</th>
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<td>Cleaner-NOMS</td>
<td>Movie-POLT</td>
<td>Zone-SCOOV</td>
<td>Motor-PESE</td>
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<td>Tongs-SPURB</td>
<td>Drunk-THROOTS</td>
<td>Steak-PHORD</td>
<td>Molecule-VINCS</td>
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<tr>
<td>Nerve-LEEFS</td>
<td>Shot-CLAPTH</td>
<td>Croak-ZIEC</td>
<td>Premier-YUIFFED</td>
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<td>Baseball-SCICKS</td>
<td>Burger-NAUSED</td>
<td>Soldier-MIRCKS</td>
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<td>Weep-STREPT</td>
<td>Thrill-BLELB</td>
<td>Happen-WHUIST</td>
<td>Blink-DEEZED</td>
</tr>
<tr>
<td>Volley-BLURNED</td>
<td>Gallop-WEABB</td>
<td>Noble-JAWQUE</td>
<td>Outline-TROOND</td>
</tr>
<tr>
<td>Chess-GHAVES</td>
<td>Soup-STELGN</td>
<td>Desk-LUXT</td>
<td>Set-LOULT</td>
</tr>
<tr>
<td>Polo-FEEPE</td>
<td>Fancy-HABE</td>
<td>Agree-TOUNNED</td>
<td>Mood-GNIRN</td>
</tr>
<tr>
<td>Once-ZUNKS</td>
<td>Chin-CLEIFS</td>
<td>Agree-TOUNNED</td>
<td>Screen-FRAXTE</td>
</tr>
<tr>
<td>Setting-TUITHEDE</td>
<td>Weather-PHRURGN</td>
<td>Soccer-BRUPT</td>
<td>Straighten-SKURGN</td>
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<td>Tenant-SESSED</td>
<td>Fresh-SHYLMN</td>
<td>Food-HOIDD</td>
<td>Dart-KAIMED</td>
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<tr>
<td>Jeep-SOURKED</td>
<td>Seafood-KNAULS</td>
<td>Pretend-QUORMS</td>
<td>Motion-TRAPHT</td>
</tr>
<tr>
<td>Swivel-PLOVES</td>
<td>Define-PROUGED</td>
<td>Forget-VEIKS</td>
<td>Tennis-FREIFED</td>
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Table O5
Mean, Standard Deviation, Range, and Significance of Mean Differences between Prime-TARGET Word Stimulus Parameters

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<th>Prime†</th>
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<th>Target†</th>
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<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Range</td>
<td>Mean</td>
<td>SD</td>
<td>Range</td>
</tr>
<tr>
<td>Number Letters</td>
<td>5.08</td>
<td>1.34</td>
<td>3-10</td>
<td>5.23</td>
<td>1.43</td>
<td>3-10</td>
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<tr>
<td>Number Phonemes</td>
<td>4.11</td>
<td>1.34</td>
<td>0-9</td>
<td>4.19</td>
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<td>Number Syllables</td>
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<td>0.65</td>
<td>1-4</td>
<td>1.53</td>
<td>0.77</td>
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<tr>
<td>Kucera-Francis* Lexical Categories</td>
<td>6.72</td>
<td>5.07</td>
<td>0-15</td>
<td>6.38</td>
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<td>Kucera-Francis* Word Frequency</td>
<td>52.06</td>
<td>78.11</td>
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<td>52.26</td>
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<td>Concreteness Score</td>
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<td>242.58</td>
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<td>Age of Acquisition</td>
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<td>5.25</td>
<td>7.24</td>
<td>0-32</td>
<td>4.40</td>
<td>5.55</td>
<td>0-25</td>
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</table>

†Prime: 62% noun, 14.6% verb, 15.6% noun/verb, 3.1% noun/adjective, 2.1% noun/verb/adjective; Target: 49% noun, 11.5% verb, 34.4% noun/verb, 4.2% noun/adjective, 1% noun/verb/adjective

*Paired samples t-test statistic

*Kucera & Francis (1967)
Appendix P: Word List Counterbalancing Procedures and Priming Sequence Allocation

Semantic Word Pairs ($n = 96$)

- Short SOA (250 ms)
  - Semantic Word Pairs ($n = 48$) Low Relatedness Proportion (RP = 25%)
  - Related Semantic Word Pairs ($n = 24$) + 48 Filler (Jumbled)
  - Unrelated Semantic Word Pairs ($n = 24$) + 48 Filler (Related)

- Long SOA (750 ms)
  - Semantic Word Pairs ($n = 48$) High Relatedness Proportion (RP = 75%)
  - Related Semantic Word Pairs ($n = 24$) + 48 Filler (Jumbled)
  - Unrelated Semantic Word Pairs ($n = 24$) + 48 Filler (Related)

96 Filler Word Pairs

- Unrelated 48 Filler $F_A1$
- Related 48 Filler $F_B1$

- Unrelated 48 Filler $F_A2$
- Related 48 Filler $F_B2$

192 Pseudo Word Pairs

- 96 Pseudo Word Pairs $G_A1$ + 96 Pseudo Word Pairs $G_B1$

- 96 Pseudo Word Pairs $G_A2$ + 96 Pseudo Word Pairs $G_B2$

Figure Q1. Word list counterbalancing procedures are shown. Four lists of semantic pairs were created (Sets A–D), counterbalanced across related/unrelated conditions for both short and long SOAs (subsets 1–4). Two lists of filler pairs were created (Sets $F_A$ & $F_B$), counterbalanced across related/unrelated conditions. Filler pairs were not counterbalanced across SOAs because they were fixed to short and long SOAs in unrelated and related forms, respectively, to manipulate relatedness proportion (RP). Two lists of pseudo pairs were created (Sets $G_A$ & $G_B$), counterbalanced across SOAs. Pseudo pairs were not counterbalanced across related/unrelated conditions because they are nonwords and thus have no semantic relationship to the prime. In total, eight unique priming sets were created using this procedure of counterbalancing (i.e., four at each SOA, see Table Q1). Sets from each SOA were then paired to create four unique priming sequences (see Table Q2). In this way, no participant saw any given word pair more than once. Priming sequences were counterbalanced across participants within each group so that an equal proportion saw each of the four sequences.
Table P1
*Prime-TARGET Pair List Allocation of Sets One to Eight*

<table>
<thead>
<tr>
<th>Sets</th>
<th>SOA</th>
<th>Short (250ms)</th>
<th>Long (750ms)</th>
<th>Short (250ms)</th>
<th>Long (750ms)</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Set 1</td>
<td>Set 2</td>
<td>Set 3</td>
<td>Set 4</td>
</tr>
<tr>
<td>Semantic Pairs</td>
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<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>List A₁</td>
<td>List A₂</td>
<td>List C₁</td>
<td>List C₂</td>
</tr>
<tr>
<td></td>
<td></td>
<td>List B₁</td>
<td>List B₂</td>
<td>List D₁</td>
<td>List D₂</td>
</tr>
<tr>
<td>Filler pairs</td>
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<td>List F₁₁</td>
<td>List F₁₂</td>
<td>List F₂₁</td>
<td>List F₂₂</td>
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<tr>
<td></td>
<td></td>
<td>Unrelated (48)</td>
<td>Related (48)</td>
<td>Unrelated (48)</td>
<td>Related (48)</td>
</tr>
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<td>Pseudo pairs</td>
<td></td>
<td>List G₁₁ (96)</td>
<td>List G₁₂ (96)</td>
<td>List G₂₁ (96)</td>
<td>List G₂₂ (96)</td>
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</table>

Table P2
*Priming Sequence Allocation*

<table>
<thead>
<tr>
<th>Priming Sequence</th>
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<tr>
<td>1</td>
<td>1 &amp; 4</td>
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<tr>
<td>2</td>
<td>2 &amp; 3</td>
</tr>
<tr>
<td>3</td>
<td>5 &amp; 8</td>
</tr>
<tr>
<td>4</td>
<td>6 &amp; 7</td>
</tr>
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</table>

*Note.* Priming sequences were counterbalanced across participants for each cohort.
Appendix Q: Pseudo Random Sequence Sets for the Probabilistic Reasoning Task

The predetermined sequence of beads for the Probabilistic Reasoning Task was taken from Colbert and Peters (2002) for the first trial (85:15 ratio), and from Dudley, John, Young, and Oliver, (1997) for the second trial (60:40 ratio). The bead sequence for both versions of trials one and two is contained in Table R1.

Table R1
Pseudo Random Bead Sequences across Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Version</th>
<th>Ratio</th>
<th>Correct Answer</th>
<th>Bead Sequence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td>85:15</td>
<td>Jar A</td>
<td></td>
</tr>
</tbody>
</table>
|       | 1       | Pink/Blue   |                 | ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ● ○
Appendix R: The National Adult Reading Test (NART; Nelson, 1981) and Conversion Formula

Word List in alphabetical order

<table>
<thead>
<tr>
<th>abstemious</th>
<th>gaoled</th>
<th>radix</th>
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<tbody>
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<td>ache</td>
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<td>procreate</td>
<td></td>
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<tr>
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<td>psalm</td>
<td></td>
</tr>
<tr>
<td>equivocal</td>
<td>puerperal</td>
<td></td>
</tr>
<tr>
<td>façade</td>
<td>quadruped</td>
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</tbody>
</table>
NART SCORE SHEET - FOR WAIS-R IQ
(MACQUARIE DICTIONARY PRONUNCIATIONS)

SCORE 'x' FOR CORRECT PRONUNCIATION AND 'o' IF INCORRECT

DATE:

EDUCATION LEVEL:
1 - some primary  
2 - some secondary  
3 - some secondary plus trade  
4 - completed secondary  
5 - begun tertiary

NART errorscore: ____________

PREDICTED WAIS-R IQ (form. QNELO 60 yrs people)

For males:
IQ = 116.3 - 0.6 ERRORSORE + 3.8 EDUCATION

For females:
IQ = 108.9 - 0.6 ERRORSORE + 3.8 EDUCATION

IPA SYMBOLS

a as in "bat" /ba:/  u as in "hwas" /hwas/  
a as in "bay" /ba:/  i as in "hera" /hera/  
a as in "boy" /bo:/  es as in "hair" /hair/  
u as in "how" /hau:/  au as in "tour" /tour/

i as in "pet" /pit/  ɔ as in "port" /pot/  
I as in "pit" /pit/  u as in "put" /put/  
s as in "pet" /pet/  ɔ as in "pool" /pool/  
s as in "pat" /pat/  ə as in "part" /part/  
ɔ as in "pot" /pot/  ɔ as in "but" /bat/  
ŋ as in "sing" /sin/  j as in "you" /jou/  
θ as in "thin" /thin/  tʃ as in "choke" /tʃouk/  
ʃ as in "shoe" /ʃo:/  dʒ as in "joke" /dʒouk/
Appendix S: The Statistical Inappropriateness of Analysis of Covariance (ANCOVA) with the current dataset

Analysis of covariance (ANCOVA) aims to evaluate whether the population means on a dependent variable are the same across all levels of a factor (i.e. the independent variable, such as participant group), after adjusting for the influence of one or more alternative variables (i.e. the covariate) (Green & Salkind, 2004; Tabachnick & Fidell, 2007). However, the research community often overlook that various conditions must first be met by any given dataset before ANCOVA is considered an appropriate analysis technique; (i) participant groups must be randomly assigned, (ii) participant groups must not differ on the covariate(s), and (iii) variables must be independent (not overlapping) constructs (Miller & Chapman, 2001). In a thorough discussion Miller and Chapman (2001) indicate that, the use of ANCOVAs to remove the influence of pre-existing group differences is erroneous and, in fact “no such analytic method is available, nor can one be developed, ” and that despite an “overwhelming case against inappropriate attempts to "control for" such group differences, they remain common in research literature...” (p. 41, see Miller and Chapman [2001] for full mathematical and theoretical argument).

Given the likelihood that pre-existing characteristics associated with traumatic brain injury and schizophrenia would influence neurocognitive performance in this research, the temptation to apply this technique is understandable. In particular, the effects of executive dysfunction are likely to be considerable, as was reinforced by correlational analyses (Chapter Eight). Nonetheless, because the current dataset violated all three of the aforementioned requirements, the application of ANCOVA was statistically inappropriate, and thus not utilised in analyses: (i) participant groups were defined by pre-existing illness and/or injury, instead of randomly assigned, (ii) group differences were demonstrated on potential covariates either by group-wise analysis or by data plots (see Table U1 and Figures U1 to U17), (iii) potential covariates overlapped with neurocognition, given that, as noted and demonstrated by correlational analyses in Chapter Eight, many of these are inextricably linked. Figures U1 to U17 demonstrate (ii) using the RBANS Total score as an example. Injury severity (PTA), SAPS current delusions, TLC Global demonstrated group similarities, however, given the violation of (i) and (iii) these remained unsuitable for ANCOVA.
Table S1

*Group-wise Significance Values on Potential Covariates*

<table>
<thead>
<tr>
<th>Potential Mediator (Covariate)</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of injury (yrs)</td>
<td>NS</td>
</tr>
<tr>
<td>Injury severity (LOC) (min)</td>
<td>NS</td>
</tr>
<tr>
<td>Injury severity (PTA) (min)</td>
<td>NS</td>
</tr>
<tr>
<td>Time since injury (yrs)</td>
<td>.004</td>
</tr>
<tr>
<td>Age of Illness Onset (yrs)</td>
<td>NS</td>
</tr>
<tr>
<td>Illness Onset Latency (mths)</td>
<td>-</td>
</tr>
<tr>
<td>Illness Duration (yrs)</td>
<td>NS</td>
</tr>
<tr>
<td>Antipsychotic Medication % Maximum Dosage</td>
<td>NS</td>
</tr>
<tr>
<td>PANSS Delusions</td>
<td>NS</td>
</tr>
<tr>
<td>PANSS Positive Scale</td>
<td>NS</td>
</tr>
<tr>
<td>PANSS Negative Scale</td>
<td>.03</td>
</tr>
<tr>
<td>PANSS General Scale</td>
<td>NS</td>
</tr>
<tr>
<td>PANSS Total</td>
<td>NS</td>
</tr>
<tr>
<td>SAPS current hallucination</td>
<td>NS</td>
</tr>
<tr>
<td>SAPS lifetime hallucinations</td>
<td>NS</td>
</tr>
<tr>
<td>SAPS current delusions</td>
<td>NS</td>
</tr>
<tr>
<td>SAPS lifetime delusions</td>
<td>NS</td>
</tr>
<tr>
<td>TLC Total Score</td>
<td>NS</td>
</tr>
<tr>
<td>TLC Global Score</td>
<td>NS</td>
</tr>
<tr>
<td>Processing Speed (TMT A)</td>
<td>.009</td>
</tr>
<tr>
<td>Attention (RBANS Index)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>HADS anxiety</td>
<td>.02</td>
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<tr>
<td>Premorbid (NART) IQ</td>
<td>NS</td>
</tr>
<tr>
<td>WASI Full Scale IQ</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Total education (yrs)</td>
<td>.05</td>
</tr>
</tbody>
</table>

* See *Chapters Six and Seven for additional group-wise statistical data*
Figure S1. Scatterplot of RBANS Total and age of injury (yrs) by group.

Figure S2. Scatterplot of RBANS Total and injury severity (LOC) (min) by group.
**Figure S3.** Scatterplot of RBANS Total and injury severity (PTA) (min) by group.

**Figure S4.** Scatterplot of RBANS Total and age of illness onset (yrs) by group.
Figure S5. Scatterplot of RBANS Total and illness duration (yrs) by group.

Figure S6. Scatterplot of RBANS Total and % maximum antipsychotic dosage by group.
Figure S7. Scatterplot of RBANS Total and PANSS Delusions by group.

Figure S8. Scatterplot of RBANS Total and PANSS Positive Scale by group.
Figure S9. Scatterplot of RBANS Total and PANSS General Scale by group.

Figure S10. Scatterplot of RBANS Total and PANSS Total by group.
Figure S11. Scatterplot of RBANS Total and SAPS Current Hallucinations by group.

Figure S12. Scatterplot of RBANS Total and SAPS Lifetime Hallucinations by group.
Figure S13. Scatterplot of RBANS Total and SAPS Current Delusions by group.

Figure S14. Scatterplot of RBANS Total and SAPS Lifetime Delusions by group.
Figure S15. Scatterplot of RBANS Total and TLC Total by group.

Figure S16. Scatterplot of RBANS Total and TLC Global by group.
Figure S17. Scatterplot of RBANS Total and premorbid (NART) IQ by group.
Appendix T: Mediators of Cognitive Neuropsychological Performance; Relationships at trend level \((p < .05)\)

*Chapter Eight* identified a number of relationships between mediators and neurocognition, where \(p < .05\). As noted, alpha was set at \(p < .01\) to correct for multiple comparisons. However, with reference to the identification of critical mediators in the literature on TBI and psychosis (*Chapter Five*), these trends are briefly presented here. Correlation coefficients for these analyses were contained in *Chapter Eight.*

For the healthy cohort; (i) slower processing speed may also be related to phonological fluency, (ii) increased attention to mental inhibition (Stroop), and (iii) increased current IQ may facilitate Immediate and Story Memory on the RBANS, phonological fluency, and verbal IQ.

Patients with TBIWP demonstrated trends between; (i) later age of injury and better mental switching on the TMT (difference score), (ii) greater injury severity according to LOC and poorer recall (List Recall and Story Recall), as well as mental switching on the Stroop, (iii) greater injury severity according to PTA and reduced memory (Immediate and Story), as well as reduced phonological fluency (‘a’), (iv) better processing speed and Stroop mental switching, (v) better attention and better Digit Span, processing speed (Stroop word), mental switching (TMT Form B and difference score), and better IQ (WASI subscale performance), (vi) better premorbid IQ and better Story Memory and Digit Span on the RBANS, (vii) better current IQ and processing speed (Stroop word), and finally, (viii) more education (yrs) and better List Recall.

In schizophrenia; (i) later age of illness onset may be related to increased IQ (Full Scale and visuo-spatial), (ii) longer illness duration with poorer Story Memory, Coding, mental inhibition (Stroop), mental switching (TMT), and reduced current and verbal IQ, (iii) higher scores on the PANSS Delusions scale with better List Recall, (iv) increased lifetime hallucinations with better phonological fluency (both ‘a’ and total), (v) higher total scores on the PANSS with reduced Figure Recall, (vi) slower processing speed with Visuo-spatial processing, Story Memory and Digit Span on the RBANS, (vii) better attention with inhibition and switching (Stroop) as well as verbal IQ, (viii) increased premorbid IQ with Story Memory and current IQ (subscales), and finally, (ix) increased current IQ with Visuo-spatial processing, Story Memory and the Total RBANS score.
For the dually-diagnosed PFTBI patients trends were identified between; (i) greater injury severity according to LOC and better Coding on the RBANS, Stroop performance (except the colour trial), and mental switching (TMT), (ii) greater injury severity according to PTA and poorer Immediate Memory, List Learning, Figure Recall, Stroop word, colour and inhibition trials, (iii) an older age of psychosis onset and better mental switching (TMT), (iv) higher percentage of the maximum antipsychotic dose and better phonological fluency, (v) increased negative symptoms on the PANSS and better Visuo-spatial processing and current IQ, (vi) increased general symptoms and better current and verbal IQ, (vii) greater lifetime hallucinations and better List Recall, (viii) PANSS Total score and better mental switching, (ix) faster processing speed with better Immediate Memory, Attention, List Learning, Digit Span, Figure Recall, phonological fluency (subtest ‘a’), and remaining Stroop trials (others were significant at $p < .01$), (x) better attention and better List Learning, (xi) higher premorbid IQ and better Immediate Memory, List Learning and verbal IQ, and finally (xii) greater education with better current IQ (Full Scale and subscales).

It is noted that akin to the findings detailed in Chapter Eight, these trends show an increase in relationships as impairment increases across cohorts. They also identify greater injury-based relationships, the potential for the effects of symptoms in both psychotic cohorts, and medication dose in PFTBI. Importantly, there was a trend for the relationship between negative symptoms and neurocognition in PFTBI, and this may warrant further investigation given that negative symptoms have been hypothesised as a diagnostic distinction. On the other hand, symptom-based relationships were counter-intuitive in direction in PFTBI. Further, the potential influence of greater education was suggested in the TBI cohorts alone. This was specific to List Recall in TBIWP which is not immediately explicable. However, in PFTBI, greater education may influence higher IQ, which could have implications for treatment. Given the issues with alpha correction for this analysis it is highly likely that some of these relationships are spurious, however because of the novel nature of this research these trends are highlighted here as variables for further investigation.
Appendix U: Peer-Reviewed Publications
Impaired semantic memory in the formation and maintenance of delusions post-traumatic brain injury: a new cognitive model of delusions

Susan L. Rossell · Rachel A. Batty · Laura Hughes

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Abstract This paper proposes a new cognitive model to explain the aetiology of delusions irrespective of diagnosis and/or phenomenology. The model hypothesises the influence of two processes in the formation and maintenance of delusions; (i) impaired perceptual abilities, particularly affect perception, which fosters the encoding of (ii) idiosyncratic semantic memories, especially those with an affective/self-referential valence. Previous research has established that schizophrenia patients with delusions have impaired semantic memory function. In the current paper we sought to provide evidence for (ii) abnormal semantic processing in persons with delusions with an alternative aetiology. Performance of four cases with a significant delusion post a traumatic brain injury was examined on a broad range of semantic memory tests. Overall semantic processing was impaired in the four cases relative to a normative healthy control sample. Cases performed better on tasks which required categorical identification, relative to the novel production of semantic information, which was poor in all four of the cases. These data offer preliminary evidence for our hypothesis of impaired semantic processing in persons with delusions. Findings will need to be empirically verified in larger sample groups and in those with alternative aetiologies.

Keywords Delusions · Psychosis · Traumatic brain injury · Semantic memory and perception

Background Delusions have traditionally been viewed as the defining characteristic of insanity. As Karl Jaspers observed “Since time in memorial … to be mad was to be deluded” [25]. In spite of this and the recognition of the prominence of delusions within psychopathology, until the last 20 years, there has been little empirical investigation into the aetiology of delusions [6]. As well as occurring in disorders such as schizophrenia, bipolar affective disorder, and delusional disorder, delusions are also present in a number of medical conditions, for example, dementia (16–70% incidence rate in Alzheimer’s type; [4]), temporal lobe epilepsy (7–23% [12]), and in up to 9% of individuals who sustain traumatic brain injury (TBI) [12]. Delusions also vary dramatically in terms of their associated phenomenology. In psychiatric cases, delusions can be widespread and multi-thematic or they can be circumscribed and monothematic. The same holds for organic delusions. Delusional symptoms associated with temporal lobe damage can be widespread and co-occur with other psychotic symptoms, whereas right hemisphere brain damage tends to result in monothematic delusions.

The multiplicity of conditions and the variable phenomenology associated with delusions are clinically important and theoretically challenging. Exploring what is
common and what is different about delusions in varying conditions, independent of phenomenology, is critical to the development of a comprehensive cognitive model of how individuals with delusions generate, evaluate, and then accept and reject (usually if implausible) candidate beliefs, and how those beliefs are then maintained. Such a comprehensive model will have practical applications. For example, common cognitive features of delusions can be used to improve and extend cognitive therapy models applicable to any delusion, rather than those that exist for paranoia only [8]. Thus, such therapy will be more diagnosisically inclusive and cost-effective.

Cognitive models

There is no encompassing cognitive model to explain all delusions, independent of aetiology or phenomenological characteristics. It may be that all types of delusions, regardless of differences in associated condition and/or phenomenology, arise from a common cognitive impairment. Alternatively, it may be that schizophrenia, affective delusions, and ‘organic’ delusions are qualitatively distinct, not only at a psychopathological level but also at a cognitive level. To date, at least four explanations have been put forward to explain delusions occurring in psychiatric disorders [20]: (a) an overconfident “jumping to conclusions” style of belief formation manifesting in abnormal performances on probabilistic reasoning tasks [20, 24], although, there are some failures to replicate [49]; (b) a self-defensive attributional style biasing individuals towards blaming other people, rather than any aspect of themselves, for negative events, especially prominent in individuals with paranoid/persecutory delusions but not other delusional types [30]; and (c) a theory of mind deficit resulting in an inability to represent the beliefs, thoughts, and intentions of other people [11, 18, 32, 33]. However, even though theory of mind deficits are highly replicable in patients with schizophrenia, there is less convincing evidence to suggest such a deficit is a factor in delusion formation or maintenance. The last approach has stated that delusions are the consequence of (d) a normal response to an anomalous experience, for example, experiencing hallucinations [34]. However, this does not account for delusions in the absence of anomalous experiences (i.e. delusional disorder and many organic delusions [9]).

New cognitive model

This paper proposes an alternative cognitive model to explain the aetiology of all delusions in all conditions. This innovative model hypothesises that delusions are the consequence of impaired perceptual abilities, visual and auditory, particularly affect perception. This results in the encoding of unusual ideas, which leads to the formation of idiosyncratic semantic memories, especially memories with an affective/self-referential valence. In deluded individuals there is continual confirmatory evidence for delusional ideas from anomalous perception, but also feedback from semantic memory that the belief concurs with previously held beliefs and past experiences. It is not within the scope of this paper to examine both aspects of this model. Thus, this current work will focus on the proposal that persons with delusions have abnormal semantic processing. Anomalous sensory processing and perception has been discussed in substantial detail in previous work [34, 47, 48].

In a review, McKenna [36] suggested that a natural link between abnormal semantics and psychopathology is the delusion; that is, they both involve aspects of meaning and belief, and the belief is equated with their knowledge-base. Delusions are commonly defined as abnormal beliefs, but could also be construed as statements and inferences based on a faulty knowledge-base or semantic system. All semantic memories are acquired, stored, and may be retrieved; if these processes were interfered with, or go unchecked, this could lead to erroneous semantic memories or false knowledge, i.e. delusions. Interestingly, impaired semantic processes have long been recognised as being central to cognitive deficits in patients with schizophrenia (e.g. [2, 10, 22, 35, 38, 44–46]). However, more recent data have established that a person’s store of knowledge—facts about the world, and the meanings of words—appears to be especially corrupt in schizophrenia patients with delusions [28, 41–43]. A semantic priming experiment showed reduced direct semantic priming but intact indirect priming in patients with prominent delusions, especially when the material had a negative valence [43]. Semantic fluency production was significantly reduced in schizophrenia, and especially so in those with delusions; the deluded patients showed more idiosyncratic word associations [42]. Finally, analysis of sentence verification errors demonstrated a bias in the deluded patients with schizophrenia to accept improbable sentences congruent with their delusional ideas [41]. The results of these three studies were interpreted as showing that the organisation of semantic information in schizophrenia patients with delusions is different from controls. In such individuals semantic information is shown to be idiosyncratically and illogically organised: some normal logical relationships between concepts are not present and some abnormal associations are present [42]; illustrated in the prototypical semantic network in Fig. 1. Thus, individuals with delusions are more prone to generating idiosyncratic, implausible ideas (the delusion) influenced by anomalous perceptions. As their semantic network is corrupt, the process of checking beliefs against information in their semantic network does not result in error detection, and is therefore accepted, in the same way...
as a plausible belief, and is also maintained. Data from this author is now confirming that it is indeed the store of information and ideas, and not the access of information that is the critical impairment [40].

Abnormalities in semantic processing have also been reported in individuals experiencing delusions more frequently associated with an organic origin, for example head trauma, dementia, or cerebral vascular disease. Edelstyn and Oyebode [15] have reviewed the Capgras Syndrome; the belief that a person, usually closely related to the patient, has been replaced by an impostor with a close resemblance to the original. They discuss how this delusion is postulated to result from a discrepancy between old stored representations, or semantic memories, and new information. Patients fail to update physical changes in their relatives, ending up with idiosyncratically stored information on these individuals. The cases they examined had mixed organic aetiology. Abe et al. [1] described a peculiar form of delusional misidentification due to Alzheimer’s disease. The patient misidentified her daughters as her sisters. The authors speculated that the misidentification was the failure to update semantic memory with new episodic and perceptual information. Finally, Feinberg et al. [16] reported a case of Fregoli delusion in a 61-year-old man after a TBI. The Fregoli delusion is the belief that a person, often a persecutor, has disguised themselves as someone known to the patient. In this case the patient misidentified 13 people around him in the hospital as family members or co-workers. This individual had marked loosening of

Four 

Fig. 1 A schematic diagram of the semantic network for the proposition ‘some food is poisonous’ in healthy and deluded individuals. Shown is a network of concepts permanently held in semantic memory relating to this proposition. Circled items are temporarily activated concepts and un-circled items are not activated upon activation of the proposition. Activation of the proposition occurs if it is heard or thought about. Temporary activation of particular concepts depends on the context of the proposition (in this example in the forest), and their frequency of use. → show accurately related concepts, ← show idiosyncratically related concepts. In healthy persons activation of the proposition may lead to other thoughts, i.e. ‘some mushrooms are poisonous/toxic, they may be harmful’ Deluded individuals have (1) less accurately related concepts available to them and (2) more idiosyncratic relations available. In all individuals some relations do not reach activation (i.e. food poisonous-allergy; mushroom-bedroom formed via clanging; food poisonous-venomous) as the context may not be appropriate or alternatively stronger relations may have been formed between other concepts (via frequency use) (i.e. food poisonous-clean; food poisonous-bedroom; food poisonous-snake).
Given that the previous literature has established a link between semantic processing deficits and delusion in schizophrenia, the current study sought to examine whether such deficits exist in individuals with delusions with an alternative aetiology. Thus, the current study examined four individuals with a significant delusion post a traumatic brain injury in comparison to a normative healthy control sample. It was expected that these individuals would show deficits across the range of semantic memory tasks, especially a marked loosening of/disordered associations within their semantic network, as previously shown in psychiatrically deluded individuals: for example, in deluded schizophrenia patients [41, 43]. This would serve as additional evidence for the model being proposed.

Materials and methods

Participants

Normative data

The control data consisted of 32 healthy controls from the general public. This sample was recruited for the study by advertisement in two local Sydney job centres. All participants tested were between the ages of 18 and 55 years and had an estimated pre-morbid IQ as scored by the National Adult Reading Test (NART) of ≥90 (see Table 1). No participant reported any psychiatric illness, confirmed by a current assessment using the Brief Psychiatric Rating Scale (BPRS [37]), a first-degree relative with a psychiatric illness, a neurological illness or a history of ECT.

Case studies background

Four cases with delusions post-traumatic brain injury were recruited from the South Western Sydney area. Prior to the TBI none of the cases had reported any history of psychiatric illness. In addition, no participant had any relative with a psychiatric illness. In each of the four cases described below psychopathology was rated using the Schedule of Negative Symptoms (SANS), and the Schedule of Positive Symptoms (SAPS) [3] (see Table 2). IQ in the four cases was determined by the NART.

Case one: ERL

ERL was a 56-year-old married woman, who worked for a bank prior to her accident. In 1995 she was involved in a car accident that resulted in a head injury. No specific lesion information was available but a right frontal pathology was implicated in case notes. During her hospital stay, she developed signs of paranoia, but returned to work 6 months after the accident, however, this was when the paranoia became prominent. The nature of ERL’s psychotic symptoms involved paranoia and delusional ideas that others were conspiring against her and her thoughts were being broadcasted. She had experienced a few episodes of auditory hallucinations. She had also experienced OCD concurrent with her paranoia, where her neurotic symptoms consisted of a cleanliness obsession and a compulsion to wash everything. ERL had a series of in and out patient admissions, and received pharmacological treatment. On the day of testing she was mildly paranoid.

Case two: DEN

DEN was a 23-year-old single male, who is the father of a young boy. He was Australian born but his family originated from Vietnam prior to his birth. He completed his schooling until age 16 and went on to complete fencing and concreting courses at Technical and Further Education College (TAFE), where he subsequently worked as a concrete labourer. In January 2000, DEN was involved in a motor vehicle accident that resulted in a head injury. A CT scan suggested a lesion within the left frontoparietal region. Since the brain injury, DEN developed the belief that he is dead and his penis has shrunk (a Koro delusion). His psychotic symptoms included hallucinations where he talks to people he believes are in his roof and paranoid delusions
where he believes that his accident was the result of a conspiracy involving his brother and sister, and believes that there is a woman in his head influencing his life. He had also become more aggressive since his accident and the onset of his delusions. DEN received pharmacological treatment for his pain and delusions. On the day of testing he had moderate to severe negative psychotic symptoms, including affective flattening, avolition, anhedonia, and poor attention. He was also experiencing a range of positive psychotic phenomena including very severe delusions, moderate bizarre behaviour, and mild thought disorder.

Case three: JL

JL was a 39-year-old single male. He completed his schooling until age 18 and went on to complete a 2-year Diploma in accountancy. JL worked as a bank teller before his accident. In January 1990, JL was hit by a car and sustained a right frontal haematoma, cerebro-spinal fluid leak, and lower fracture of the face and fracture of the hip. As a result of his injuries he lost his sense of smell. JL returned to work in late 1990 but began to develop psychotic symptoms approximately one year later where he developed concerns that he smelt. As a consequence, JL left the bank for an outdoor job to escape this problem. He had been diagnosed with bipolar disorder where he experiences periods of mania. The nature of JL’s psychotic symptoms included olfactory hallucinations where he felt that he emitted a “dead body” smell, somatic delusions that involve himself as “Mr Smell”, and thought disorder. His monothematic delusion of smell and decay was not mood-congruent, occurring independently of his mania. JL had received pharmacological treatment and commented that his psychotic symptoms were mostly under control; on the day of testing he was experiencing moderate thought disorder and mild bizarre behaviour.

Case four: BS

BS was a 30-year-old single male. BS moved to Australia from Fiji with his family at the age of 10 years. He and his family are Hindus. He completed his schooling until age 18 and then went on to study bookkeeping and office duties courses and worked as a train maintenance person for the Railways. The seven years leading up to his injury, BS worked full time in various positions in a bank and more recently in accounting. In May 2002, BS was involved in a motor vehicle accident that resulted in multiple trauma to his head (right temporal subarachnoid and subdural haemorrhage, and lacunar infarct) and body (damage to ribs, thorax, liver, and right brachial plexus), with residual memory and cognitive problems. Since his accident, BS had become excessively religious and attributed his survival to special magical powers due to his connection with God; he had experienced visual hallucinations of the God he prays to (Shiva) and had developed some beliefs in telepathic abilities. Subsequent to his head injury and delusions, BS experienced depression and some anxiety symptoms, such as obsessive checking, and was taking medication. On the day of testing he was experiencing mild delusions, thought disorder, and bizarre behaviour.

Cognitive tasks

The following tasks were approved by South Western Sydney Area Health Service ethics and were carried out in accordance with the latest version of the Declaration of Helsinki. Informed consent was obtained from them after the study procedures had been explained to the participants. The semantic task battery is described briefly below, more detail on each task can be found in Rossell and David [40].

(A) Synonyms

Using the stimuli from Psycholinguistic Assessment of Language Processing in Aphasia (PALPA [26]) task 49 we examined the participant’s ability to correctly identify synonyms. 60 word pairs (30 synonyms and 30 non-synonyms) of which 50% were high- and 50% were low-frequency, were randomly presented centrally on a computer screen. The first word in the pair was presented for 200 ms, there was a 550 ms blank screen followed by the second word for 200 ms. There was a blank screen between trials of 2,500 ms and the subjects were able to respond for up to 2,000 ms after the second word presentation. Participants were asked to indicate whether or not the pair was a synonym using a two-button press. Accuracy was recorded for high- and low-frequency conditions separately.

(B) Word associations

Using the stimuli from PALPA [26] task 51 we examined the subject’s ability to correctly identify word associations. 30 key words (15 high- and 15 low-frequency) were compared to 4 other words; one related, one semantic foil and two unrelated (Example: key word-fog, related-mist, semantic foil-steam and unrelated-bolt, and lock). This was a paper and pencil task with key words on the left-hand side of the page in bold followed by the four possible associates on the same line. The participant was asked to indicate, by underlining, which of the 4 other words were related/associated by meaning to the key word. Accuracy was recorded for high- and low-frequency conditions separately.
(C) Definitions

As much as 42 words, between 4 and 8 letters long were used (see [44]). They were taken from the MRC Oxford Psycholinguistic Database. From these words two task versions were created; generate and forced choice. Participants always performed generate first and then, after approximately 90 min, the forced choice. (1) Generate: after hearing and seeing each word, the participant was required to generate a definition, i.e. what each word meant. The participant’s performance was monitored for the first 5 words. If they were not completing the task correctly the instructions were repeated and an example of a correct definition was given. For each word the participant’s definition was compared against Oxford Concise English Dictionary entries, and was awarded between 2 and 0 points depending on its accuracy and completeness. When an answer scored 0 points it was further rated as one of 5 possibilities for an incorrect answer: (a) an association i.e. army–navy, (b) an opposite response i.e. shallow–deep, (c) no obvious sense in the definition i.e. dusk–not finished 1,000 years to go, (d) an incorrect answer, may be for an alternative spelling of the word i.e. lain = small narrow road, and finally, (e) missing or no response. Total accuracy as well as % of errors to each of the five categories above was recorded. (2) Forced choice: the same 42 words were presented with four definitions: two foils, one incorrect and one correct answer (for example, GREEN: foil1 = the colour between red and yellow; foil2 = the colour of the sun; incorrect = solid, firm or rigid material; and correct = the colour between blue and yellow). The foil answers were created using a thesaurus and finding definitions of similar words or concepts. The participants were required to indicate the correct definition. The % of correct, incorrect, and foil answers were recorded for each participant.

(D) Categories

We used a revised version of the category task reported in Chen et al [10]. 18 categories were selected from the norms of Battig and Montague [5] and Hampton and Gardiner [21], e.g. VEHICLES. For each category 5 different exemplar words were selected to provide different degrees of relatedness, resulting in 90 trials. These exemplar words were either: (1) high frequency (VEHICLE—bus), (2) low frequency (VEHICLE—ferry), (3) borderline (VEHICLE—ski), (4) related but outside the category (VEHICLE—horse), and (5) unrelated (VEHICLE—banker). Stimuli were presented in random order centrally on a computer screen. First, category names appeared in capital letters for 1,000 ms. After a delay of 550 ms exemplar words appeared in lower case for 200 ms followed by a 2,000 ms response window. After the exemplar word was shown, participants were asked to indicate whether it belonged to the category or not by pressing one of two buttons, YES or NO. For four of the categories there was clearly a single obviously correct answer, ‘YES’ for high frequency and low frequency, and ‘NO’ for the related and unrelated categories. This was not the case for the borderline condition where classification of category membership was supposed to be ambiguous. For simplicity when calculating accuracy ‘YES’ was taken as the correct answer. Accuracy for the five categories is reported.

(E) Pyramids and palm trees (PPT)

The PPT [23] is a test of semantic associative knowledge. The participants viewed 3 pictures, a prime and two targets. They were asked to indicate which of the targets was related to the prime. Accuracy was recorded.

(F) Fluency

Category fluency was examined using the category animals. Participants were asked to give as many category exemplars as they could over 60 s. The total number of words generated for the category was calculated minus errors (i.e. category inappropriate words) and perseverations.

Results

Data for the seven semantic memory tasks for the four case studies and the healthy control group are presented in Table 3. If the case study demonstrated deficient performance on any of the measures this was noted in terms of the number of standard deviations (SD) difference from the healthy control groups performance (* = 1SD ** = 2SD and *** = 3SD). A summary of performance of each case study is described below and the salient deficits are presented in Table 4.

Case studies

Case one: ERL

ERL demonstrated intact synonym performance. Alternatively, she produced less correct responses (2SDs) on the word association task to the low-frequency stimuli only. This was due to her greater selection of semantically related responses. She generated fewer definitions on the definition task (1SD from the norms). Of note within the definitions generate task is that ERL made more associative errors (two SD’s from the norm). Her performance on the definitions forced choice component was comparable to the
healthy controls. On the categories task ERL was able to correctly identify the categories to which words belonged. No impairment was shown on the pyramid and palm trees task. ERL produced fewer words on the category fluency task, 1SD below controls.

**Case two: DEN**

DEN showed deficits across all semantic tasks (the majority of his scores were more than three standard deviations from the healthy control group), with the

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**Table 3** Task data across the four cases and the control group

<table>
<thead>
<tr>
<th>Task</th>
<th>Condition</th>
<th>Variable</th>
<th>Controls N = 32</th>
<th>ERL</th>
<th>DEN</th>
<th>JL</th>
<th>BS</th>
</tr>
</thead>
<tbody>
<tr>
<td>(A) Synonyms</td>
<td>High freq</td>
<td>% Correct</td>
<td>94.2 (5.6)</td>
<td>93.3</td>
<td>70.0***</td>
<td>100.0</td>
<td>53.3***</td>
</tr>
<tr>
<td></td>
<td>Low freq</td>
<td>% Correct</td>
<td>88.2 (9.0)</td>
<td>86.7</td>
<td>30.0***</td>
<td>80.0</td>
<td>63.3***</td>
</tr>
<tr>
<td>(B) Word associations</td>
<td>High freq</td>
<td>% Correct</td>
<td>89.9 (7.1)</td>
<td>86.6</td>
<td>53.3***</td>
<td>86.6</td>
<td>60.0***</td>
</tr>
<tr>
<td></td>
<td>Low freq</td>
<td>% Correct</td>
<td>9.5 (7.1)</td>
<td>6.7</td>
<td>6.7</td>
<td>6.7</td>
<td>40.0***</td>
</tr>
<tr>
<td></td>
<td></td>
<td>% Semantic errors</td>
<td>9.6 (2.0)</td>
<td>6.7</td>
<td>33.3***</td>
<td>6.7</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>% Unrelated responses</td>
<td>0.6 (2.0)</td>
<td>6.7</td>
<td>33.3***</td>
<td>6.7</td>
<td>0.0</td>
</tr>
<tr>
<td>(C) Definitions</td>
<td>(1) Gen</td>
<td>% Correct</td>
<td>80.9 (23.8)</td>
<td>50*</td>
<td>18**</td>
<td>49*</td>
<td>39*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>% Associative errors</td>
<td>26.9 (12)</td>
<td>7.1</td>
<td>3.2</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>% Opposite errors</td>
<td>4 (6.8)</td>
<td>7.1</td>
<td>3.2</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>% Nonsense errors</td>
<td>6.9 (9.9)</td>
<td>7.1</td>
<td>38.7***</td>
<td>0.0</td>
<td>4.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>% Incorrect</td>
<td>38 (31.3)</td>
<td>7.1</td>
<td>3.2</td>
<td>9.1</td>
<td>4.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>% No response</td>
<td>20.8 (26.6)</td>
<td>21.4</td>
<td>12.9</td>
<td>9.1</td>
<td>42.8</td>
</tr>
<tr>
<td></td>
<td>(2) Forc</td>
<td>% Correct</td>
<td>61.5 (21.7)</td>
<td>92.9</td>
<td>64.3</td>
<td>88.1</td>
<td>59.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>% Incorrect</td>
<td>25.3 (19.9)</td>
<td>0.0</td>
<td>7.1</td>
<td>0.0</td>
<td>9.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>% Foils</td>
<td>13.2 (5.5)</td>
<td>4.8</td>
<td>28.6***</td>
<td>11.9</td>
<td>31.0***</td>
</tr>
<tr>
<td>(D) Categories</td>
<td></td>
<td>% Correct</td>
<td>78.7 (7.5)</td>
<td>84.4</td>
<td>70.0*</td>
<td>81.1</td>
<td>70.0*</td>
</tr>
<tr>
<td></td>
<td>High</td>
<td>% Correct</td>
<td>94.9 (5.2)</td>
<td>94.4</td>
<td>94.4</td>
<td>88.9*</td>
<td>94.4</td>
</tr>
<tr>
<td></td>
<td>Low</td>
<td>% Correct</td>
<td>86.4 (10.1)</td>
<td>77.7</td>
<td>72.2*</td>
<td>88.9</td>
<td>77.8</td>
</tr>
<tr>
<td></td>
<td>Borderline</td>
<td>% Correct</td>
<td>70.7 (6.6)</td>
<td>72.2</td>
<td>88.9</td>
<td>50.0***</td>
<td>83.3</td>
</tr>
<tr>
<td></td>
<td>Related</td>
<td>% Correct</td>
<td>72.7 (9.8)</td>
<td>88.9</td>
<td>33.3***</td>
<td>77.8</td>
<td>27.8***</td>
</tr>
<tr>
<td></td>
<td>Unrelated</td>
<td>% Correct</td>
<td>89.4 (7.2)</td>
<td>88.9</td>
<td>61.1***</td>
<td>100</td>
<td>61.1***</td>
</tr>
<tr>
<td>(E) Pyramid and palm trees</td>
<td></td>
<td>% Correct</td>
<td>92.3 (5.8)</td>
<td>90.4</td>
<td>94.2</td>
<td>90.4</td>
<td>94.2</td>
</tr>
<tr>
<td>(F) Category fluency</td>
<td></td>
<td>Animals Words produ</td>
<td>20.3 (5.1)</td>
<td>11*</td>
<td>12*</td>
<td>20</td>
<td>13*</td>
</tr>
</tbody>
</table>

> **Table 4** Summary of salient semantic deficits in the four case studies

<table>
<thead>
<tr>
<th>Task name</th>
<th>Task type (I vs. P)</th>
<th>ERL</th>
<th>DEN</th>
<th>JL</th>
<th>BS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Synonyms</td>
<td>I</td>
<td>✔</td>
<td>×</td>
<td>✔</td>
<td>×</td>
</tr>
<tr>
<td>Word association</td>
<td>I</td>
<td>✔</td>
<td>×</td>
<td>✔</td>
<td>×</td>
</tr>
<tr>
<td>Low-freq. correct</td>
<td>I</td>
<td>×</td>
<td>×</td>
<td>✔</td>
<td>×</td>
</tr>
<tr>
<td>Definitions</td>
<td>P</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
</tr>
<tr>
<td>Generate associativ</td>
<td>P</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
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<tr>
<td>Errors</td>
<td>P</td>
<td>×</td>
<td>×</td>
<td>×</td>
<td>×</td>
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<td>I</td>
<td>✔</td>
<td>×</td>
<td>✔</td>
<td>×</td>
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<tr>
<td>Forced choice</td>
<td>I</td>
<td>×</td>
<td>×</td>
<td>✔</td>
<td>×</td>
</tr>
<tr>
<td>Categories</td>
<td>P</td>
<td>×</td>
<td>×</td>
<td>✔</td>
<td>×</td>
</tr>
<tr>
<td>Total correct</td>
<td>I</td>
<td>✔</td>
<td>×</td>
<td>✔</td>
<td>×</td>
</tr>
<tr>
<td>Category fluency</td>
<td>P</td>
<td>×</td>
<td>×</td>
<td>✔</td>
<td>×</td>
</tr>
</tbody>
</table>

✔ intact, × impaired, I identification, P production

NB: × at least >1SD from norm
exception of the pyramid and palm trees task. Notable were his responses on the word association task; while his performance was poor to both high- and low-frequency words, his errors were confined to making unrelated responses and his semantic errors were comparable to the controls. Similar to ERL, DEN made a high number of associative errors when asked to define words (definitions generate task), and a high number of nonsense errors. The definitions forced choice component of this task reflected that DEN was distracted by foil definitions, and he was only able to identify word categories to high-frequency and borderline words on the category task. DEN produced fewer words on the category fluency task, 1SD below controls.

Case three: JL

JL had mostly intact semantic processing performance with some notable exceptions. He had poor definition generation, due to a large number of associative errors. Interestingly his performance on the definitions forced choice component was comparable to the norms. On the categories task his overall accuracy matched the norm data, however, he showed an unusual pattern of performance on the borderline condition, only selecting 50% yes responses in comparison to 70% in the healthy controls. JL had intact synonym recognition, word association recognition, category fluency, and pyramid and palm trees performance.

Case four: BS

Similar to DEN, BS showed deficits across all semantic tasks except for the pyramid and palm trees task. His performance too, was in general three SD’s from the norms. He demonstrated poor synonym and word association identification. BS made a large number of semantic errors when identifying word associations for high-frequency words, but a large number of unrelated responses when identifying low-frequency words. When attempting to generate word definitions his poor performance was split between making associative errors and no response, and similar to DEN, the forced choice component of this task reflected that BS was distracted by foil word definitions. BS again showed a pattern of performance similar to DEN when identifying word categories; he was only able to correctly categorise high-frequency and borderline words.

Results summary

All four cases showed impairments when asked to generate definitions for words. Furthermore, the errors made on the definitions generate task were predominantly errors of association. Three out of the four cases had poor category fluency. Conversely, all cases were able to identify which target was related to the prime on the pyramid and palm trees task. Cases two and four (DEN and BS, respectively) were unable to identify synonyms, word associations, forced choice definitions and word categories (see Table 4).

Discussion

Deficits in semantic processing were shown by all of our cases. These results support our proposal that individuals with delusions have abnormal semantic processing (some individuals were more extensively impaired than others i.e. DEN and BS versus JL and ERL; this will be discussed below), and is congruent with evidence of disordered semantic networks in deluded schizophrenia patients [41, 43], and one previous study of delusions post a traumatic brain injury [17]. As such, these cases provide additional evidence for the relationship between delusions and abnormal semantic processing, independent of aetiology.

An interesting behavioural pattern emerged during the analysis, that is, all cases were particularly impaired on tasks that required the individual to produce or generate semantic information (definitions generate and category fluency). Whereas the remainder of tasks, which required categorical identification were, overall, more successfully completed (by at least two of the four cases on any given task, see Table 4). Rossell has previously postulated that individuals with delusions have (i) idiosyncratically and illogically organised semantic information, where some typical logical relationships between concepts are present but some abnormal associations are also present [41] (see Fig. 1), and (ii) that these idiosyncrasies and abnormalities are represented by inaccurate storage of information and ideas rather than the access to this information [44]. In this study the existence of some typical logical associations or relationships between concepts may have been sufficient to generally allow the correct categorical identification of words when the correct response, acting as a prompt or memory cue, is offered amongst a group of alternatives. This would allow for supported performance on the synonyms, words association, definition forced choice, categories, and pyramids and palm trees tasks. However, when required to produce semantic information unaided, cues or alternative choices are not available. Thus, resulting in the inability of all cases to perform the definition generate task within normal ranges, and three out of four cases showing poor category fluency.

Another important behavioural pattern is with regard to the errors produced on the tasks. When the cases were asked to generate definitions their incorrect responses were
predominantly classified as ‘associative errors’. This is a further indication of the loose associative links inherent within an idiosyncratically organised semantic network (as previously shown in a deluded brain-injured patient [16]). Thus, deluded individuals have (i) less accurately related concepts available to them and (ii) more idiosyncratic relations available. For example, when asked to define the word ‘army’ an associated response would be ‘navy’, this illustrates that stronger relations may have been formed between these two concepts in the deluded individual than the association of ‘army’ with its correct definition ‘the military force of a nation’. We argue that these idiosyncratic associations are formed during the encoding of new information, although clearly this needs experimental testing. DEN additionally showed an increased rate of nonsense errors; again this can be used as evidence for a severe disruption in the semantic information held for the concepts tested on this task. Significantly, the errors produced by the four cases are very different from the healthy controls. The healthy controls had the greatest percentage of incorrect responses, that is, defining a word with a similar spelling. Idiosyncratic semantic organisation may also explain the increased rate of ‘foil’ responses on the definitions forced choice task, especially in DEN and BS. That is, the cases had some general understanding of the concept but were not able to be specific. Although this study did not directly test the access-store dichotomy, that is, whether semantic memory is abnormal because of impaired storage versus impaired access, the pattern of findings, especially the pattern of errors, suggests that the deficits in semantic processing are due to the manner in which semantic information is stored and not with the access and retrieval of semantic information [see 40].

Importantly, increased associative errors and reduced incorrect errors on the definitions generate task, replicates the response pattern previously shown in patients with schizophrenia [44]. Further, reduced category fluency has been reported in schizophrenia, particularly in patients with delusions who produce more idiosyncratic word associations on this task [41]. In this study, some of the responses recorded for category fluency task were idiosyncratic, for example; one of DEN’s responses was ‘alpaca’, while JL named both an Indonesian elephant and an African elephant, as well as a sloth. ‘Teddy bear’ was generated in amongst the responses by BS, which is a further example of loose and uniquely organised semantic networks. Together this data provides evidence for the proposal that abnormal and idiosyncratic organisation of the semantic network is a common feature in individuals with delusions, irrespective of diagnosis and phenomenology.

Ceiling performance on the pyramid and palm trees task by all our cases is postulated to be the consequence of the simple requirements of this task, which are to indicate a semantic match, and also the simple nature of the stimuli, common pictures. Thus, this task was unable to tap into the uncued semantic processes we are arguing to be impaired.

Word frequency influenced task performance for both the cases and healthy controls; high-frequency words were generally correctly identified at higher rates than low-frequency words (synonyms, word associations, and categories tasks). The ‘commonality’ of words has been shown to promote more expedient encoding [7, 44]. On two occasions however, a higher rate of correct responses were shown to the low-frequency words relative to the high; BS and DEN on the synonyms and word association tasks, respectively. This reverse pattern is predicted to reflect subtle differences specific to the semantic organisation of these two individual cases.

Lesion location and severity may have also influenced semantic memory performance. Three patients had a frontal pathology; ERL, DEN, and JL. The two patients with some intact semantic abilities both had a right frontal lesion. BS had a temporal lobe pathology. Interestingly, DEN and BS had more extensive injuries that ERL and JL. Further group studies are needed to confirm the role of brain region on delusions and semantic processing. Interestingly, recent MRI studies have implicated both temporal and frontal involvement in delusion formation [30].

Limitations

The cases DEN and BS warrant closer inspection. Both revealed greater deficits across all tasks relative to the other two case studies, commonly scoring more than three standard deviations below the norm. Both experienced multi-themed delusions; DEN was identified with four delusional themes and BS with three, which was more than the other two cases that had one or two delusional themes. This is further evidence for the proposal that individuals with multiple delusional themes have more severe semantic memory abnormalities, shown previously in schizophrenia patients with delusions [44]. Interestingly, both of these cases also had delusions congruent with their cultural identities. However, low pre-morbid IQ estimates were obtained for these cases, which is a limitation of these findings, as low IQ would have impinged on language and reading abilities necessary for the tasks. Importantly, the other two cases had IQs within the normal range and still exhibited semantic processing problems. Pre-morbid IQ would need to be matched in any further investigations to elucidate and remove its effect on semantic memory performance.

There are a number of limitations to this research that should be mentioned. Due to time restrictions we were unable to assess other neuropsychological abilities. Thus, it
is not known whether the patients also showed similar attention, executive function and other memory difficulties; and whether these other neuropsychological abilities were related to psychotic psychopathology. However, previous research in delusion formation in schizophrenia suggests that finding such a relationship between these other neuropsychological abilities and delusions is unlikely, and was not the rationale for completing this project. Further, the cases did exhibit other positive symptoms of psychosis, for example thought disorder and hallucinations. Hallucinations have not been linked to a semantic processing pathology but some authors (but not all) argue that semantic processing is involved in thought disorder. However, in all four cases the predominant psychotic symptom was delusions, with thought disorder being mild. Future studies may also benefit from comparing TBI psychosis patients with TBI patients with no history of psychosis. These patient groups will need to be closely matched for lesion location and extent.

Conclusions

We have shown atypical semantic processing in deluded individuals who have sustained a TBI. Importantly, the pattern of semantic performance recorded by our cases is consistent with schizophrenia patients with delusions, although in some cases they did not show such global semantic processing impairments. Taken together, we consider this as preliminary evidence for consistent abnormal semantic processing in persons with delusions, irrespective of diagnosis and phenomenology. This finding will need to be verified in larger sample groups of persons with delusional beliefs across a range of diagnoses, and matched for pre-morbid IQ. Group-based studies will allow for correlational analysis with other positive symptoms to examine whether semantic processing abnormalities are unique to delusions. The new distinction shown between the production and identification of semantic information warrants further investigation, and the extent of anomalous affect perception in deluded individuals needs to be determined before this new cognitive model of delusions can be confirmed.

References

20. Garety PA, Hemsley DR, Wessely S (1991) Reasoning in deluded individuals who have sustained a TBI. Importantly, the pattern of semantic performance recorded by our cases is consistent with schizophrenia patients with delusions, although in some cases they did not show such global semantic processing impairments. Taken together, we consider this as preliminary evidence for consistent abnormal semantic processing in persons with delusions, irrespective of diagnosis and phenomenology. This finding will need to be verified in larger sample groups of persons with delusional beliefs across a range of diagnoses, and matched for pre-morbid IQ. Group-based studies will allow for correlational analysis with other positive symptoms to examine whether semantic processing abnormalities are unique to delusions. The new distinction shown between the production and identification of semantic information warrants further investigation, and the extent of anomalous affect perception in deluded individuals needs to be determined before this new cognitive model of delusions can be confirmed.

References


Elucidating semantic disorganisation from a word comprehension task: Do patients with schizophrenia and bipolar disorder show differential processing of nouns, verbs and adjectives?

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Abstract

Memory deficits have been reported in schizophrenia and bipolar disorder. However, the precise impact of semantic memory deficits on word comprehension, particularly across grammatical categories, has not been adequately investigated in these disorders. Furthermore, previous studies examining semantic memory have predominantly been designed so that most healthy controls perform at ceiling, questioning the validity of observed differences between patient and control groups. A new word definition task examined word comprehension across grammatical categories, i.e. nouns, verbs and adjectives, and was designed to overcome the ceiling effect. It was administered to 32 schizophrenia patients, 28 bipolar disorder patients and 32 matched healthy controls. Schizophrenia patients had a global impairment on the task but bipolar patients were only impaired on a recognition memory component. Word comprehension, however, across grammatical categories was comparable across groups.

Keywords: Schizophrenia; Bipolar disorder; Word comprehension; Semantic disorganisation

1. Introduction

Semantic memory refers to an individual’s stored knowledge. It is impersonal and includes knowledge of words and their meanings, knowledge of objects and their interrelationships, and general knowledge about the world. Abnormalities in semantic memory are commonly proposed to be central to cognitive abnormalities in schizophrenia, with deficits being reported on a wide variety of tasks, for example, categorisation (Rossell and David, 2006), fluency (Rossell et al., 1999) and priming (Rossell et al., 2000). Semantic deficits are, consequently, predicted to underlie disturbances in thought and language in schizophrenia, which might not only explain the deficits observed in other cognitive domains (i.e. reasoning), but also provide a cognitive explanation for common symptoms in schizophrenia, for example, delusions, thought disorder and alogia. While memory deficits in bipolar disorder are also reported, the impact of semantic memory deficits in bipolar has not
been adequately investigated (Bearden et al., 2006; Rossell, 2006).

Additionally, many previous studies of semantic memory in schizophrenia have used semantic assessments where healthy controls perform at ceiling, as the measures used were designed for assessing neuropsychological deficits in obvious brain disease. When measures have been designed to specifically examine deficits in schizophrenia interesting qualitative differences have been reported (for example in Rossell et al., 1998). Thus, to address our current hypotheses a new word definition task was developed which prevented controls performing at ceiling.

Investigators have been interested in the organisation of words in semantic networks, with both neuropsychological and functional neuroimaging studies advocating the differentiation of grammatical-class in the brain’s neural networks (e.g. Bedny and Thompson-Schill, 2006); that is, differences in the processing of verbs, nouns and adjectives.Crudely, it is argued that verbs and nouns differ semantically, with nouns equated to objects, which correspond to objects stored in semantic memory, whilst verbs reflect actions. It might, therefore, be predicted that deficits in schizophrenia may be restricted to words that consist of a greater number of semantic features, that is, nouns. Currently there are three studies that have examined grammatical-class differences in schizophrenia. Two have shown impaired verb generation (Marvel et al., 2004; Woods et al., 2007), and the third poorer performance in the generation of both common nouns and verbs (Elvavag et al., 2001). No study has explored word comprehension effects in bipolar disorder.

Thus, while the present research is not the first to examine grammar-based word effects in schizophrenia, it is the first study to consider performance differences across grammatical categories in two patient groups, schizophrenia and bipolar disorder, when compared to healthy controls. We are also examining the comprehension of adjectives, which has remained largely uninvestigated. Two word comprehension tasks were developed; generate, in which participants had to generate a definition of the presented word, and forced choice, where they needed to select the correct definition from four possible choices. We hypothesized that schizophrenia patients would show reduced word comprehension accuracy, on both generate and forced choice tasks, particularly to nouns.

2. Method

2.1. Participants

Two patient samples were recruited from the inpatient and outpatient departments of Liverpool Hospital, Sydney and via the NISAD research register (National Institute for Schizophrenia and Allied Disorders). 32 patients were diagnosed as DSM IV schizophrenia and 28 as DSM IV bipolar disorder using the Diagnostic Interview for Psychosis (Castle et al., 2005). 32 healthy controls were recruited by advertisement in two Sydney job centers. Exclusion criteria for all groups were a history of traumatic brain injury, epilepsy, alcohol or substance abuse, neurological or co-existing psychiatric conditions including depression as screened for using the Beck Depression Inventory (Beck et al., 1961), and administration of ECT. All participants were between the ages of 18 and 55 years and had an estimated pre-morbid IQ as scored by the National Adult Reading Test (NART; Nelson, 1981) of >90 (Table 1). There were no significant group differences in age or education. There was, however, a difference in IQ as scored by the NART (Nelson, 1981). The bipolar and control groups were matched on NART IQ, and were different from the schizophrenia patients. There were more males in the control and schizophrenia samples, and more females in the bipolar sample.

Current psychopathology was rated using the Schedule of Negative Symptoms (SANS), the Schedule of Positive Symptoms (SAPS) (Andreasen and Olsen, 1982), and the Bech–Rafaelsen Mania Scale (Bech et al., 1979) (Table 1). The two patient groups were matched on their five global SAPS scores; in contrast, the schizophrenia patients demonstrated greater affective flattening and anhedonia on the SANS. The bipolar sample was currently manic1. There was no significant difference in the age of onset or number of years experiencing illness between the two patient samples. Schizophrenia patients were on the following medication: 21 atypical antipsychotics and 11 neuroleptics. Bipolar patients were taking the following: 18 mood stabilisers and 10 atypical antipsychotics.

2.2. Definition task

120 words, between 4 and 8 letters long were used2. They were nouns, verbs and adjectives and were taken from the MRC Oxford Psycholinguistic Database. The words were divided into two frequency bands using Kucera and Francis (1967): low frequency words (1–30 words per million) and high frequency words (>30 words per million). The words were counterbalanced between 6 word conditions: low frequency nouns, high frequency

1 There were no correlations between the definition task variables and mania as scored by the Bech-Rafaelsen. Thus, there was no need to co-vary for current status of mania.

2 Partial task results were reported in Rossell and David (2006). The current manuscript reports on all definition task results.
nouns, low frequency verbs, high frequency verbs, low frequency adjectives, and high frequency adjectives. The six conditions were carefully matched for length, concreteness, imageability, neighbours and number of syllables (the task can be downloaded from www.srossell.com). Two task conditions were created (1) Generate (2) Forced choice. Generate was always performed first. After a delay of 90 min, in which participants were administered other cognitive tasks, the forced choice component was completed. In both conditions the 120 words were presented in one of 3 random orders (counterbalanced across subjects).

2.2.1. Generate
The experimenter read each word and the participant was then required to generate a definition of each word, i.e. what they thought the word meant. The score sheet was placed on the table so the participant could see the spelling of each word. The participants’ performance was monitored for the first 5 words, if they were not completing the task correctly the instructions were repeated and an example was given of a correct definition. These definitions were then compared to Oxford Concise English Dictionary entries, and each answer was awarded between 2 and 0 points depending on its accuracy and completeness. Accuracy or the mean % correct was calculated for each of the 6 conditions (correct was defined as 2 points for a fully correct answer and 1 point for a partially correct answer). Further, when an answer scored 0 points it was rated as one of 5 possibilities for an error: (1) an association i.e. army — navy, (2) an opposite error i.e. shallow — deep, (3) a nonsense error i.e. dusk — cooking, (4) an incorrect answer, may be for an alternative spelling i.e. lain=small narrow road, and lastly, (5) missing or no response. The scoring scheme was first pilot tested to ensure inter-rater (accuracy $r=0.86$, inter-error $r=0.82$) and intra-rater (accuracy $r=0.89$, intra-error $r=0.88$) reliability. The mean % of errors for the 5 categories of errors is reported.

2.2.2. Forced choice
All the words were presented with accompanying definitions. The definitions were created using the Oxford Concise English Dictionary. Two foil answers, one incorrect answer and one correct answer were allocated to each word. The foil answers were created using a thesaurus and finding definitions for similar words. Participants were required to indicate which definition they thought best fit the word. Accuracy (i.e. mean % correct) was calculated for each of the six word conditions.

3. Results
A repeated measures ANOVA with three groups (controls, schizophrenia and bipolar), two task conditions (generate, forced choice), three word types (nouns, verbs and adjectives) and two frequencies (high and low) was performed with the accuracy data (covarying for NART IQ) (see Table 2). There were main effects for group [$F(2,89)=13.4$ $p<.001$], the controls (81%) were more accurate than the schizophrenia (61%) and bipolar

### Table 1
Demographic and symptom characteristics (mean (SD)) of the three participant groups

<table>
<thead>
<tr>
<th></th>
<th>Controls $N=32$</th>
<th>Schizophrenia $N=32$</th>
<th>Bipolar $N=28$</th>
<th>Group comparisons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/female</td>
<td>21/11</td>
<td>20/12</td>
<td>8/20</td>
<td>Chi=9.1 $p=0.007$</td>
</tr>
<tr>
<td>Age</td>
<td>36.6 (12.3)</td>
<td>36.4 (10.3)</td>
<td>38.8 (11.0)</td>
<td>NS</td>
</tr>
<tr>
<td>No. of years education</td>
<td>13.8 (2.2)</td>
<td>13.4 (2.6)</td>
<td>13.9 (2.6)</td>
<td>NS</td>
</tr>
<tr>
<td>NART</td>
<td>115 (10.9)</td>
<td>107 (13.4)</td>
<td>117 (10.6)</td>
<td>$F=6.1$ $p=0.003$ S &amp; B/C</td>
</tr>
<tr>
<td>Age of onset</td>
<td>-</td>
<td>22.8 (5.9)</td>
<td>22.6 (7.8)</td>
<td>NS</td>
</tr>
<tr>
<td>No. of years ill</td>
<td>-</td>
<td>13.6 (8.9)</td>
<td>16.3 (11.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Bech–Rafaelsen mania rating</td>
<td>-</td>
<td>0.3 (1.2)</td>
<td>17.0 (8.4)</td>
<td>$F=90$ $p&lt;.001$</td>
</tr>
<tr>
<td>SANS</td>
<td>-</td>
<td>1.25 (1.2)</td>
<td>0.50 (1.3)</td>
<td>$F=5.5$ $p&lt;.02$</td>
</tr>
<tr>
<td>Alogia</td>
<td>-</td>
<td>0.78 (1.2)</td>
<td>0.25 (0.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Avolition</td>
<td>-</td>
<td>1.69 (1.7)</td>
<td>1.00 (1.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Anhedonia</td>
<td>-</td>
<td>2.25 (1.6)</td>
<td>0.96 (1.5)</td>
<td>$F=10.2$ $p&lt;.002$</td>
</tr>
<tr>
<td>Attention</td>
<td>-</td>
<td>0.34 (1.0)</td>
<td>0.11 (0.6)</td>
<td>NS</td>
</tr>
<tr>
<td>SAPS</td>
<td>-</td>
<td>1.75 (1.8)</td>
<td>1.36 (1.9)</td>
<td>NS</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>-</td>
<td>2.50 (1.8)</td>
<td>2.50 (1.9)</td>
<td>NS</td>
</tr>
<tr>
<td>Delusions</td>
<td>-</td>
<td>0.97 (1.3)</td>
<td>1.36 (1.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Bizarre behaviour</td>
<td>-</td>
<td>1.66 (1.5)</td>
<td>1.86 (1.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Thought disorder</td>
<td>-</td>
<td>0.34 (1.0)</td>
<td>0.61 (1.3)</td>
<td>NS</td>
</tr>
</tbody>
</table>

S & B/C=Student Newman Keuls post-hoc test established schizophrenia patients significantly different from bipolar patients and controls. NS=Non-significant.
patients (69%); task condition \([F(1,89)=64.2 \ p<.001]\), with lower accuracy for generate (63%) than forced choice (79%); word type \([F(2,89)=13.4 \ p<.001]\), the accuracy to nouns (69%) and verbs (70%) was similar, and less than, adjectives (72%); last, frequency \([F(1,89)=23.5 \ p<.001]\), with greater accuracy for high (72%) compared to low (69%) frequency words. There was an interaction between group and task condition \([F(2,89)=3.1 \ p<.05]\). Schizophrenia patients showed the greatest difference in accuracy between generate and forced choice, whilst controls and bipolar patients showed a similar performance difference (schizophrenia generate=50%, forced choice=73%, difference=23%; controls generate=74%, forced choice=88%, difference=14%; and bipolar generate=64%, forced choice=75%, difference=11%). Thus, generate resulted in a prominent reduction in accuracy for schizophrenia patients only. Interestingly, both patient groups showed reduced performance on the forced choice condition. There was also an interaction between word type and frequency \([F(2,89)=5.1 \ p<.01]\); the frequency of word use had the most impact on task accuracy for the nouns, then the adjectives and verbs (noun high=72% low=67%; adjective high=74% low=71%; verb high=70% low=69%).

For the generate task a 3×5 repeated measures ANOVA with three groups (controls, schizophrenia and bipolar) and five error types (associative, opposite, nonsense, incorrect and no response) was performed using the % of each error type data and covarying for NART IQ (NART IQ=113) (see Table 3). There was a main effect for error type \([F(1,88)=4.6 \ p<.04]\), with more associative errors produced overall than the other four error types (associative=36%, opposite=5%, nonsense=9%, incorrect=30% and no response=20%). There was also an interaction between group and error type \([F(2,88)=4.7 \ p<.01]\). Controls were most likely to give an incorrect error, whilst both the patient groups were more likely to produce an associative error. Type of errors did not correlate with symptoms as

Table 2
% mean (SD) accuracy scores for the 6 word conditions across groups

<table>
<thead>
<tr>
<th></th>
<th>Controls N=32</th>
<th>Schizophrenia N=32</th>
<th>Bipolar N=28</th>
<th>F p SNK post-hoc</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Generate component</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High nouns</td>
<td>75.5 (21.4)</td>
<td>50.8 (22.5)</td>
<td>64.1 (28.3)</td>
<td>8.5 (p&lt;.001) C &amp; B&gt;S</td>
</tr>
<tr>
<td>Low nouns</td>
<td>70.4 (17.1)</td>
<td>45.8 (18.8)</td>
<td>62.4 (24.9)</td>
<td>12.2 (p&lt;.001) C &amp; B&gt;S</td>
</tr>
<tr>
<td>High verbs</td>
<td>74.9 (22.8)</td>
<td>49.1 (24.3)</td>
<td>63.1 (28.4)</td>
<td>8.5 (p&lt;.001) C &amp; B&gt;S</td>
</tr>
<tr>
<td>Low verbs</td>
<td>73.2 (18.3)</td>
<td>49.8 (20.9)</td>
<td>62.3 (27.7)</td>
<td>8.7 (p&lt;.001) C &amp; B&gt;S</td>
</tr>
<tr>
<td>High adjectives</td>
<td>75.2 (19.4)</td>
<td>52.2 (24.0)</td>
<td>66.2 (28.3)</td>
<td>7.5 (p&lt;.001) C &amp; B&gt;S</td>
</tr>
<tr>
<td>Low adjectives</td>
<td>75.6 (18.4)</td>
<td>50.3 (23.7)</td>
<td>64.2 (30.7)</td>
<td>8.6 (p&lt;.001) C &amp; B&gt;S</td>
</tr>
<tr>
<td>Total</td>
<td>74.1 (17.8)</td>
<td>49.7 (20.4)</td>
<td>63.7 (27.0)</td>
<td>10.1 (p&lt;.001) C &amp; B&gt;S</td>
</tr>
<tr>
<td><strong>Forced choice component</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High nouns</td>
<td>91.4 (8.4)</td>
<td>75.3 (17.7)</td>
<td>73.9 (21.7)</td>
<td>10.6 (p&lt;.001) C&gt;S &amp; B</td>
</tr>
<tr>
<td>Low nouns</td>
<td>83.8 (6.8)</td>
<td>69.1 (19.9)</td>
<td>70.9 (16.6)</td>
<td>8.5 (p&lt;.001) C&gt;S &amp; B</td>
</tr>
<tr>
<td>High verbs</td>
<td>86.9 (6.9)</td>
<td>74.5 (14.3)</td>
<td>72.5 (20.4)</td>
<td>8.7 (p&lt;.001) C&amp;S &amp; B</td>
</tr>
<tr>
<td>Low verbs</td>
<td>87.5 (9.5)</td>
<td>68.3 (17.3)</td>
<td>75.4 (17.8)</td>
<td>12.9 (p&lt;.001) C&gt;S &amp; B</td>
</tr>
<tr>
<td>High adjectives</td>
<td>91.3 (7.5)</td>
<td>77.5 (18.9)</td>
<td>80.7 (16.0)</td>
<td>7.4 (p&lt;.001) C&gt;S &amp; B</td>
</tr>
<tr>
<td>Low adjectives</td>
<td>87.3 (10.4)</td>
<td>71.3 (20.0)</td>
<td>76.9 (20.2)</td>
<td>7.1 (p&lt;.001) C&amp;S &amp; B</td>
</tr>
<tr>
<td>Total</td>
<td>88.0 (5.6)</td>
<td>72.7 (16.0)</td>
<td>75.1 (17.0)</td>
<td>11.6 (p&lt;.001) C&gt;S &amp; B</td>
</tr>
</tbody>
</table>

C=Controls, B=Bipolar, S=Schizophrenia SNK=Student Newman Keuls post-hoc test.

Table 3
Error classification: the % of errors (SD) to each error type for the generate component

<table>
<thead>
<tr>
<th>Error</th>
<th>Controls N=32</th>
<th>Schizophrenia N=32</th>
<th>Bipolar N=28</th>
<th>F p SNK post-hoc</th>
</tr>
</thead>
<tbody>
<tr>
<td>% associative errors</td>
<td>28.8 (29.5)</td>
<td>38.4 (15.6)</td>
<td>42.2 (23.8)</td>
<td>2.9 (p&lt;.05) C&lt;S&amp;B</td>
</tr>
<tr>
<td>% opposite errors</td>
<td>3.4 (4.9)</td>
<td>5.2 (7.6)</td>
<td>5.4 (7.9)</td>
<td>NS</td>
</tr>
<tr>
<td>% nonsense errors</td>
<td>8.5 (10.1)</td>
<td>9.7 (10.5)</td>
<td>7.7 (8.3)</td>
<td>NS</td>
</tr>
<tr>
<td>% incorrect</td>
<td>42.1 (31.2)</td>
<td>24.8 (12.2)</td>
<td>22.6 (25.2)</td>
<td>6.1 (p=.003) C&gt;S&amp;B</td>
</tr>
<tr>
<td>% no response</td>
<td>17.3 (23.9)</td>
<td>21.9 (20.5)</td>
<td>21.9 (22.9)</td>
<td>NS</td>
</tr>
</tbody>
</table>

C/<S & B=Student Newman Keuls post-hoc test established control patients significantly different from schizophrenia and bipolar patients. NS=Non-significant.
scored by the SAPS. Although, there were non-significant trends towards correlation between thought disorder and ‘associative’ errors in both patient groups ($p=0.09$).

4. Discussion

In comparison to healthy controls the definition task revealed semantic processing deficits in both patient groups. In general, patients were poorer at providing an accurate definition of single words and at selecting the correct definition from a list of alternatives. These findings are complimentary to other papers that have shown word comprehension impairments in schizophrenia, as illustrated by impaired verb generation (Marvel et al., 2004; Woods et al., 2007), and verb and noun generation (Elvavag et al., 2001). There was, however, an interesting interaction between diagnosis and task condition; whereby, the schizophrenia patients showed a greater deficit on the generate condition compared to the forced choice; but the bipolar patients were relatively intact on the generate condition, whilst as impaired as the schizophrenia patients at the forced choice. The overall pattern of findings could be interpreted as reflecting a shortfall in both patients groups’ ability to organise and categorise word meanings, which would accordingly impact on their ability to distinguish the correct word meaning in the presence of alternatives, especially when some of those alternatives are very closely related in meaning. Not only would this notion be supported by previous research on categorisation and word associations (Rossell and David, 2006) in schizophrenia, but it would further explain the prominence of ‘associative’ errors demonstrated by the two patient groups on the generate task. This interpretation, however, does not explain why the patient groups differed on the generate condition. It could be generate is more reliant on intact memory, and therefore, represents a more difficult task only for patients with schizophrenia. This suggests that greater “free-recall” memory retrieval deficits are present in schizophrenia than in bipolar disorder. Alternatively, our data suggests that bipolar patients are able to compensate for memory retrieval deficits on certain tasks. The bipolar patients provided longer responses on the generate condition (representative of pressure of speech), thus increasing the likelihood of obtaining a correct, or partially correct, answer (the bipolar group produced an average of 20 words (SD=8) for each definition compared to 8 (SD=6) by schizophrenia patients). Finally, one could argue that the generate condition has a stronger executive component, which is more likely to be impaired in schizophrenia. In agreement with this speculation is data from a letter fluency task, a standard executive function task. Schizophrenia patients showed reduced performance on this measure compared with the other groups, and also demonstrated a significant correlation between generate performance and letter fluency ($r=0.5$ $p=0.004$).

Symptoms were well-matched across the two patients groups, except for mania, which was not correlated with task performance. Further, even though one might have predicted that thought disorder would have interacted with the task, especially with regard to producing ‘associative’ errors, there were only non-significant trends towards correlation between thought disorder and ‘associative’ errors in the patient groups. Interestingly, there was no interaction between word type and diagnosis, suggesting that neither patient group differs from healthy controls in the processing of different grammatical-category word types. Thus, all groups were better at defining the meaning of adjectives when compared to nouns and verbs. Therefore, the semantic deficits in the patient groups were not at a grammar-based categorical level. This finding is complimentary to Elvavag et al. (2001), who did not record any differences in grammatical-category processing in schizophrenia. We are the first to have reported this finding in bipolar disorder.

Word frequency influenced overall comprehension accuracy as predicted. Our findings indicate that this effect is mediated by grammatical-category, but again is not differentiated by the presence of psychosis. Specifically, the most accurate word comprehension was illustrated for high frequency words, primarily in nouns, then adjectives, and then verbs. This finding is similar to results obtained by Brebion et al. (2005), who suggested that during word comprehension patient groups take advantage of the ‘commonality’ of a word to the same degree as healthy controls; namely, high frequency words foster more expedient encoding.

As the task was not designed for the neuropsychologically impaired no individual from any of the three groups performed at ceiling. One possible limitation, however, was the time required for administration (generate=30–40 min and forced choice=20 min). As a result some participants, particularly patients, became restless. To resolve this problem an equally reliable 42-item version has been developed (see www.srossell.com).

In conclusion, the data illustrates that semantic processing deficits in psychosis are not demonstrated at a grammar-based categorical level; that is, schizophrenia and bipolar patients did not show differential processing of nouns, verbs and adjectives, compared to healthy controls. The interaction between task condition and diagnosis may be indicative of organisation and
categorization deficits in schizophrenia. The comparative performance of controls and bipolar patients on the generate task may also illustrate that bipolar patients are able to compensate for some of their memory retrieval deficits. Finally, the new word definition task was successful in preventing controls from performing at ceiling, and was thus a useful task for differentiating between patients and controls.

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Contributors
SLR designed the study and performed clinical interviews and cognitive assessments. RB undertook the statistical analysis and prepared the first draft. All authors contributed and approved the final manuscript.

Conflict of interest
The authors declare no conflict of interest.

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