SCHIZOPHRENIA AND HEMISPHERIC BRAIN FUNCTIONING:

A neuropsychological case study of a monozygotic twin case

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ABSTRACT

Schizophrenia is a debilitating mental illness which is complex and multifactorial in nature. Currently a full understanding of the exact aetiological and treatment pathways is yet to be understood, with effective treatment of the debilitating and pervasive negative symptoms particularly lacking. However recent advances in neurophysiological and neuropsychological research seem to be converging on theories of the central role of lateralised functional systems. These models implicate right hemispheric hyperactivation in negative symptom patterns, while positive symptoms are thought to be associated with left frontal hypoactivation resulting in compensatory left temporal hyperactivation.

Through the use of the Cognitive Neuropsychological case study methodology, this research took an inductive and exploratory approach to a unique case of 41 year old monozygotic twins concordant for schizophrenia and discordant for a right frontal cerebrovascular accident (CVA). From various records the CVA seemingly had a positive effect on the affected-twin's negative symptoms.

By means of a selected battery of neuropsychological tests this research focused on patterns of test performance for known functional systems and identified neuropsychological correlates of the CVA and the negative symptom improvement. Statistically significant differences were found between the twins, particularly in the right medial and ventral prefrontal areas. These areas, with their projections to the limbic system and other sub-cortical structures, were highlighted as being important to these differences. From these findings working hypotheses regarding specific lobal structures, relating to existing theories and research in schizophrenia, were posited for future research.

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Declaration of Originality:

The author hereby declares that this dissertation, unless specifically indicated to the contrary in the text, is her own original work.

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CHAPTER 1

INTRODUCTION

Schizophrenia is a debilitating mental illness which affects up to 1.5 % of the population (APA, 2000; Sawa & Snyder, 2002). Like many mental illnesses it has been argued that schizophrenia is multifactorial in nature with biological, genetic and environmental contributions playing a role in the expression of the symptoms (Sawa & Snyder, 2002; Tsuang & Faraone, 2002). However a full understanding of the exact aetiological and treatment pathways in schizophrenia is yet to be achieved, with various differing symptom expressions making unified classification, aetiological and treatment models problematic (Higashima et al., 2005). Literature highlights the importance of linking such models in an attempt to improve not only the understanding of the various symptoms of the disorder, but also for the development and improvement of increasingly effective treatment strategies (Carpenter & Buchanan, 1994; Higashima et al., 2005; Tsuang & Faraone, 2002; Sadock & Sadock, 2000).

Dating back to early conceptions of schizophrenia there has been a proliferation of research in the area, with many studies specifically focusing on the aetiology of the disorder (Coffey, 1998; Higashima et al., 2005; Meehl, 1962; Sadock & Sadock, 2000; Savage, Jackson & Sourathathone, 2003; Stratta, Donda, Rossi & Rossi, 2005). Much of this research has focused on identifying a range of neurobiological abnormalities as major contributing factors to the symptoms (Lewis, 2003; Sadock & Sadock, 2000; Sawa & Snyder, 2002; Stratta et al., 2005). Additionally, further research into environmental and biopsychosocial models have contributed to the broadening of various aetiological models to include environmental, social and intra-personal factors (Tsuang & Faraone, 2002). Despite a growing understanding of the disorder's

structures - especially frontal and temporal systems (Barnett et al., 2005; Blanchard & Neale, 1994; Davidson, 1998, 2001; Moller, 2003).

More specifically, research implicates the dysfiinction (hyperactivation) of the right frontal and limbic systems with the negative symptoms, while left frontal hypoactivation is hypothesised to play an auxiliary role in these symptoms (Barnett et al., 2005; Blanchard & Neale, 1994; Davidson, 1998; 2001; Moller, 2003). The positive symptoms are hypothesised to arise from left frontal dysfunction (hypoactivation), which leads to compensatory left temporal hyperactivation resulting in hallucinations and delusions (Barnett et al., 2005; Blanchard & Neale, 1994).

There was no truly efficacious treatment for schizophrenia until the early 1950's when the benefits of chlorpromazine were discovered (Sadock & Sadock, 2000; Sawa & Snyder, 2002). Despite current research gains into the description and aetiology of schizophrenia, these common treatments remain fairly unchanged since their early inception in the world of psychiatry. Chlorpromazine, as with it's 21^{SI} century counterparts, often has a sedating effect and ameliorates many of the positive symptoms of the disorder (despite working mechanisms remaining unclear), but fails to have substantial effects on the negative symptoms of schizophrenia (Olie, 2006; Sawa & Snyder, 2002). Treatment of the more pervasive negative symptoms remains largely under-researched and less successful (Carpenter, Conley & Kirkpatrick, 2000; Kalat, 1998; Moller, 2003; Olie, 2006; Rector, Beck & Stolar, 2005; Roth, Flashman, Saykin, McAllister & Vidaver, 2004; Silver, 2003).

There is a prospect that research into specific brain systems may yield a new understanding of the disorder, and new aetiological models. As more is known about lateralisation of functions and the contributions of left and right hemispheres to behaviour, these new ideas may lead to

working hypotheses which may help with research into negative and positive symptom patterns, and perhaps offer a way of bridging the gap between aetiology and treatment. This may in turn increase the possibility of finding improved alternative treatment options for schizophrenia, and specifically for the pervasive and often debilitating negative symptoms (MoHer, 2003; Roth et al., 2004; Tsuang & Faraone, 2002).

This research focuses on the case study of 41-year-old monozygotic twins, Abbey and Gail (pseudonyms), who are concordant for schizophrenia (currently Residual subtype, with early onset) and discordant for a right hemisphere frontal anterior (premotor and prefrontal area) cerebral arterial dissection cerebrovascular accident (CVA) which affected only Gail (CVA)[1]. The CVA occurred four years prior to the research. From clinical interview, psychiatric records and collateral information the CVA has seemingly had a differential effect on the negative symptoms of the affected twin Gail (CVA). From psychiatric and collateral observation Gail's (CVA) negative symptoms seem to be decreased in comparison to her pre-morbid pre-CVA state, with currently increased motivation, pleasure seeking, positive affect and seeking of social contact and support. Abbey's symptoms remain largely unchanged and stable.

While this study clearly was not able to use traditional quantitative methodology with randomised design and large statistical power (Howell, 2002), it sought to make use of a rather unique opportunity to use the methods of Cognitive Neuropsychology to study and explore the effects of right hemisphere CVA in schizophrenia in monozygotic twins. While the clinical methods of Cognitive Neuropsychology are to some extent inductive, the discipline has a long tradition of studying the effects of lesions, and has made a unique, and indispensable

[1] Note for ease of reading only, and is not intended to be a label in any way

contribution to our understanding of brain-behaviour relationships (Shallice, Burgess & Frith, 1991; Shallice, 1988; Yin & Campbell, 2003).

Considering the uniqueness of monozygotic twins not only concordant for schizophrenia but additionally discordant for a right hemisphere CVA, this seemed to be a unique and potentially valuable opportunity for an in-depth neuropsychological exploration of changes in the participants' symptom expression and functional status which might be associated with the CVA. Potentially such changes might have importance for an understanding of the role of different hemispheres and functional regions in schizophrenia (Yin & Campbell, 2003).

This research therefore aims to compare the functioning of the twins by means of a selected battery of neuropsychological tests, with a particular interest-focus on tests which are understood to be sensitive to patterns of lateralised brain damage. Further there is a specific interest in trying to relate patterns of test performance with known functional brain systems, and to try to identify neuropsychological correlates of:

1. The right hemisphere CVA in Gail.
2. The improvement in negative symptoms in Gail (CVA).

The primary aim of this research is to generate working hypotheses which relate to existing theories and research in schizophrenia, and which may have implications for future research.

CHAPTER TWO

REVIEW OF THE LITERATURE

This literature review attempts to expand on some of the controversies and difficulties referred to in the Introduction. Because of the complexity, and the vast number of interrelationships between the contributing variables to the aetiology of schizophrenia, the selection of material and organisation of this review was difficult. This review has not sought to survey all schizophrenia research, but rather is a select review of literature relevant to its particular focus. However due to the scarcity of literature concerning schizophrenia and twin studies with CVA (highlighting the unique nature of this research) this literature review covers relevant literature divided into various sections. The review consists of sections which deal with the following topics:

1. A brief overview of the disorder of schizophrenia and the various classification systems used to described it.
2. An examination of various aetiological models of schizophrenia.
3. The nature and neuropsychological implications of CVA, focusing on the CVA-type experienced by Gail (CVA).
4. An examination of the changes in functioning of the various brain structures and hemispheres implicated in neurophysiological aetiological models.
5. An exploration of the implications of schizophrenia from neuropsychological and neuroscience viewpoints.
6. Current neuroscientific theories, pf affect and their potential implications for schizophrenia.

7. Schizophrenia, neuropsychological findings of lateralised brain systems and twin study contributions.

2.1 An exploration of the disorder of schizophrenia

Schizophrenia was first described by Emile Kraepelin in 1896 as 'dementia praecox', and was later given the name of'schizophrenia' by Eugene Bleuler in 1911 (Coffey, 1998). Broadly, the psychiatric disorder of schizophrenia is considered specifically a disorder of human functions, affecting much of the functioning which makes human interaction unique from that of other mammals (Beebe, 2003; Bradshaw & Mattingley, 1995; Coffey, 1998). In schizophrenia social interaction and information processing are disturbed, the individual's personality 'fragments' with a loss of reality, hallucinations (abnormal perceptions), delusions (fixed false beliefs), incoherent thought, disordered memory and confusion (Anderson, 1994; Bradshaw & Mattingley, 1995; Coffey, 1998).

Since its initial description by Kraepelin schizophrenia has been classified and described largely by psychiatrists (Coffey, 1998). Despite conflicts, various classification systems for the disorder have been offered. The two main texts currently used in clinical settings are the Diagnostic and Statistical Manual of Mental Disorders-IV-Text Revised (DSM-IV-TR) and the International Classification of Diseases-10 (ICD-10) (APA, 2000; Coffey, 1998). The ICD-10 describes schizophrenia as a syndrome with a variety of causes, and outcomes dependent on a balance of genetic, physical, social and cultural factors (Coffey, 1998). The ICD-10 describes the subtypes of schizophrenia as being paranoid, hebephrenic, catatonic, undifferentiated, and residual (Coffey, 1998).

The DSM-1V-TR (APA, 2000) defines schizophrenia as a psychotic disorder which may be characterised by the presence of two or more of the following symptoms: positive symptoms include delusions; hallucinations; disorganised speech; disorganised or catatonic behaviour; and negative symptoms characterised by a 'decrease' in functioning and behaviour (which may include alogia; avolition; anhedonia and affective flattening). These symptoms have a duration dimension and should be present for a significant portion of time during a 1-month period with some signs of the disorder persisting for at least 6 months, and should cause some social or occupational disturbance to the individual (APA, 2000).

Depending on the symptoms mentioned above, individuals with schizophrenia may be diagnosed into one of a number of subtypes (APA, 2000). The types recognised are: Paranoid type (characterised by paranoid preoccupations, delusions or auditory hallucinations); Disorganised type (characterised by disorganised speech and behaviours and flat or inappropriate affect); Catatonic type (characterised by excessive, decreased or peculiar motor activity); Undifferentiated type (where the criteria for the symptoms are met but the criteria for any of the other specific subtypes are not) or Residual type (where there is a continued disturbance in the absence of prominent positive symptoms) (APA, 2000). Blanchard, Horan and Collins (2005) posit that a profile of negative symptoms and cognitive decline, with largely absent positive symptoms, is clear for individuals with Residual schizophrenia.

The usual age of onset for schizophrenia is mid-20's for males and early-30's for females however, symptoms may commence anywhere between 8 and 60 years of age (APA, 2000; Bradshaw & Mattingley, 1995; Coffey, 1998).

Despite the wide use of the above mentioned classification systems Bradshaw and Mattingley (1995) and Tsuang and Faraone (2002) point out that schizophrenia is a complex and heterogeneous disorder which shows multiple and variable symptoms which cannot always be neatly differentiated and packaged within the diagnostic process. As such, alternative views of symptom clustering to define the syndrome of schizophrenia, along various different continua, have emerged. These alternative classification theories are outlined below.

Crow (1985), posits that individuals with schizophrenia could be described as belonging to one of two basic groups according to their differing symptomatology, namely those with predominantly type I schizophrenia and those with predominantly type II schizophrenia (Crow, 1985; Rotenberg, 1994). Individuals affected predominantly by type I symptoms of schizophrenia experience mostly 'positive' symptoms (such as delusions; hallucinations and disorganised speech and/or behaviour), are thought to respond well to neuroleptic intervention, and are hypothesised to have an increased number of dopamine receptor sites (Crow, 1985). Those affected by type II symptoms experience mostly the 'negative' symptoms mentioned above, are thought to have a poorer response to neuroleptic intervention, and are hypothesised to have increased cell loss and structural changes in the brain, particularly in the frontal regions (Crow, 1985; Rotenberg, 1994).

Another classification system, by Carpenter and Buchanan (1994), builds on Crow's (1985) theory by dividing the psychopathology of schizophrenia into three relatively independent clusters of symptoms. These clusters are namely positive psychotic symptoms (hallucinations and delusions) similar to Crow's (1985) type I classification; negative symptoms (including diminished affect and social drives, poverty of speech and anergia) similar to Crow's (1985)

type II classification; and a cognitive impairment cluster (including tangentiality of thought, memory difficulties, various cognitive deficits, loss of goals, incoherence and loosening of associations) (Carpenter & Buchanan, 1994). This system considers the cognitive dimension of schizophrenia often not considered in other systems, despite cognitive deficits becoming increasingly accepted as a remarkably robust characteristic of the diagnosis in the last decade (Heinrichs, 2005; Lewis, 2003). Additionally, a distinct cognitive profile of individuals with schizophrenia has emerged lending further support to this classification system (Lewis, 2003).

Lastly Tsuang and Faraone's (2002) dimensional model of schizophrenia posits that vulnerability to schizophrenia can occur in low, moderate or high risk degrees. These risk degrees put individuals at risk for developing schizophrenia symptoms along a continuum. These symptoms range from schizotypal personality traits, negative symptoms or neuropsychological impairment to positive symptoms and are collectively termed 'schizotaxia' (Meehl, 1962). Meehl (1962) defined schizotaxia as the unexpressed genetic predisposition to schizophrenia. This indicates that symptoms are the manifestation of a neuro-biological predisposition to the development of such symptoms (Tsuang & Faraone, 2002). Unlike the current commonly used diagnostic models, the dimensional model of schizophrenia is most consistent with biopsychosocial aetiological models of multigene inheritance, neuro-physiology and familial transmission combined with various environmental factors (Tsuang & Faraone, 2002).

Consistent with psychological practice within South Africa the DSM-1V-TR diagnostic criteria were used for the classification and diagnosis of the participants in this research. However, one cannot ignore the various dimensional and cluster approaches to the classification and diagnosis of schizophrenia when considering various aetiological models of the disorder. These models more fully integrate issues of description, classification, diagnosis, aetiology and treatment

(Tsuang & Faraone, 2002). Additionally, these various alternative models highlight the complexity and heterogeneity inherent to the disorder of schizophrenia which is now becoming more widely discussed in the literature.

2.2 Aetiological models of schizophrenia

In recent years, with ever proliferating aetiological research, there have been many advances in the knowledge of the causal factors at play in the disorder of schizophrenia. While no single causative agent has been identified, broad clusters of causal factors have been divided into three main aetiological models, namely biological models (including genetic factors); environmental models (including intra- and inter-personal interactions); and biopsychosocial models (Beebe, 2003; Coffey, 1998; Tsuang & Faraone, 2002). As yet, no one theory seems to have been successful in explaining the totality of the disorder which is schizophrenia (Beebe, 2003; Sadock & Sadock, 2000). Given the nature of the research presented here, with its aetiological and treatment focus as well as its selected methodology, an exploration of biological, non-interpersonal environmental and biopsychosocial models were considered pertinent.

2.2.1 Biological models

Schizophrenia has been linked to a range of neurobiological abnormalities throughout the brain including neuro-chemical dysregulation, and neuro-anatomical and functional neuronal changes (Beebe, 2003; Blanchard & Neale, 1994; Sawa & Snyder, 2002). However, there has been contradicting research regarding the precise nature of these changes, and the specific roles of the left and right hemispheres and various lobes in the symptoms of schizophrenia (Beebe, 2003; Blanchard & Neale, 1994; Kalat, 1998; Rector et al., 2005; Sadock & Sadock, 2000).

2.2.1.1 Neuro-chemical models

Many different neuro-chemicals have been well-researched for their implications in the aetiology of schizophrenia, some more successfully than others. A well researcher neurotransmitter model, named the Dopamine Hypothesis (originally posited by Carlson and Linqvist, no date, cited in Sadock & Sadock, 2000) is a neuro-chemical hypothesis which holds that the symptoms of schizophrenia are due to a specific dopamine imbalance, namely an excess of dopamine or dopamine receptors in the brain (Carfagno, Hoskins, Pinto, Yeh & Raffa, 2000; Kolb & Whishaw, 2003; Sadock & Sadock, 2000). Dopamine is a neurotransmitter found in the basal ganglia, the limbic system, prefrontal areas and temporal lobes of the brain (Beebe, 2003; Kalat, 1998; Kolb & Whishaw, 2003). It is hypothesised that the dopamine pathways in the mesolimbic and mesocortical regions have been disrupted in individuals with schizophrenia, with excessive dopamine receptor activity resulting in hallucinations and delusions (Beebe, 2003; Kalat, 1998). Additionally, this neuro-chemical hypothesis posits genetic causative factors in serotonin and dopamine receptor gene malformations (Beebe, 2003; Coffey, 1998). However, the Dopamine hypothesis model has been criticised for its lack of explanation and understanding of the role of negative symptoms of schizophrenia, the lack of causal mechanism knowledge (after administering dopamine-blockers the positive symptoms still take a number of weeks to subside) as well as its lack of widespread applicability within the population of individuals with schizophrenia (Beebe, 2003; Carfagno et al., 2000).

Although the importance of dopamine for prefrontal cognitive functioning is widely recognised the nature of the dopamine interactions in this area remains controversial (Tseng & O'Donnell, 2004). Research has expanded on the dopamine hypothesis to look at the complexity of this

neurotransmitters interactions in the brain. A critical component in dopamine action is in its modulation of glutamate transmission (an excitatory neurotransmitter) which plays an essential role in prefrontal cortical control of executive functions and goal-directed behaviour (Kolb & Whishaw, 2003; Tseng & O'Donnell, 2004). This hypothesis is named the Dopamine-Glutamate hypothesis, and posits that dopamine-glutamate co-activation (resulting in an imbalance between dopamine neurons and glutamate neurons) leads to disruptions in executive functioning, working memory and attention through abnormal co-ordination of pyramidal neuron firing and changes in amygdala inhibition (Kolb & Whishaw, 2003; Tseng & O'Donnell, 2004). Despite this theory having a large basis of support in animal studies, it lacks empirical support in humans, especially in individuals with schizophrenia (Lezak, 2004).

2.2.1.2 Neuro-anatomical models

Although much of the previous research in this area consisted of autopsy research, modern technology has enabled detailed research with living participants. Over many years research into neuro-anatomical abnormalities in individuals with schizophrenia has revealed three main areas of cerebral anatomical abnormalities (Beebe, 2003; Kalat, 1998; Sawa & Snyder, 2002). These are decreased overall brain volume, specific cortical neuronal degeneration and ventricular enlargement (Beebe, 2003; Kalat, 1998; Roth et al., 2004; Van Haren et al., 2004). Firstly, broadly in brain volume findings the brains of individuals with schizophrenia have been found to be an average of 6 percent lighter than brains of other patients with mental illnesses (Beebe, 2003; Kalat, 1998; Sadock & Sadock, 2000). Secondly neuronal degeneration has been found in the cerebral cortex, particularly the frontal area, as well as in the amygdala and hippocampus (Kalat, 1998; Roth et al., 2004; Sadock & Sadock, 2000). Lastly enlargement of ventricles has

been consistently found in the brains of individuals with schizophrenia (Kalat, 1998; Sadock & Sadock, 2000).

These changes have been investigated by Computerised Tomography (CT) and Magnetic Resonance Imaging (MRI) with scans confirming that roughly one-third of all individuals diagnosed with schizophrenia exhibit some cerebral atrophy (Bradshaw & Mattingley, 1995; Roth et al., 2004; Sawa & Snyder, 2002). More specifically, consistent widening of the lateral ventricles or the cortical sulci (or both), especially in the amygdala (frontal) and hippocampal (temporal) areas has been discovered (Bradshaw & Mattingley, 1995; Roth et al., 2004). Frontal atrophy has been reported from anterior dorsolateral (where 'intentionality' is mediated), orbitofrontal (with its involvement in social behaviours), and cingulate regions as well as involvement in the supplementary motor area (Bradshaw & Mattingley, 1995; Heinrichs, 2005; Lezak, 2004). Additionally, Bradshaw and Mattingley (1995) point out that cerebral atrophy is likely to extend well beyond the frontal lobes and may involve a cortico-cortical re-entrant loop via the striatum, pallidum and thalamus (as well as other sub-cortical structures).

Hemispheric asymmetry has been noted in neuro-anatomical studies (Bradshaw & Mattingley, 1995; Heinrichs, 2005; Lezak, 2004). A pattern of diffuse mild cerebral atrophy seems to be more common in those individuals with schizophrenia who have predominantly negative symptoms (Bradshaw & Mattingley, 1995; Rector et al., 2005). Recent research indicates that a large percentage of individuals with predominantly positive symptoms have reduced left frontal lobe brain volumes (Heinrichs, 2005). This frontal cerebral atrophy resulting in dysfunction has been linked to the positive symptoms of schizophrenia as the inferior and medial prefrontal regions have connections to the auditory and visual regions in the temporal lobe, as well as the amygdala (Bradshaw & Mattingley, 1995; Sawa & Snyder, 2002). Damage to these areas is

hypothesised to give rise to compensatory functioning in the temporal regions, causing hallucinations and delusions (Bradshaw & Mattingley, 1995).

2.2.1.3 Neuro-functional models

Early functional assessment of neural blood flow with methods like the xenon inhalation technique were superseded in the 1990's by methods such as Positron Emission Tomography (PET) and functional MRI (fMRl) enabling high definition and harmless neuro-functioning research (Heinrichs, 2005). Research has found overall decreases in brain metabolism in those individuals with schizophrenia (Beebe, 2003; Kalat, 1998; Roth et al., 2004). Specifically, decreased metabolic function in the frontal and temporal areas has been found (Beebe, 2003; Heinrichs, 2005; Kalat, 1998). Additionally, fMRI scans have shown altered brain functioning in the amgydala areas in individuals with schizophrenia (Beebe, 2003). These functional findings may be reciprocal as Davidson (2001) points out that PET findings have indicated that glucose metabolism in the left medial and lateral prefrontal cortex is reciprocally associated with glucose metabolic rates in the amygdala. These dysfunctions in the frontal and amygdala regions have been linked to both positive and negative symptoms (Kalat, 1998).

The causal basis of the neuro-chemical, neuro-anatomical and neuro-functional changes outlined above has yet to be discovered, however, various neurodevelopmental hypotheses have been developed to explain these neuro-specific changes. Coffey (1998) highlights research examining these neurobiological abnormalities as a result of brain changes during adolescence. Such theories hypothesise that the 'synaptic pruning' which occurs during adolescence may go beyond its normal developmental limits in those individuals with a vulnerability to the development of schizophrenia (Coffey, 1998; Lewis, 2003). However, the lack of gliosis

(scarring) in many of these atrophied areas points to early foetal neuro-developmental as opposed to later damage (Bradshaw & Mattingley, 1995; Coffey, 1998).

Other theories link both neurobiological as well as genetic theories and suggest that abnormal neuro-anatomy is a result of genetically linked vulnerability during the gestation period resulting in foetal neuro-developmental anomalies (Coffey, 1998; Sawa & Snyder, 2002). This early neuro-developmental damage highlights the convergence of genetic predispositions, neuro-anatomical changes and neuro-chemical alterations or dysfunctions (Sawa & Snyder, 2002). Additionally, twin studies further highlight the likelihood of early foetal neuro-developmental damage (Segalowitz, 1999; Van Haren et al., 2004).

Meta-analysis of large volumes of neuro-chemical, neuro-anatomical and neuro-functional research data, ranging from autopsy to MRI and fMRI, to PET and cerebrospinal fluid volume (CSF) research, has revealed some consistencies in the literature (Beebe, 2003). The literature has consistently identified frontal and temporal lobe anatomical and metabolic anomalies in a significant number of individuals with schizophrenia (Beebe, 2003; Bradshaw & Mattingley, 1995; Lewis, 2003; Sadock & Sadock, 2000). However, the exact brain locality or laterality of the symptoms, as well as structural interactions with neuro-chemicals, have yet to be identified (Beebe, 2003; Kalat, 1998). This lack of clarity around exact brain structures, neuro-chemistry and metabolic functioning which contribute to the symptoms of schizophrenia may be related to the diffuse nature of the expression of schizophrenia, which in itself may point to multiple brain structure and functional implications (Lewis, 2003; Sadock & Sadock, 2000; Tsuang & Faraone, 2002).

2.2.2 Environmental models

The environmental factor of birth season (winter and early spring births with viral influenza in the third trimester) has been linked to the development of schizophrenia (Bradshaw & Mattingley, 1995; Coffey, 1998). It is hypothesised that exposure to seasonal viral or toxic agents during gestation may play a role in increasing an individual's risk for the development of schizophrenia (Beebe, 2003; Coffey, 1998). These theories link to other neurobiological theories which suggest a role for early neuro-developmental anomalies (Bradshaw & Mattingley, 1995). However, there has yet to be conclusive research linking environmental or toxic agent exposure in early foetal development to the later expression of symptoms of schizophrenia (Lewis, 2003).

2.2.3 Biopsychosocial models

There has been a range of theories focusing on an integrated aetiology of schizophrenia. Zubin and Steinhauer's (1981) 'Vulnerability model' of schizophrenia moved beyond unidimensional aetiological models and integrated several paradigms, namely genetic and neuro-physiological, environmental, learning theory and internal environment in an attempt to understand the complexities of the disorder. The vulnerability model posits that symptoms of schizophrenia are produced by complex interactions among biological, environmental, psychological, and cultural factors (Beebe, 2003). This model provides a structural framework for articulating the interaction among physiological, psychological, and environmental factors that, taken together, are posited to act to produce the symptoms of schizophrenia (Beebe, 2003; Zubin & Steinhauer, 1981). Zubin and Steinhauer's (1981) model describes the onset of an episode of schizophrenia as being the product of the interaction between vulnerability markers (being developmental factors, biological factors and social factors) and trigger events (endogenous or exogenous

events). This interaction could be affected by moderating variables such as social networks, coping style and personality which may act as protectants from the onset of an episode (Zubin & Steinhauer, 1981).

Building on the vulnerability model hypothesis Rabkin (1982), Hultman and Ohmna (1998) and Ishiguro, Okuyama, Toru and Arinami (2000) posit that biological vulnerability is a precondition for the appearance of the symptoms of schizophrenia, however, the appearance of the symptoms, and the form they may take, may be mediated by the various other social, environmental and developmental factors. These vulnerability models of multiple causal aetiologies leading to the expression of various symptoms of schizophrenia relate closely to Tsuang and Faraone's (2002) classification model of schizotaxia. As such, biopsychosocial models may offer the unique ability to capture the complexity of the disorder.

Additionally, biopsychosocial aetiological models are based upon more than neurobiological and environmental factors alone (as posited by other models), and take into account an individual's wider social and developmental context. These factors seem essential not only to the unpacking and exploring of the nature and course of schizophrenia but also in the linking of the aetiological models of schizophrenia to various classification and diagnostic as well as treatment models.

2.3 Cerebrovascular accidents and neuropsychological implications

CVA's may cause a disruption or alteration to the metabolism or blood supply to neurons in various areas of the brain (Lezak, 2004). If the disruption approaches a duration of 10 minutes or longer, cell death is likely to occur (Bradshaw & Mattingley, 1995; Kolb & Whishaw, 2003).

The 2 most common CVA-types are thrombotic (clotting) and haemorrhagic (bleeding) CVA (Kolb & Whishaw, 2003).

Individuals over the age of 55 years have a higher risk of CVA, and of those individuals affected by CVA only 3 - 4 percent are under the age of 45 years (Cohen, 2000; Robinson, 1998). However, arterial dissection, resulting in cerebral haemorrhage, occurs in 6 - 22 percent of the individuals in this age group (Cohen, 2000). In this under 45 year age group arterial dissection occurs most commonly in the frontal or temporal internal carotid arteries, as well as arterial or ventral cerebral arteries (Cohen, 2000; Robinson, 1998).

Arterial dissection is caused by a lesion in a cerebral artery causing the penetration of blood into the arterial wall, which in turn forms an intramural hematoma or pooling of blood, leading to cerebral haemorrhage as the arterial wall is broken by the pressure (Cohen, 2000; Robinson, 1998). This event is related to decreased blood flow to surrounding areas (ischaemia), increased intracranial pressure and neurological cell infarct (Cohen, 2000; Lezak, 2004; Robinson, 1998). Risk factors for cerebral haemorrhage include hypertension, congenital cerebral artery defect, arterial dissection (acute or chronic), blood disorders, and neuro-toxins (Kolb & Whishaw, 2003).

Symptoms of acute or chronic arterial dissection vary between individuals, however, some commonalities are noted (Cohen, 2000). Individuals may experience CVA-sided homolateral headaches, changes in intracranial pressure, contralateral hemiparesis and hemiplegia, aphasia, memory loss and visual field deficits (Cohen, 2000; Kolb & Whishaw, 2003; Robinson, 1998). More specifically, right hemisphere CVA's may produce neuropsychological difficulties including left sided hemiparesis or hemiplegia; memory loss (both short-term and long-term);

spatial and Gestalt deficits, related constructional deficits, cognitive deficits, altered range or expression of emotion and an increased chance of becoming significantly depressed (Davidson, 2001; Lezak, 2004).

2.4 Exploration of hemispheric and lobal functioning and dysfunction

Despite some lack of specificity the research outlined earlier consistently identifies frontal and temporal lobe abnormalities, as well as overall asymmetrical hemispheric contributions to the symptoms of schizophrenia (Beebe, 2003; Bradshaw & Mattingley, 1995; Lewis, 2003; Mo Her, 2003; Roth et al., 2004; Sadock & Sadock, 2000). A further exploration of the roles of these lobes, and hemispheric functioning in healthy and schizophrenia or lesion-affected brains, is therefore necessary.

The frontal lobes are generally asymmetrical in functioning with the left-frontal lobe having a preferential role in language-related movements and the right playing a greater role in other movements such as facial expression (Kolb & Whishaw, 2003). Additionally, Lezak (2004) outlines the links between the right-frontal lobe and the limbic system, specifically the amgydala, which aids in the setting of emotional tone. These differing functions have important contributions to the symptoms of schizophrenia, with the left-frontal areas consistently implicated in the positive symptoms and the right-frontal implicated in the negative symptoms (Bradshaw & Mattingley, 1995; Chan, 2004).

The frontal lobes comprise all of the tissue in front of the central sulcus and are divided into three general regions namely the motor, premotor and prefrontal regions (Kolb & Whishaw, 2003). The motor region provides a mechanism for the execution of individual movements,

while the premotor cortex functions as a selector of the movements to be executed, essentially choosing behaviour in response to external cues (Kolb & Whishaw, 2003). While the motor cortex makes movements and the premotor cortex selects movements, the prefrontal cortex controls cognition processes so that the appropriate movements are selected at the correct time and in the correct place (Kolb & Whishaw, 2003; Lezak, 2004). This relates to temporal memory processes (the neural record of recent events) which aids humans in control of behaviour through internal knowledge rather than behaviour based solely on external environmental cues (Lezak, 2004). Damage to these areas has been related to movement disturbances including movement planning and inhibition of behaviour in relation to environmental cues (Kolb & Whishaw, 2003). Additionally, frontal lobe dysfunction has been related to decreases in intellectual performance, particularly in divergent thinking abilities (Lezak, 2004). All of these deficits have been linked to individuals with schizophrenia (Chan, 2004).

The prefrontal region in particular, which has been significantly linked to symptoms of schizophrenia, can be further broken down into three distinct sub-areas, namely the dorsolateral prefrontal area (connected to the posterior parietal areas, superior temporal sulcus and basal ganglia, and where intentionality is mediated), the ventral prefrontal area (connected to the superior temporal gyrus, somatosensory cortex and the amgydala, and where social behaviours and perception are mediated) and the medial prefrontal area (connected to the tegmentum and related to affective mediation) (Kolb & Whishaw, 2003; Lezak, 2004). Prefrontal dysfunction has been related to decreased behavioural spontaneity (including speech, verbal fluency and facial expression), an increase in behavioural inflexibility, self-regulation dysinhibition and a loss of ability to formulate strategies for problem solving (Kolb & Whishaw, 2003; Lezak, 2004). Due to their affective and social response importance neuro-anatomical research has highlighted

both the medial and ventral prefrontal areas as significant for explaining the symptoms of schizophrenia (Beebe, 2003; Chan, 2004).

The left temporal lobe commonly implicated in individuals with schizophrenia, are primarily concerned with auditory functioning but also contain limited components of the visual system (Lezak, 2004). The interaction between the temporal lobes and the limbic system (specifically the amygdala and hippocampus) aids in the addition of affective tone to sensory input and memories (Kolb & Whishaw, 2003; Lezak, 2004). Temporal lobe dysfunction has been linked to comprehension difficulties and impairments in the interpretation of facial expressions and non-literal meanings (Kolb & Whishaw, 2003; Lezak, 2004). The temporal lobe has been implicated in the positive symptoms of schizophrenia, especially auditory and visual hallucinations (Beebe, 2003; Bradshaw & Mattingley, 1995).

The right hemisphere is more diffusely organised than the left and Lezak (2004) describes its overall functioning in the processing of information which is not easily verbalised, including social cues, and spatial and tactile information. This information is processed in a gestalt manner (the processing of many elements in a single stage as a configural whole) (Lezak, 2004).

Right hemisphere dysfunctions result in deficits ranging from illogical thought and facial misinterpretations to difficulty in dealing with complex verbal and social patterns, common to individuals with schizophrenia (Beebe, 2003; Chan, 2004; Rotenberg, 1994). Broader cognitive deficits may include poor planning and visuospatial orientation, visual memory deficits as well as poor abstract concept formation or gestalt problem solving (Lezak, 2004; Rotenberg, 1994). Emotional and personality changes may occur with right hemisphere dysfunction and could possibly include an increased range and intonation (rhythm) of affect which may at times be

inappropriate, additionally, dysinhibition is a common effect of right hemispheric lesion (Lezak, 2004).

2.5 The neuropsychology of schizophrenia: Views from neuropsychology and neuroscience

Given the predominance of biological aetiological models, both neuropsychology and the neurosciences are commonly used methodologies to investigate aetiological models of schizophrenia (Chan, 2004). Neuropsychological studies suggest that there are wide scale deficits seen in individuals with schizophrenia (Bradshaw & Mattingley, 1999; Chan, 2004; Chan, Chen, Cheung, Chen & Cheung, 2004; Kolb & Whishaw, 2003; Lewis, 2003; Roth et al., 2004).

Cognitive performance, understood to be complex and dynamic, is dependent on the integrity of the brain systems which mediate information processing, with integrity compromise leading to significant difficulties (Heinrichs, 2005). Sixty one to 78 percent of individuals with schizophrenia exhibit largely stable cognitive deficits manifesting as below normal neuropsychological test scores on all tests of cognitive functions (Chan et al., 2004; Lewis, 2003). This assertion has been supported by both monozygotic and dizygotic twin studies (Heinrichs, 2005; Lewis, 2003; Van Haren et al., 2004).

Research describes a particular profile of cognitive deficits in individuals with schizophrenia (Lewis, 2003). This profile manifests as borderline to low average full-scale IQ scores and specific deficits in attention and sustained attention, memory (global), perception and visuo-motor abilities and executive functioning (including abstract reasoning, problem solving, planning and initiating, sequencing and cognitive set-shifting ability) (Bradshaw & Mattingley,

1999; Chan, 2004; Chan et al., 2004; Heinrichs, 2005; Kolb & Whishaw, 2003; Lewis, 2003; Lezak, 2004; Roth et al., 2004). In standardised assessments of executive functioning, individuals with schizophrenia showed significantly more rule-breaking, rigidity, impulsivity and longer execution time than non-schizophrenic controls (Chan et al., 2004). Additionally, problematic goal-formulation as well as poverty of action were significantly increased in individuals with schizophrenia (Chan, 2004).

Lewis (2003) notes as a caveat that transient severe cognitive impairment is common in acute psychotic states, resulting from the level of the disorganisation of thought processes in these states. However, research indicates that a chronic diagnosis of schizophrenia, with or without large periods of the active phase of positive symptoms, results in a consistent cognitive impairment across this population (Chan, 2004; Chan et al., 2004; Kolb & Whishaw, 2003; Lewis, 2003; Lezak, 2004; Roth et al., 2004). The degree to which these cognitive deficits are chronically stable has been the subject of some debate (Lewis, 2003). There appears to be an emerging consensus that cognitive deficits are mostly constant and neurodevelopmental in nature, although in those individuals with early onset of the disorder a neuro-degenerative component has been identified (Lewis, 2003). However, confounding this may be the likelihood that those individuals with early onset of the disorder may have had significantly less or disrupted education, in comparison to later-onset individuals, possibly contributing to lower than average cognitive performances (Heinrichs, 2005).

Bradshaw and Mattingley (1995) and Kolb and Whishaw (2003) point out that the specific pattern of frontal and prefrontal deficits common to individuals with schizophrenia (specifically those with predominantly negative symptoms) are likely to effect cognition broadly, but particularly executive functioning. Those with any form of frontal, temporal or hippocampal

deficit (this temporal limbic structure interconnects with prefrontal regions in the context of working memory) may result in working memory problems, disorganised behaviour as well as psychotic symptoms. Additionally, Lewis (2003) point out that a post-psychotic decline in cognitive functioning may represent an inability to acquire new information as well as neuronal degeneration due to psychotic states.

Chan et al. (2004) have found further evidence of frontal involvement, including the medial and ventral prefrontal areas in the poor planning ability, inability to maintain goal-directed behaviour, mental rigidity, impaired social judgement as well as impulsivity prevalent in the cognitive profile of those with schizophrenia. Findings highlighted that a specific right hemisphere frontal dysfunction seems to be prevalent in individuals with schizophrenia (Bradshaw & Mattingley, 1995; Chan et al., 2004; Moller, 2003). Roth et al. (2004) linked an increase in the negative symptom of apathy to poorer visuomotor sequencing and short-term memory, thereby hypothesising increased right hemisphere contributions. Gabrovska-Johnson et al.'s (2003) preliminary findings highlighted a specific profile of cognitive impairment common to individuals with schizophrenia was linked to a profile of right hemisphere impairment.

On neuropsychological investigation Josman and Katz (2006) found that individuals with schizophrenia and individuals who had suffered a CVA performed significantly worse on cognitive tests and daily tasks than normal controls. Additionally, these two groups performance was found to be similar in terms of executive function difficulties (Josman & Katz, 2006). However, no research has been found investigating the effects of comorbid schizophrenia and CVA.

In summary, a clear pattern of broad cognitive deficits including attention, perception, memory and executive function deficits has been consistently identified in individuals with schizophrenia. The literature suggests a cognitive profile of individuals with schizophrenia can be clearly differentiated from non-mentally ill individuals, as well as from other individuals with differing mental illnesses (Heinrichs, 2005; Lewis, 2003). From the literature the cognitive profile, affective deficits and psychotic symptoms, in individuals with schizophrenia are broadly related to the frontal areas, with temporal connections. In particular the medial and ventral prefrontal regions, particularly in the right hemisphere, have been highlighted as extremely pertinent.

2.6 Neuroscience and affect: Implications for schizophrenia

Affective style, as described by Davidson (1998; 2000; 2001; 2002; 2004) is the broad range of differences in varied affective phenomena governed by emotion regulation (a broad constellation of processes that serve to amplify, attenuate or maintain the strength of emotional reactions). Emotions are the key to successful adaptation and interact seamlessly with other cognitive functions as well as support motivated behaviour (Davidson, 2000). As such, Davidson (2001) describes affect as one of the key components which govern the risk for psychopathology (others include biological risk factors etc.). The concept of affective style is important to the disorder of schizophrenia, particularly in relation to emotion regulation and the differentiation between positive and negative mood.

Although other areas do come into play in the complex formation and expression of emotions Davidson (1998; 2000; 2001; 2002; 2004) and Jackson et al. (2003) focus on the importance of the prefrontal cortex and the amygdala as essential key components of affect. Broadly the prefrontal cortex is linked with affective processing, affect-guided planning and anticipation

(Davidson, 1998; 2000; 2001). The amygdala has been linked to negative affect in particular, as well as the direction of attention to affectively salient stimuli and cortical arousal (Davidson, 1998; 2000). Additionally, asymmetries between the hemispheres have been found to be significant (Davidson, 2000; 2002; 2004; Davidson, Shackman & Maxwell, 2004). In his relating of these systems to the prefrontal cortex Davidson (2000; 2001; 2004) highlights the differentiated nature of the prefrontal cortex (into the dorsolateral, ventromedial and orbitofrontal structures discussed above) as well as the importance of the asymmetries between the left and right hemispheric prefrontal cortices. However, the exact nature of the interface of these two systems has yet to be delineated (Davidson, 1998; 2000).

Two basic circuits have been proposed to mediate different forms of motivation and emotion, namely the approach system (called the behavioural activation system or BAS) and the withdrawal system (known as the behavioural inhibition system or BIS) (Davidson, 1998; 2000; 2001; Sutton & Davidson, 1997). Firstly, the BAS facilitates appetitive behaviour and generates positive affects that are approach-related and goal directed (Davidson, 2000; 2004; Sutton & Davidson, 1997). The BAS is mediated by the medial prefrontal region which projects to the nucleus accumbens and areas of the temporal lobes, and is specific to the left prefrontal cortex (Davidson, 2000). This zone is a major convergence point for motivationally relevant information from many limbic structures (Davidson, 1998; 2001).

Secondly the BIS facilitates the withdrawal of an individual and generates pessimism and negative affect (such as fear and disgust) (Davidson, 2000; 2001; Sutton & Davidson, 1997). The BIS is mediated by the right medial orbital prefrontal cortex with many connections to the limbic system, particularly the amygdala (specifically right sided) (Davidson, 2000; Sutton & Davidson, 1997). Additionally, research has shown that those individuals with more right-sided

prefrontal activation had increased neurotransmitter anomalies, specifically relating to the stress hormone Cortisol (Davidson, 1998). Hypo- and hyperactivations may result from various neurophysiological changes, including neuronal changes related to CVA (Davidson, 1998).

A pattern of left prefrontal hypoactivation is viewed as a neuronal reflection of a decreased capacity for pleasure, a loss of interest and a generalised decline in goal-related behaviour (Davidson, 1998; 2000; Davidson, Shackman & Maxwell, 2004; Jackson et al., 2003; Sutton & Davidson, 1997). Right-sided hyperactivation is associated with increased withdrawal and avoidance, pessimism and negative mood (symptoms common to individuals with schizophrenia) (Davidson, 1998; 2000; Jackson et al., 2003; Sutton & Davidson, 1997). Neuro-imaging studies have revealed that the left prefrontal region may have an inhibitory role on the amygdala, without which amygdala hyperactivation results in increased negative mood and fear reactions, particularly in learned aversive reactions (Davidson, 1998; 2001; Jackson et al., 2003).

The amygdala may therefore be a linking component, allowing communication between the left and right prefrontal regions, and may be involved in many disorders with affective components (Davidson, 1998; 2001). The extent to which learning theory plays a role in amygdala fear responses is still a debated issue with initial versus continuous learning being discussed (Davidson, 2001). However, lesion research has shown that medial prefrontal cortex lesions show dramatically slower extinction of learned aversive responses implying a descending pathway link between the medial prefrontal cortex and the amygdala (Davidson, 2001).

Despite recognising individual affective differences the strength of this model has been apparent over much research (Davidson, 1998). However, much of the research into the neuroscience of affective style relates to affective and anxiety disorders and there is a lack of research on

schizophrenia in this area. Additionally, criticisms of this model include methodological issues (namely the use of self-report scales for the investigation of negative and positive mood) as well as the neglect of the role of brain plasticity in affective regulation in individuals with lesions.

Although the cognitive picture of individuals with schizophrenia relative to those with affect disorders is specifically different, the affective components may be likened on various levels (Lewis, 2003; Sawa & Snyder, 2002). Research on differences between negative affect (described as avoidance, withdrawal, negative mood and pessimistic appraisal) and flat affect (described as lack of affective component or negative mood) has shown that those individuals with flat or negative affect perform significantly more similarly than those with significant positive or normal affect (Sawa & Snyder, 2002; Suslow, Roestel & Arolt, 2003). Additionally, Niethammer and Weisbrod (2000) support Davidson's (1998; 2000; 2001; 2004) findings of prefrontal hemispheric asymmetries in individuals with schizophrenia. Right-sided frontal hyperactivation and left-sided hypoactivation, outlined in much of the neuropsychological literature, support Davidson's (2000; 2001; 2004) theories of the neurobiology of affect (Niethammer & Weisbrod, 2000).

Therefore, despite a lack of literature clearly applying Davidson's (1998; 2000; 2001; 2004) theories to individuals with schizophrenia, these theories may be applied to the affective components of schizophrenia.

Hypothesising from Davidson's (1998; 2000; 2001; 2002; 2004) theories in individuals with schizophrenia it may be assumed that the B AS system, located in the left prefrontal cortex, and which is biased towards positive mood, engagement and optimism, may be hypoactivated, with the right prefrontal cortex of the BIS system, biased towards avoidance, withdrawal, negative

mood and pessimism, being hyperactivated (consistent with literature on affective changes in other psychopathologies). Additionally, from Davidson's (2001; 2002; 2004) work this hypoactive left prefrontal cortex fails in its function to inhibit the amygdala, leading to hyperaction of the amygdala which further decreases regulation and increases negative affect and low motivation.

Further hypothesising from Davidson's (1998) lesion theories regarding the effects of a right hemispheric CVA-associated lesion on an individual with schizophrenia, the right-sided hyperactivity may have been decreased by the infarct caused by the CVA. This may possibly lead to a decrease in withdrawal, avoidance and negative mood and increased dysinhibition. Additionally, amygdala function may have been affected (due to the changed metabolism associated with the prefrontal lesion) with a decrease in the amygdala's negative affective influence.

Not only do Davidson's (1998; 2000; 2001; 2002; 2004) theories give an account for the negative symptoms of schizophrenia, they are also compatible with recent neuropsychological research (outlined above) on the negative symptoms of schizophrenia.

2.7 Schizophrenia: Twin studies, neuropsychology and hemispheric brain functioning

Twin studies have established themselves as playing an important role in the study of the disorder of schizophrenia, highlighting both genetic and pathophysiological aetiological models (Singh, McDonald, Murphy & O'Reilly, 2004). Van Haren et al.'s (2004) meta-analytic study of monozygotic twins concordant and discordant for schizophrenia supported general findings of neuro-anatomic research showing that twins with schizophrenia, whether concordant or

discordant, had smaller whole brain volumes than control twins. Additionally, Van Haren et al. (2004) showed variation in hippocampal and ventricular volumes between the concordant and discordant twins indicating that individuals with schizophrenia are more likely to have anatomically abnormal hippocampi and ventricular volumes which is in line with previously discussed neuro-anatomical research.

Although much of the literature linking physiological abnormalities and genetic predisposition's is based upon twin-research data, Joseph (2001; 2002) warns against blind faith in these studies. Besides methodological problems many of the conclusions drawn from twin studies are based upon largely unsupported theoretical assumptions (such as the equal environment assumption or 'EEA') as well as assumptions not taking into account possible biological confounds and the non-additive nature of genetic influence (Joseph, 2001; 2002; Meaney, 2001; Segalowitz, 1999). Although Joseph (2002) does concede that his theoretical position is itself based upon large unsupported assumptions, his argument does highlight the critical stance with which all research, including twin studies, should be approached. Twin studies, although often seen as the 'gold standard' of genetic research should be considered within the larger biopsychosocial aetiological models they are based within. However, what is clear is that twin, family and adoption studies have established themselves in playing an important role in the study of the disorder of schizophrenia, especially in the study of gene-environment interactions (Meaney, 2001; Singh et al., 2004). Additionally, Segalowitz (1999) states that monozygotic twin studies are less likely to hold such problematic assumptions as monozygotic twins share a chorion, blood supply, and are subject to the same early hormonal influences and possible infections and therefore are generally significantly more similar on a variety of personality and cognitive measures than dizygotic twins or individual siblings.

Schizophrenia research outlined above has hypothesised various hemispheric and laterality asymmetries in affected individuals (Beebe, 2003; Bradshaw & Mattingley, 1995; Chan, 2004; Chan et al., 2004; Kalat, 1998; Kolb & Whishaw, 2003; Lewis, 2003; Niethammer & Weisbrod, 2000; Roth et a1, 2004). While the direct relationship between schizophrenia symptoms and brain localisation remains fairly elusive, from neuro-anatomical, neuro-metabolic as well as neuropsychological studies, a picture of right hemisphere based abnormalities in the frontal area and connections to temporal areas seems to have emerged (Barnett et al., 2005; Chan et al., 2004; Cutting, 1994; Gabrovska-Johnson et al., 2003; Robinson, 1998; Rotenberg, 1994). Upon a meta-analytic review of the mass of literature in this area, as well as taking into account various classification models of schizophrenia, clearly the right hemisphere particularly the frontal areas, plays a key role in the development of many of the symptoms of schizophrenia.

As outlined above, in individuals with schizophrenia, pathological inhibition of the left hemispheric prefrontal regions may result in both the hyperactivation or functioning of the right hemispheric prefrontal region and an uninhibited right amygdala resulting in decreased approach behaviours and goal attainment, and increased inhibition and negative affect (Davidson, 1998, 2004).

Barnett at al. (2005), Cutting (1994) and Robinson (1998) point out the neuropsychological similarities between the various symptoms of schizophrenia and the symptoms experienced by persons with specific right hemisphere damage, specifically in the areas of inhibition of behaviours and affective changes. Cutting (1994) supplies further neuropsychological test evidence showing that the use of tests specifically formulated to focus on individual hemispheric damage show definite right hemisphere effects in individuals with schizophrenia (specifically in

the areas of facial and speech emotion perception and right hemisphere linguistic tasks). Rotenberg (1994) points out that many of the peculiar behaviours and specific disturbances exhibited in individuals with schizophrenia are non-verbal in nature and as such, are under right hemisphere control, a point which Sadock and Sadock (2000) also make clear.

Functional neurological tests have confirmed that abnormal blood flow and metabolic reactions in several brain regions, including the temporal and prefrontal regions are altered in a large number of individuals with schizophrenia, with right dorsolateral hypermetabolism as well as altered blood flow specifically linked to individuals experiencing negative symptoms (Rotenberg, 1994; Sadock & Sadock, 2000).

Additionally, the left hemisphere plays a reciprocal role to the right hemisphere's hyperfunction with left hemispheric hypofunctioning linked to decreased goal attainment, uninhibited amygdala and (with links to the temporal areas) psychotic symptom formation. The research indicates that a distinct delineation of the hemispheres and their contributions to the symptoms may be more complicated than initially considered with reciprocal roles and connections between the hemispheres and lobes making clear delineation of function (or dysfunction) difficult. This is a difficulty inherent to the nature of neuropsychological investigation and, as Davidson (2001) and Lezak (2004) point out, in our attempts to research and organise brain functioning some of the finer interactional and relational elements seem to be lost.

It is clear that there is a delicate balance between the many variables within this proposed model, with minute changes leading to slightly different expressions of the disorder of schizophrenia, as well as differing vulnerabilities to neurobiological change which in turn may affect the

individuals expression of their symptoms of schizophrenia, contributing to the heterogeneous nature of schizophrenia.

Additionally, differences between active phases of schizophrenia and residual phases need to be taken into account. During an active psychotic phase of schizophrenia full expression of the dysfunctions described above in the neuro-anatomical and neuro-chemical interactions is at play (APA, 2000). However, in a residual schizophrenia diagnosis many of the positive symptoms have stabilised with some residual negative symptomatology (APA, 2000; Lewis, 2003). Blanchard, Horan and Collins (2005) and Lewis (2003) posits that although positive symptoms may be minimal in the residual diagnosis (commonly controlled through psychotropic medication) the often persistent negative and cognitive symptoms common to the residual diagnosis continue to be affected by the right and left hemispheric dysfunctions outlined above. As such, the theories of affective and cognitive dysfunction are specifically more pertinent to the residual schizophrenia diagnosis, and form the basis of a model for the development of a treatment for such symptoms.

2.8 Conclusion

Despite connections between the left and right hemispheres as demonstrated by Davidson (2001) this theory supports Cuttings (1994) and Rotenberg's (1994) theories of primarily left hemispheric involvement in positive symptoms and primarily right hemispheric involvement in negative symptoms. The neuropsychological and neuroscience literature presented above converges on a pattern of right hemispheric hyperactivation (dysfunction) contributing to negative symptoms and left hemispheric hypoactivation (dysfunction) contributing to positive symptoms (as well as some degree of negative symptom overlap).

Neuropsychological deficits in frontal, specifically prefrontal areas, are well founded in the research. Additionally, right hemispheric lesion studies have linked right hemispheric dysfunction to symptoms similar to those of the negative symptoms of schizophrenia, strongly implicating this hemisphere in the negative symptoms.

Neuroscience links inferior and medial prefrontal cortex (especially left hemispheric) dysfunction to positive symptoms via temporal lobe connections (both auditory and visual connections to the temporal lobe). Cerebral atrophy and neuronal disorganisation are posited to be the cause of the malfunctioning in these areas. In terms of exact mechanisms, Davidson's (1998, 2000; 2001; 2002; 2004) theories link left hemispheric prefrontal hypofunctioning to a decrease of approach and goal direct behaviours (as in schizophrenia). Left hemispheric prefrontal hypoactivation has been linked to a lack of amygdala inhibition, so contributing to possible negative symptoms. Additionally, Davidson (1998; 2000; 2001; 2002; 2004) links right hemispheric prefrontal hyperactivation (specifically in the medial area) to a lack of motivation and increased inhibition of behaviours as well as negative mood.

Taking from this unified theory and relating it to the specific case in hand, it is hypothesised that the right hemisphere hyperfunctioning (through cerebral neural atrophy or changes) may have contributed to a vulnerability not only to the expression schizophrenia symptoms, but to CVA. The CVA, through damage to the right hemisphere, may have contributed to some change in the expression of schizophrenia symptomatology.

Despite the assumptions around monozygotic twins, no two people share exactly the same life experiences even if they share the same genes. Although it is unclear as to why only one of the

twins was affected by a CVA, considering Zubin and Steinhauer's (1981) vulnerability model it is possible that trigger events or moderating variables may have differed between the participants. The current case-based research hopes to explore the theories mentioned above with a view to a greater understanding of the hemispheric role in the symptoms of schizophrenia and the role a major CVA may have on such symptoms.

From the selected literature outlined above it is clear that not only does schizophrenia present as a complex and multifaceted disorder but the study of the classification, aetiology and neuropsychological effects of schizophrenia is just as complex. Multiple diagnostic classification systems and aetiological models have led to disconnection between diagnosis, aetiological considerations and the treatment of schizophrenia. However, recent research does seem to be having a slight funnelling effect on the aetiological and treatment models of schizophrenia. As neuroscience and neuropsychological research gain consistency, aided by case study and twin study methodology, a more unified picture of symptom expression and psychological and neuropsychological effects may become clearer, which is positive for renewed efforts in treating not only the positive symptoms of schizophrenia but likewise addressing both negative symptoms and cognitive deficits.

CHAPTER THREE

RESEARCH AIMS, RATIONALE AND QUESTIONS TO BE ADDRESSED

The current research takes a clear exploratory and inductive approach (Terre Blanche & Durrheim, 1999). Observations regarding the neuropsychological performance of the participants will be consolidated in order to speculate broader hypotheses relevant to the literature discussed above. The Cognitive Neuropsychology methodology of in-depth case study analysis, which is particularly beneficial in inductive exploratory research, was selected as an applicable and relevant methodology for this research (Shallice et al., 1991). The aims of this methodology, which explicitly utilises case studies to make inferences about processes underlying human behaviour, include the comparison of normal cognitive functioning to abnormal functioning and the creation of cognitive profiles of different illnesses and brain damage (Harley, 2004; Shallice et al, 1991; Shallice, 1988). As such, the Cognitive Neuropsychology methodology was considered ideal for the exploration of the current participants.

3.1 Research rationale and aims

The rationale of this research is to contribute to an understanding of the role of the right hemisphere in the negative symptoms of schizophrenia by studying the relationship between the neuropsychological effects of right hemisphere CVA and negative symptoms of schizophrenia. The logic of the research design involves a comparison of two monozygotic twins' performance on selected neuropsychological measures in an attempt to understand the effects of right hemispheric CVA on negative symptoms. It is hoped that this will aid an understanding of the

specific contribution made by the right hemisphere to the symptoms of schizophrenia; as well as aiding in possible new directions for future research into the nature and treatment of the negative symptoms of schizophrenia. Although this research is certainly not advocating right hemispheric lesioning as a treatment for schizophrenia, this unique opportunity to study genetically identical individuals who vary with respect to organic pathology, but who are concordant for schizophrenia, offers a perspective on future aetiological and treatment models.

Primary aims of this research are the establishment of psychometric differences in negative symptomatology between the participants'. Establishing a decline in cognitive functioning (as predicted by the literature) from pre-morbid functioning due to early onset of schizophrenia is considered important in terms of applicability of this case to the broader literature. Further, guided by the literature, the participants' overall pattern of cognitive functioning will be compared to the pattern of cognitive functioning common to those with schizophrenia in order to lend credence to the applicability of this case to the literature.

The main aim of this research is to compare the performance of the participants with one another on a number of neuropsychological tests, and to explore the differences. Guided by existing literature on known patterns of functional lateralisation (in individuals with and without schizophrenia), this research will attempt to relate the performance differences to these patterns.

More specifically an investigation of various (putative) right hemisphere and frontal lobe functions (as suggested by Barnett et a1, 2005) will form the basis of the working research questions in an attempt to understand the differences between the participants - specifically with regard to the effects of the premotor and prefrontal anterior cerebral artery CVA, and the paradoxical improvement in the negative symptoms of schizophrenia. In this way, a set of

working hypotheses, termed research questions, will be implemented to analyse the test data. Areas to be investigated, as per convention, are (Barnett et al., 2005; Chan et al., 2004; Kolb & Whishaw, 2003; Lezak, 2004):

1. General cognitive ability: full scale IQ, verbal IQ, performance IQ.
2. Attention, tracking and concentration.
3. Perception and visual reasoning.
4. Praxis, constructional ability and Gestalt functioning.
5. Memory and learning.
6. Verbal functions and language skills.
7. Executive function.
8. Somatosensory difficulties and motor ability.
9. Facial recognition.

3.2 Research questions

As stated above this is exploratory case study research therefore causal hypotheses are largely problematic as causality and generalisability of case studies is considered to be low (Terre Blanch & Durheim, 1999). However, case studies offer the unique opportunity to explore and describe, in depth, the nature of a specific phenomenon (Harley, 2004; Shallice et al., 1991; Shallice, 1988; Terre Blanch & Durheim, 1999; Yin & Campbell, 2003).

Broadly this research aims to address, firstly, whether there are differences in functioning between the participants (both in terms of decline in functioning, and in general cognitive functioning of an individual with schizophrenia, compared to the literature) and secondly, to

compare these differences linked to the CVA. The specific questions to be addressed by this research are:

1. Is the twins' negative symptom presentation different from one another?
2. Does the twins' pattern of cognitive functioning suggest a decline from pre-morbid functioning?
3. Is the twins' pattern of neuropsychological functioning comparable to the existing literature?
4. Is there any difference in neuropsychological functioning between the twins?
5. Is there any pattern to any difference of neuropsychological functioning between the twins?
6. If there is a meaningful pattern of differences in functioning between the twins, can this be of potential value in explaining the improvement in negative symptoms seen with right hemispheric CVA?

It is expected that, although this case is a unique and complex case study, the twins neuropsychological test data should largely fit the pattern of neuropsychological dysfunction common to individuals with schizophrenia as described by Barnett et al. (2005), Chan (2004), Chan et al. (2004), Heinrichs (2005), Lewis (2003) and others.

Although monozygotic twins are genetically identical, life experiences and un-controlled for premorbid anatomical differences, may contribute to differences in test data (Joseph, 2001). However, the basis of twin study methodology asserts that these differences should not be statistically significant, especially in monozygotic twins, and that through statistical analysis any statistically significant differences between the twins neuropsychological functioning may be exposed (Harley, 2004; Segalowitz, 1999). Therefore, it can be safely assumed that the main contribution to these differences would be due to the CVA as many of the other life-spanning

variables between the twins are comparable (for example age of onset of schizophrenia; psychotropic medication dosage and duration of usage; course of the illness; education levels achieved and general life experiences).

From the literature cited above general differences between the participants are expected to be predominantly right hemispheric in nature. Abbey is expected to have a cognitive profile common to individuals with schizophrenia (as outlined by Barnett et al., 2005 and Roth et al., 2004), with global right hemispheric dysfunction, and specific difficulties in emotional recognition and expression, visuo-spatial processing, memory and gestalt information processing. Gail (CVA) is expected to have lesion-specific right hemisphere dysfunction, with more severe difficulties in visuo-spatial, sensory and gestalt processing but with fewer difficulties in emotional recognition and expression. Slight left hemispheric functioning differences are also expected between the twins with Abbey having poorer self-regulational abilities compared to Gail (CVA). Additionally, differences in executive function, self-regulation and conceptual abilities are expected to emerge.

Table 3.1: Tabulation of expected differences between the research participants

	Left Hemisphere Overall self regulation	Right hemisphere(RH) Gestalt function	RH Visuo-spatial function	RH Emotion expression, recognition	Frontal lobe (FL) Executive function	FL Memory function	Concept formation
Abbey Non-CVA	—	—	—	—	—	—	—
Gail CVA	—			+	+	+	+

Legend: - denotes below average, — denotes below Abbey, + denotes above Abbey.

CHAPTER FOUR

METHODOLOGY

4.1 Research methodology rationale

The chosen methodology for this research is that of a case study. Its aims are partly descriptive, but it also seeks to tentatively draw inferences from the different patterns of neuropsychological functioning between the two individuals. Essentially, it is hoped that differences in functioning can be seen between the twins, based on the established fact that one has suffered a CVA and the other has not. Furthermore, it is hoped that these can be tentatively fitted to current models of brain dysfunction with regard to negative symptoms of schizophrenia.

It would be naive to believe that causal explanations are possible in this inductive approach. However, it must be noted that neuropsychological research has benefited greatly from a number of famous single case studies which demonstrate the effects of brain lesions on behaviour (Harley, 2004; Kalat, 1998; Shallice, 1988). The example of Phineas Gage is certainly a case in point, and it is hard to find a textbook on neuropsychology which does not allude to this case in demonstrating the effects of frontal lobe lesions. Thus, this research aims to extend the development of pre-existing theories regarding schizophrenia, negative symptoms and hemispheric contributions. The case study methodology, outlined below, should not be confused with the one-group, post-test only, quasi-experimental research design (where causal hypotheses are formalised), as case study methodology is a sound method in its own right (Terre Blanch & Durrheim, 1999; Yin & Campbell, 2003).

4.1.1 Critique of large scale research methodology

As stated above, there have been many studies of the neuro-anatomical, neuro-chemical and neuropsychological correlates of schizophrenia, with some debate regarding the localisation or lateralisation of dysfunction (Blanchard & Neale, 1994; Savage et al., 2003; Stratta et al, 2005). Much of the large scale randomised double (or single) blind experimental-control group research into the area of the neuropsychology of schizophrenia has been criticised for various methodological failings (Shallice et al., 1991; Yin & Campbell, 2003).

Some of the methodological problems raised in the study of schizophrenia are related to the problem of poor general health including long-term neuroleptic drug effects (Shallice et al., 1991). The research of medication-naive individuals with schizophrenia, those never having been medicated, as opposed to those on suspended drug treatments, are important to neuropsychological research (and is a valid criticism of the research presented here). However, these studies present with various ethical and practical constraints (Heinrichs, 2005). Phillips, Howard and David (1997) do note that although anti-cholinergic medications may affect neuropsychological test results, antipsychotic medication is not associated with major performance impairments on cognitive tasks in participants with schizophrenia. However, Lewis (2003) and Heinrichs (2005) caution that although no clear performance deficits are currently related to antipsychotic medication use, they may have a sedating effect and therefore may affect overall test performance through some cognitive slowing.

Further criticisms of experimental design highlight that although single-blind randomised research is possible it is difficult to find matched controls to individuals who have chronic

schizophrenia and who have been exposed to prolonged neuroleptic medication (Yin & Campbell, 2003). Additionally, as outline above, diagnostic and symptom heterogeneity has been highlighted as a further difficulty within larger scale schizophrenia research, and has poor test-retest reliability (Shallice et al., 1991; Yin & Campbell, 2003). Large group experiments have often utilised poor neuropsychological strategies including employing a limited range of neuropsychological tests which could lead to interpretation difficulties as teasing out various neuropsychological functions from a small test battery may lead to confounded results (Shallice et al., 1991). Despite such criticisms, large scale randomised research designs remain important in furthering the generalisibility and application of theory. However, alternative methodologies may offer more unique and in-depth insights into the complex phenomena of the functioning and dysfunction in individuals with schizophrenia.

4.1.2 Rationale for Cognitive Neuropsychological methodology

Shallice et al. (1991) describe the methodology of neuropsychology broadly, and particularly that of Cognitive Neuropsychology, as being one of the most beneficial in exploratory research. Cognitive Neuropsychology methodology dates back to the nineteenth century, However, modern Cognitive Neuropsychological methods were first applied in the 1970's (Shallice, 1988). Aims of Cognitive Neuropsychology include

> "explaining patterns of impaired and intact performance seen in people with brain damage to one or more components of a model of normal cognitive functioning" (Caramazza, 1988, as cited in Harley, 2004, p. 5).

and

> "to draw conclusions about normal, intact cognitive processes from the patterns of performance observed in people with brain damage" (Caramazza, 1988, as cited in Harley, 2004, p. 5).

With these aims in mind Cognitive Neuropsychology methodology supports the use of case studies as a more specific hemispheric or lobe focused approach which may be employed to not only elicit richer data but also allow investigation of interesting differences between individuals (Harley, 2004; Shallice et al., 1991; Shallice, 2004). This assertion underlies the third aim of Cognitive Neuropsychology, that is

> "to make inferences about the processes underlying human behaviour using single case studies" (Harley, 2004, p. 6).

Although Cognitive Neuropsychology methodology has been criticised, namely for its lack of distinct localisation ability and neuroimaging data, Fiez (2001), Harley (2004) and Shallice (2004) point out that the identification of distinct neural structures in the brain (especially through neuro imaging alone) does not contribute to the understanding of cognition.

Despite the criticism of both Cognitive Neuropsychology methodology and twin study methodology (Fiez, 2001; Joseph, 2001; 2001) both of these methodologies remain important contributors to research in the areas of neuropsychology and schizophrenia. Given the current unusual case, and taking into account time, resources and participant limitations, the methodology of Cognitive Neuropsychology was selected as it offers the opportunity to quantify and study behaviour in a number of different cognitive domains. Additionally, there is

the possibility of exploring double dissociations as a means of drawing inferences about possible brain dysfunction.

4.1.3 Rationale of data analysis

Data analysis within the area of cognitive neuropsychology case studies is commonly done through the comparison of the participants' performance to either a modestly sized control group, or alternatively to population norms, with the listing of descriptive statistics alone being insufficient (Crawford, Garthwaite, Howell & Gray, 2004). Issues of statistical power continue to be difficult in case study methodology data analysis as both Type I (erroneously concluding that a participant's score is significantly different than those of controls/the population) and Type II (erroneously concluding that the participant does not differ from controls/the population) statistical errors are not methodologically controlled for (Crawford et al, 2004). However, statistical control (as opposed to methodological control) of both Type I and Type II error may be a more valid method of control in the case of Cognitive Neuropsychology as this area is interested in the particulars of specific populations as opposed to the general (Crawford et al., 2004).

Crawford et al. (2004), Crawford and Garthwaite (2002) and Crawford et al. (2006) highlight the usefulness of z-score inferential statistics when control sample data is not available as being statistically and methodologically sound. Additionally, Crawford and Garthwaite (2002) highlight that a z-score below -1.64 is considered statistically significant. However, Crawford and Garthwaite (2002) caution that the z-score method with a single case study may over-exaggerate the rarity or abnormality of an individual's score, but add that an estimation of the z-score confidence limits may decrease this error.

4.2 Research methodology

Within the framework of Cognitive Neuropsychology the design of this research was conceptualised through the review of relevant CVA and schizophrenia neuropsychological methodological material (Barnett et al, 2003; Blanchard & Neale, 1994; Harley, 2004; Savage et al., 2003; Shallice et al., 1991; Yin & Campbell, 2003). The specific framework for the tests used (as outlined below in section 4.4), including specific ordering of tests and the assessment of the various hemispheres and frontal functions, was based on the literature outlined in Chapter 2 (Blanchard & Neale, 1994; Cutting, 1994; Davidson, 2001; Hobart, Goldberg, Bartko & Gold, 1999;Rotenberg, 1994).

4.2.1 Research frame

The framework of this research was conceptualised into two phases. The first phase commenced with a detailed history-taking and collateral gathering component, including a full medical history, psychiatric history and general life conditions (including education, occupational history and social capacity), which is standard practice in creating a context within which neuropsychological data is gathered and interpreted (Lezak, 2004; Mansfield, 2002). The collateral apsects also provided vital information regarding long-term personality or affective information which could not be elicited from the participants or through neuropsychological testing.

The second phase of the research comprised testing of the participants (separately and consecutively) on a number of neuropsychological and psychological tests and batteries over an

eight session period. A full spectrum of assessment measures was used to gain a global understanding of the participants' various cognitive capabilities and range of functioning, as well as tests for specific hemispheric and lobal functioning. This research aims at a broader approach than much research in the area, which generally use limited assessment measures and are largely designed to identify only generalised organic brain damage and lack a focus on specific hemispheric functioning (Bartnett et al., 2003; Cutting, 1994; Yin & Campbell, 2003).

4.2.2 Neuropsychological testing considerations

Despite most neuropsychological tests holding a single set (or multiple sets) of American based norms the primary goal of a cognitive neuropsychological assessment (as outline above) is determining brain pathology of an individual by comparing a person's performance to available normative standards on the various neuropsychological tests (Grant & Adams, 1996; Harley, 2004). Despite many of the selected assessment methods being standardised and demonstrating adequate reliability and validity statistics, the tests were largely developed and standardised in western settings (primarily the United States of America) and as such, may not be the most suitable assessment measures for non-westernised settings such as South Africa. With the exception of the WAIS-III there is no data available to support the reliability or validity of these tests on a South African population. However, due to their world-wide use, in line with other research in this area, for lack of more reliable or valid tests, and considering the favourable participant variables (outlined below) these tests were deemed most appropriate for this research.

Demographic variables which must be taken into account when conducting neuropsychological assessment are gender, educational level, language, test-wiseness and ethnicity (Foxcroft &

Roodt, 2001; Grant & Adams, 1996; Nell, 1999). However, the participants are considered test-wise, are English-first language speakers and were educated through to M-levels (grade 12 equivalent) in a British-based education system. As such, the neuropsychological and psychological tests used in this research were deemed suitable.

4.2.3 Other variables to consider

A non-social, helper-helpee relationship existed between the researcher and the participants prior to the research therefore, researcher objectivity could be questioned (Terre Blanche & Durrheim, 1999). However, the researcher does not consider this a disadvantage. Rather it is important when considering that, due to the participants' limited social skills, a large amount of time is needed to build up a relationship of trust. Therefore, a prior relationship may be considered beneficial in obtaining a best performance. Lezak (2004) and Mansfield (2002) reiterate this and stress the importance of good rapport with subjects to obtain the best possible performances.

4.3 Ethical considerations

Although neither twin has been admitted to a psychiatric hospital or been sequestrated, and both are legally competent adults, when considering ethical implications of this research the twins were considered a special population given their diagnosis and cognitive capacity.

Due to this informed consent and other ethically important factors (such as participant withdrawal and findings feedback) was carefully negotiated with both twins and, with their consent, with the family members with whom they reside.

4.4 Data collection

4.4.1 Procedure

The procedure consisted of the phase-one intake sessions (gaining consent and history taking done in two sessions) and eight phase-two assessment sessions. After gaining consent from all parties involved, history taking included individual and family meetings. The participants were assessed individually and consecutively to prevent test contamination and decreased validity due to participant communication. The assessment administration procedure was as follows:

Session 1:

1. Mental Status Examination (MSE).
2. Positive And Negative Symptom Scale (PANSS).
3. Skin Writing Test.
4. Bender Gestalt Test.

Session 2:

5. Wechsler Adult Intelligence Scales, 3rd Edition (WAIS-III).

Session 3:

6. Stroop Test.
7. Rey Complex Figure Test (RCFT) and Recognition Trial.
8. Symbol Digit Modalities Test (SDMT).
9. Single Double Simultaneous Stimulation Test (SDSS).

Session 4:

10. Trail Making Test (TMT).
11. Line Bisection Test.
12. Hooper Visual Organisation Test (Hooper VOT).

Session 5:

13. Rey Auditory Verbal Learning Test (RAVLT).
14. Facial Recognition Test.
15. Austin Maze Test.
16. Controlled Oral Word Association Test (COWA).

Session 6:

17. Wisconsin Card Sorting Test (WCST).

Session 7:

18. Wechsler Memory Scales, 3rd Edition (WMS-III).

Session 8:

19. Minnesota Multiphasic Personality Inventory, 2nd Edition (MMPI-II).

4.4.2 Instruments

1. Mental Status Examination (MSE):

Current general mental status and superficial cognitive function assessment were examined for appropriateness for neuropsychological investigation (to assess presence of confusion, disorientation, and coarse assessment of cognitive functions). Preliminary assessment of concept formation ability, attention and concentration and verbal functions were assessed through the use of proverbs, the 'serial sevens' test and through conversation respectively (Mansfield, 2002).

2. Positive And Negative Symptom Scale (PANSS):

The PANSS is an assessment measure commonly used to assess the clinical severity of the symptoms of schizophrenia and to distinguish between the positive and negative symptoms (Barnett et al, 2003). This measure was used to establish current schizophrenia symptomatology in both of the participants. The PANSS is a 30-item scale which distinguishes 3

symptom dimensions: 7 items constitute the positive scale, 7 the negative scale and 16 items a general psychopathology scale (Kay, Fizbein & Opler, 1987). The normative and standardisation data is based on an American sample which revealed satisfactory internal scale consistencies (0.8) as well as inter-rater reliability (0.73) (Lancon, Auquier, Nayt, & Reine, 2000). However, there is little research on this measure within a South African population.

3. Skin Writing Test:

Rey (1964, as cited in Lezak, 2004) developed this test as a formalised skin writing procedure assessing tactile perception and visual reasoning important for lateralising the site of possible brain damage. The test consists of 5 subtests where the examiner writes, one by one, a pre-determined series of letters or numbers on the participants' dominant or non-dominant hand or forearm (Lezak, 2004). Rey's (1964, as cited in Lezak, 2004) original study provided statistical data on 4 different adult American-based groups, namely manual and unskilled workers, skilled technicians and clerks, people with a baccalaureate degree and finally persons between the ages of 68 and 83. Further validity and reliability data on this measure, and specifically within a South African population, is unavailable. However, in this research the test was used in a more individual-centred, clinical approach to assess differences between the participants, rather than quantitative with a normative comparison focus.

4. Bender Gestalt Test:

The Bender Gestalt test was originally developed by Bender in 1938 (Bender, 1938). The adapted Bender Gestalt test commonly used in modern testing consists of 9 designs which were originally used to demonstrate the brain's tendency to organise visual stimuli into Gestalten

(configural wholes) and examines the participants visuo-constructional abilities inherent to the right hemisphere (Hutt, 1985). Poor performance on the Bender Gestalt test is associated with general right hemisphere lesioning, specifically parietal lesions (Lezak, 2004). Psychometric data reveals an inter-rater reliability for the total assessment measure of 0.96. Within psychiatric populations performance on the Bender-Gestalt is significantly correlated to their WAIS-III test scores with a correlation coefficient of 0.50 (Lezak, 2004).

5. Wechsler Adult Intelligence Scales, 3rd Edition (WAIS-III):

The WAIS-III was originally developed, normed and standardised in 1997 in the United States of America (Wechsler, 1997a). After South African norms became available for the WAIS-III (through the South African Human Sciences Research Council) the WAIS-III has become a commonly used assessment measure within South Africa (Nell, 1999). The WAIS-III consists of 14 compulsory and 2 optional subtests which are calculated into a number of intelligence scores, namely full scale intelligence score, a performance IQ score and a verbal IQ score (Wechsler, 1997a). Additional subscale indices may be calculated via various subtests, being the working memory index, processing speed index, perceptual organisation index, and verbal comprehension index (Wechsler, 1997a).

Table 4.1: WA1S-I11 Subscales and Index composition

Subtests	A	B	C	D	E	F	G
Picture Completion	*		*		*		
Vocabulary	*	*		*			
Digit Symbol - Coding	*		*				*
Similarities	*	*		*			
Block Design	*		*		*		
Arithmetic	*	*				*	
Matrix Reasoning	*		*		*		
Digit Span	*	*		*		*	
Information	*	*					
Picture Arrangement	*		*				
Comprehension	*	*					
Symbol Search	*		*				*
Letter-Number Sequencing	*	*				*	
Object Assembly	*		*				

Legend for table:
A: Full Scale IQ
B: Verbal IQ
C: Performance IQ
D: Verbal Comprehension Index
E: Perceptual Organisation Index
F: Working Memory Index
G: Processing Speed Index

From the various subtests information on both current and premorbid (where applicable) estimations of intelligence, as well as various other dimensions of cognitive functioning can be ascertained (Jones, van Schaik & Witts, 2006; Nell, 1999; Wechsler, 1997a). Although scale validity and reliability data was gained through analysis of the American based norms of the WAIS-III, South African based norms for the WAIS-III are available (Nell, 1999).

6. Stroop Test:

Initially developed by John Stroop in 1935 this measure assesses attention, information processing and cognitive slowing (Lezak, 2004). This test is sensitive to subtle attentional deficits and left frontal injuries (Lezak, 2004; Mansfield, 2002). The test consists of a Form C

(colour task) sheet and a Form C-W (colour word task). The Form C consists of a list of colour words printed in coloured (but not corresponding) ink. The individual's task is to read as many of the words as possible within the time allowed (Lezak, 2004). The Form C-W is an identical sheet, however, the individual is instructed to state the colour of the ink rather than read the word, and to do as many as possible within the time allowed (Lezak, 2004). Although adequate reliability and validity data are available for this test (Lezak, 2004), there are no South African norms available.

7. Rey Complex Figure Test (RCFT) and Recognition Trial:

The RCFT (Meyers & Meyers, 1995) is a popular measure of visuospatial constructional ability, visual memory and organisational approaches to visual constructional tasks. Specifically the RFCT has been noted to be an important assessment tool for assessing lateralised damage, particularly pertaining to right hemispheric, frontal or prefrontal deficits (Deckersbach et al, 2000; Mansfield, 2002). Although some administration procedures do differ the test involves the copying of a complex geometric figure, followed by an immediate recall trial (original figures not present), a 3-minute immediate recall trial (original figures not present), a 30-minute delayed recall trial (original figures not present) and a recognition trial involving the recognition of the correct components of the original figure amongst various other distractor components (Meyers & Meyers, 1995). The RCFT normative data was derived from a screened American and Canadian based sample through categorical and age-matched norming procedures (Meyers & Meyers, 1995). Psychometric property analysis of the RCFT reveals an inter-rater reliability of 0.94 (Pearson's coefficient), temporal stability of 0.87 (test-retest reliability coefficient), as well as adequate discriminant and factorial validity (Meyers & Meyers, 1995). However, South African standardisation and norms are not available for this measure.

8. Symbol Digit Modalities Test (SDMT):

The SDMT was originally designed by Smith (1982) as a measure of complex scanning and visual tracking, psychomotor speed and agility and an indicator of overall processing speed and efficiency. The test involves the conversion of meaningless geometric designs into written and (or) oral number responses (Smith, 1982). This screening measure can differentiate between deficiencies relating to impaired perceptual processes or cerebral dysfunction secondary to suspected brain damage (subnormal oral and written scores), impairment of speech performance (subnormal oral scores with normal written scores) and motor or writing skills deficit (subnormal written scores with normal oral scores) (Smith, 1982). Standardised scores are available for adults separated into ten age groups with separate scores for various educational levels (Smith, 1982). Psychometric analysis of the SDMT reveals atest-retest reliability of 0.76 (Pearson's coefficient), additionally the SDMT has been found to be a valid test of general brain defects as well as sensitive to various types of brain injuries including lateralised lesions (Bird, Papadopoulou, Ricciardelli, Rossor, & Cipolotti, 2004; Smith, 1982). South African standardisation and norms are not available for this assessment measure.

9. Single Double Simultaneous Stimulation Test (SDSS):

The SDSS is a simple test of somatosensory functioning and can be used together with the SDMT in sensitively detecting lateralised brain lesions (Centofanti & Smith, 1986; Lezak, 2004). This 20-itemtest of perception and visual reasoning consists of 8 single stimulation items and 12 double simultaneous stimulation items touching the hand or cheek (or both) on one or both sides of the body (Centofanti & Smith, 1986). Normative and standardised data was

accumulated from a diverse American population and revealed adequate validity in identifying lesion sites (Centofanti & Smith, 1986). South African standardisation and norms are not available for this assessment measure, however, this test was used with a more individual-centred clinical purpose, assessing differences between the participants' qualitatively.

10. Hooper Visual Organisation Test (Hooper VOT):

The Hooper VOT was originally developed by H. Elston Hooper in 1958 and is a sensitive and reliable indicator of brain lesions (Hooper, 1958). The Hooper VOT assesses the individuals ability to organise visual information as well as concept formation, and is specifically sensitive to right hemispheric and posterior lesioning (Hooper, 1958; Lezak, 2004; Merten & Beal, 2000). The test consists of 30 line drawings depicting simple objects which have been cut into a number of pieces in a puzzle-like fashion (Neurosciences unit, 1983). The participant is asked to identify what each object would be if it were put back together correctly (Neurosciences unit, 1983). Psychometric property assessment reveals atest-retest reliability of 0.78 (Pearson's coefficient) for a psychiatric population and a split-half reliability coefficient of 0.80, indicating that 80 percent of the variance in test scores is attributable to true variance in the traits measured by the Hooper VOT, with only 20 percent due to measurement error (Hooper, 1958; Neuroscience unit, 1983). Additionally, the Hooper VOT was assessed as being adequately valid in detecting and differentiating between psychopathology and normal controls as well as psychoneurotic and schizophrenic reactions (Hooper, 1958). However, South African standardisation and norms are not available for this assessment measure.

11. Trail Making Test (TMT):

The TMT was originally developed by American Army psychologists and is a measure sensitive to concept tracking, visuomotor tracking, visual scanning, attention and psychomotor speed (Lezak, 2004). The test is given in 2 parts, A and B, with the participant drawing lines to connect consecutive numbered circles on one sheet, and then connecting the same number of consecutively numbered and lettered circles by alternating between the two sequences on another with both trials being timed (Lezak, 2004). Poorer performance on Part B of the test is associated with frontal lobe lesions (Lezak, 2004). From psychometric data the TMT has a reliability coefficient of between 0.60 and 0.90 depending on the test population (Lezak, 2004). However, South African standardisation and norms are not available for this assessment measure.

12. Line Bisection Test:

The Line Bisection test developed by Albert in 1973, is sensitive to spatial or contralateral neglect specifically relating to right hemispheric dysfunction (Blanchard & Neale, 1994; Ferber & Karnath, 2001; Lezak, 2004). This test consists of a total of 20 lines of different sizes, arranged so that two are centred on the top and bottom of the page, six are centred to the left of the midline of the page, six to the right, with a central column of six lines which must be centrally crossed by a single line by the participant (Lezak, 2004). This test compares favourably to other commonly used visuospatial tests of inattention, and has a test-retest reliability coefficient ranging from 0.84 to 0.93 (Ferber & Karnath, 2001; Lezak, 2004). South African standardisation and norms are not available for this assessment measure.

13. Rey Auditory Verbal Learning Test (RAVLT):

The RAVLT provides information on immediate memory span, rate at which words are learnt, reveals proactive and retroactive inhibition tendencies, measures short term and longer term retention and is sensitive to subtle cognitive deficits (Hawkins, Dean & Pearlson, 2004; Lezak, 2004; Mansfield, 2002). The test consists of 5 presentations of a 15-word list (List A), followed by a single presentation of another list (List B), an immediate recall trial (List A), a 30-minute delayed recall trial (List A) as well as an optional recognition trial where the participant identifies words from List A in amongst various distrac tor words (Lezak, 2004). Participants with frontal lobe lesions tend to do less well than healf ly participants on recall trials but may show a normal learning pattern, additionally left temporal lesioned participants do significantly more poorly on the RAVLT than right lesioned participants (Lezak, 2004). Reliability coefficients for the RAVLT are between 0.38 and 0.77 and the test has been shown to be adequately valid (Lezak, 2004). However, South African standardisation and norms are not available for this assessment measure.

14. Facial Recognition Test:

The facial recognition test was specifically developed 10 examine the ability to recognise faces without involving a memory component (Lezak, 2004]). The test involves the participant matching identical front views and front with side views from 22 stimulus cards to form 54 separate matches (Lezak, 2004). Neuropsychological findings reveal that this measure is sensitive to right hemisphere lesions, with right parietal lesions inducing significantly poor performances (Blanchard & Neale, 1994; Lezak, 2004). Psychometric data reveals an internal

consistency reliability coefficient of 0.57 and a test-retest reliability coefficient of 0.60 with acceptable validity findings (Lezak, 2004). However, South African standardisation and norms are not available for this assessment measure.

15. Austin Maze Test:

The Austin Maze test is a test of frontal lobe functions testing attention, concentration, learning, motor ability, self-regulation as well as assessing overall mental efficiency (Mansfield, 2002). A pattern of frontal lobe lesion errors include 'running on errors' where participants are unable to inhibit erroneous responses and many of the errors on this test tend to mirror difficulties the participant may be having in everyday life (Mansfield, 2002). The test consists of a board with a matrix of identical keys, a green light indicator (indicating a correct response) and a red light indicator (indicating an incorrect response) (Mansfield, 2002). Additionally, there is a error counter on the side of the board and a reset button (Mansfield, 2002). The participant attempts to navigate the maze (ultimately with zero errors) from start to finish over a number of trials (Mansfield, 2002). Psychometric data was unavailable for this assessment measure.

16. Controlled Oral Word Association Test (COWA):

The COWA test is sensitive to frontal lesions, with left frontal lesions depressing overall scores, right frontal lesions depressing fluency on the test and bilateral lesions resulting in even greater impairment than either hemispheric lesion alone (Blanchard & Neale, 1994; Lezak, 2004). The test involves 3 trials, each asking the participant to list as many words beginning with 'C, 'F' and 'L' respectively (Lezak, 2004). The participant lists as many words as possible with the exception of proper nouns, numbers, and repetitions with a different suffix, within a time limit

(Lezak, 2004). The COWA test has been found to be valid in distinguishing between healthy and brain lesioned individuals, as well as those with degenerative brain diseases (Lezak, 2004). British psychometric data on this test reveals a test-retest reliability of 0.82 (Pearson's coefficient) and satisfactory validity (Bird et al., 2004). However, South African standardisation and norms are not available for this assessment measure.

17. Wisconsin Card Sorting Test (WCST):

The WCST was originally formed by Berg, Berg and Grant in 1948 (Lezak, 2004). This test is an executive function test sensitive to frontal lobe pathology and tests abstracting and conceptual shifting ability (Blanchard & Neale, 1994; Lezak, 2004). The test is sensitive to strategic planning, organised searching, utilising environmental feedback to shift cognitive sets, directing behaviour toward achieving a goal and modulating impulsive responding (Tate, Perdices, & Maggiotto, 1998). The test consists of 4 stimulus cards which are placed before the participant, the participant is then given a pack of cards (no two cards are the same) and the participant must place them one by one under one of the stimulus cards according to the pattern deduced from the examiner's responses of 'right' or 'wrong' (Lezak, 2004). The examiner's procedure is to start with the colour criteria and move on to the form and number criteria without any indication to the participant. This pattern is repeated after 10 consecutive correct responses have been recorded (Lezak, 2004). Satisfactory inter-rater reliability as well as validity statistics have been reported (Bird et al, 2004; Bowden et al., 1998; Lezak, 2004; Tate, Perdices & Maggiotto, 1998). However, South African standardisation and norms are not available for this assessment measure.

18. Wechsler Memory Scales 3rd Edition (WMS-III):

The WMS-III were published in 1997 in an attempt to update the previous WMS-R (Wechsler, 1997b). The scale consists of 17 subtests (optional and compulsory) which are calculated into auditory and visual immediate memory scales, auditory and visual general (delayed) memory scales, general memory scale and working memory scale (Nell, 1999; Wechsler, 1997b).

Table 4.2: WMS-III subscales and Index composition

Subtests	A	B	C	D	E	F	G	H
Logical memory I	*		*					
Faces I		*	*					
Verbal paired associates I	*		*					
Family Pictures I		*	*					
Letter-Number sequencing								*
Spatial span								*
Logical memory II				*			*	
Faces II					*		*	
Verbal paired associates II				*			*	
Family pictures II					*		*	
Auditory recognition						*	*	

Legend for table:
A: Auditory immediate scale
B: Visual immediate scale
C: Immediate memory sclae
D: Auditory delayed scale
E: Visual delayed scale
F: Auditory recognition delayed scale
G: General memory scale
H: Working memory scale

Indices which may be obtained from the various subtests include working memory and information on broader current memory functioning (Nell, 1999; Wechsler, 1997b). Scale validity and reliability data was gained through analysis of the American based norms of the WMS-III (Tulskey, 2004; Wechsler, 1997b).

19. Minnesota Multiphasic Personality Inventory, 2^{n} Edition (MMPI-II):

The MMPI-II was used to gain a global personality pattern of the participants, as well as specific psychological indicators such as paranoia, schizophrenia and social introversion (Butcher et al., 2001). The MMPI-II consists of 567 true-false answer test items which the participant manually checks of the answer sheet (Butcher et a1, 2001). Psychometric property analysis reveals the MMPI-II has adequate test-retest reliability coefficients between 0.34 and 0.91 for all subscales and internal consistency estimates (coefficient alpha) between 0.37 and 0.90 (Butcher et al., 2001). However, South African standardisation and norms are not available for this assessment measure.

4.5 Data analysis

From twin study methodology, monozygotic twins' neuropsychological performance is expected to have no statistically significant differences, especially when the twins are concordant for schizophrenia (Segalowitz, 1999). Therefore, the participants' results are assumed to have no statistically significant differences in neuropsychological performance. From the case history (below) the CVA presents as a seemingly lone significant difference between the twins. This difference was assumed to account for any differences found between the twins neuropsychological performance (overall differences as well as differences in specific areas of functioning. Additionally, the CVA was assumed to account for the change in Gail's (CVA) negative symptoms in the lack of other significant changes or differences to account for this. Therefore, any significant differences found between the participants' neuropsychological performance is assumed to be due to the CVA and to be important in terms of the changes in

the negative symptoms. This rationale was used in terms of the data analysis. Handling of the participants raw data and the data analysis proceeded in five phases.

4.5.1 Treatment of raw data

The raw data was prepared for analysis by scoring according to the various manual recommendations. As various tests consist of multiple sub-tests and indexes (for example WAIS-III, WMS-I1I, RCFT etc) the data set was broken down into 50 data points (see Table 4.3). This breakdown enabled fuller investigation into the various areas of functioning (outlined below) in order to capture the complexity of the participants functioning. However, MMPI-II data was not included in this data set as, not only does this test not include single scores applicable to this scoring system but, in line with other literature, this test was used for symptom exploration and description only.

Table 4.3: Sub-division of data points for both participants'

Test	**Sub-test/s**
1-2. SDMT	SDMT - Written SDMT - Oral
3-4. TMT	TMT-A TMT-B
5. Stroop test	-
6. PANSS	-
7. VOT	-
8. Skin Writing test	-
9. SDSS	-
10. Line Bisection test	-
11. Facial Recognition test	-
12. WCST	-
13. Austin Maze	-
14-16. COWA test	COWA test C COWA test F COWA test L
17. Bender Gestalt test	-
18-34. WAIS-III	WAIS-III FIQ WAIS-III VIQ WAIS-III PIQ WAIS-III Picture completion WAIS-III Vocabulary WAIS-III Digit Symbol WAIS-III Similarities WAIS-III Block design WAIS-III Arithmetic WAIS-III Matrix reasoning WAIS-III Digit span WAIS-III Information WAIS-III Picture arrangement WAIS-III Comprehension WAIS-III Symbol search WAIS-III Letter-number sequencing WAIS-III Object assembly
35-42. WMS-III	WMS-III Auditory immediate WMS-III Auditory delayed WMS-III Visual immediate WMS-III Visual delayed WMS-III Immediate memory WMS-III Auditory recognition delayed WMS-III General memory WMS-III Working memory
43-46. RAVLT	RAVLT List A total RAVLT List B total RAVLT Recall RAVLT Recognition
47-50. RCFT	RCFT Copy RCFT 3-minute immediate recall RCFT 30-minute delayed recall RCFT Recognition

As raw data comparisons are difficult (rather like comparing apples with oranges) the raw data was converted into z-scores for each data point (for each participant) and explored through descriptive statistics. This analysis is in line with the methodology of case study data analysis outlined above. From the z-scores the participants' data was coded (along convention, see Table 4.4) to classify ability levels, creating categorical data (Howell, 2002; Lezak, 2004). Namely the data was given one of 7 codes as outlined below:

Table 4.4: Z-score classification of ability level

Classification	**Code**	**z-score**	**Percent Included**	**Lower limit of percentile range**
Very superior	**7**	+2 and above	**2.2**	98
Superior	**6**	+1.3 to 2.0	**6.7**	91
High average	**5**	+0.6 to 1.3	16.1	75
Average	**4**	+/- 0.6	50.0	25
Low average	**3**	-0.6 to-1.3	16.1	9
Borderline	**2**	-1.3 to-2.0	**6.7**	2
Defective	**1**	-2.0 and below	**2.2**	-

Adapted from Mansfield (2002).

Although parametric assumptions of homogeneity of variance and normal distribution do not apply to the current statistical analysis (given the sample, methodology and research questions) descriptive statistics were used as a means of gaining a fuller understanding of the data set (Howell, 2002; Terre Blanche & Durrheim, 1999). More specifically the descriptive data was used to explore whether the participants pattern of neuropsychological functioning was comparable to the existing literature (see Chapter 3, research question 3).

4.5.2 Parametric and non-parametric inferential analysis

The coded data was then explored inferentially. The coded data was used to investigate differences between the participants, utilising various parametric and non-parametric methods (Howell, 2002). The non-parametric Wilcoxon rank sum and Sign tests were utilised rather than parametric tests due to violation of parametric test assumptions (small sample size and non-normal distribution of test scores) (Howell, 2002).

The Wilcoxon rank sum test is one of the most common non-parametric tests and is often considered the non-parametric analogue of the t-test (Howell, 2002). This tests looks for differences in central tendencies between samples (assumed to be sampled from identical populations) (Howell, 2002). A significant Wilcoxon rank sum test indicates rejection of the null hypothesis with the groups being found to be significantly different from each other (Howell, 2002).

Additionally, the parametric Chi-square distribution test (applicable as its assumptions are more flexible than other parametric tests) was used (Harley, 2004; Howell, 2002). The Chi-square statistic measures associations between categories of nominal data with the assumptions that observations are independent, non-occurrences were taken into account and the total sample size is larger than the number of cells (Howell, 2002; Morgan, Reichert & Harrison, 2002). Although no formal hypotheses were posed, this section addressed the research question of patterns of differences in neuropsychological functioning between the participants (see Chapter 3, research questions 1 and 4).

4.5.3 Between participants: Differences in cognitive domains

Within the tests the data was organised into various cogent categories, using *a priori* behavioural and cognitive domains in an attempt to tease out various dimensions of differences between the participants (Lezak, 2004, p.334; Mansfield, 2002). The data was divided into test sub-groupings (see Table 4.5) as suggested by Lezak (2004, p. 334) with the aim of investigating any pattern to the difference of neuropsychological test scores of the participants (see Chapter 3, research question 5). Although Lezak (2004) and Kolb and Whishaw (1999) concede that such coarse division of tests could be problematic they reiterate that many of the cognitive functions involved in the various tests may be generally divided along such accepted guidelines. Following these divisions each sub-grouping of tests was analysed through the Chi-square test for differences between the participants.

Table 4.5: Division of tests into sub-groupings

Attention, Tracking & Concentration	**Perception & Reasoning**	**Memory & Learning**	**Verbal Functions & Language skills**	**Construction**	**Executive Function**
Stroop test	WAIS Picture Completion	RAVLT (all sub-tests)	COWAtest (all sub-tests)	Bender Gestalt test	WCST
SDMT	Facial Recognition test	WMS-III (all sub-tests)	WAIS Vocabulary	VOT	WAIS Comprehension
TMT	VOT	RCFT (all sub-tests)	WAIS Information	RCFT (all sub-tests)	WAIS Arithmetic
WAIS Digit Span	SDSS			WAIS Block Design	WAIS Picture Completion
WAIS Arithmetic	Skin Writing test				WAIS Picture Arrangement
WAIS Digit Symbol	WAIS Picture Arrangement				WAIS Similarities
Line bisection test					Austin Maze

4.5.3.1 Attention, tracking and concentration

The attention, tracking and concentration sub-grouping includes the Stroop test which is sensitive to both left and right hemispheric difficulties, but is particularly sensitive to executive difficulties (Lezak, 2004). The SDMT is sensitive to acute organic cerebral dysfunction (Lezak, 2004). The TMT is linked to frontal activation with both the SDMT and TMT being affected by motor speed (Lezak, 2004). The WAIS-III arithmetic, WAIS-III digit span and WAIS-III digit symbol are sensitive to diffuse versus focal hemispheric damage (Lezak, 2004). The Line bisection test is sensitive to right hemisphere lesions. Right hemisphere lesions may in fact lead to bilateral deficits - this is an interesting contrast to left hemispheric lesions which usually lead only to right-sided deficits (Lezak, 2004).

4.5.3.2 Perception and reasoning

The sub-grouping of perception may be divided into visual, tactile, olfactory and auditory perceptual functioning (Kolb & Whishaw, 2003). Perceptual and memory functions are necessarily related since experience provides a framework for interpreting information. The same overlap therefore applies to tests of perception, memory, learning, and constructional ability, which one must bear in mind when interpreting results (Lezak, 2004).

This subgrouping includes WAIS-III Picture Completion, WAIS-II1 Picture Arrangement, the Facial recognition test (sensitive to right lesions especially temporal lesions) and the Hooper VOT (sensitive to right frontal lobe lesions) (Lezak, 2004). Tactile perception tests include the SDSS and Skin writing tests. These tests are sensitive to medial hemispheric surfaces and can lateralise areas of damage (Lezak, 2004). No auditory or olfactory perceptual tests were utilised.

4.5.3.3 Memory and learning

The memory and learning sub-grouping comprises tests which appear to measure complex brain systems which include span of immediate memory, learning, retrieval, visual memory and verbal memory (Lezak, 2004). Memory and learning functions are linked to many areas in the brain including frontal, temporal and limbic systems (Kolb & Whishaw, 2003; Lezak, 2004).

This sub-grouping included the WMS-III which tests a relatively large number of memory functions. The RAVLT (verbal memory) is sensitive to frontal difficulties (Lezak, 2004). Such

difficulties often result in a poor learning curve (Lezak, 2004). The RCFT (visual memory) is sensitive to right sided and frontal lesions leading to poor recall and impoverished designs (Lezak, 2004).

4.5.3.4 Verbal functions and language skills

This sub-grouping consists of the COWA which is sensitive to left hemispheric, particularly frontal, lesions (Lezak, 2004). However, right hemispheric lesions may impair verbal fluency on this test (Kolb & Whishaw, 2003; Lezak, 2004). The WAIS-III Vocabulary and Information sub-tests are sensitive to left hemispheric lesions (Lezak, 2004).

4.5.3.5 Construction

The construction sub-grouping includes perceptual, motor and spatial abilities and can be divided into drawing, building and assembling (Lezak, 2004). The tests in this area included the Bender Gestalt test which is specifically sensitive to right hemispheric parietal lobe lesions leading to piecemeal designs (Lezak, 2004), the Hooper VOT and WAIS-III Object Assembly and the RCFT where planning difficulties indicating frontal involvement (Lezak, 2004). The WAIS-III Block Design is sensitive to many lesion types, however, right-sided lesions are often associated with increased errors (Lezak, 2004).

4.5.3.6 Executive function and concept formation

The executive function and concept formation sub-grouping assesses conceptual concreteness, mental flexibility and planning (Lezak, 2004). This sub-grouping consisted of the WCST, Austin Maze, WAIS-III Comprehension, Arithmetic, Picture Completion, and Picture Arrangement.

The Austin maze is sensitive to executive problems indicated by slower maze completion times, perseveration of errors and poor planning (Lezak, 2004). WAIS-III Comprehension test which is sensitive to right-sided lesions and is a good indicator of pre-morbid abilities. WAIS-III Arithmetic has a verbal component and generally left sided lesions impair performance more significantly than right sided lesions (Lezak, 2004). WAIS-III Similarities are sensitive to frontal lesions (Lezak, 2004). WAIS-III Picture Completion and Picture Arrangement are sensitive to right frontal involvement (Lezak, 2004).

4.5.4 Between participants: Lobal and hemispheric functioning

Composite scores reflecting various lobal and hemispheric functioning (as opposed to cognitive) domains, as outlined by Lezak (2004) and Blanchard and Neale (1994), were created and evaluated for differences (see Table 4.6). Despite possible differences in cognitive functioning an investigation into specific lobal and hemispheric functioning was deemed useful. Blanchard and Neale (1994) separated out a number of tests according to their hemisphere or lobal primary functioning. This analysis explored the question around the pattern of differences between the twins hemispheric functioning (see Chapter 3, research question 6). Following the division of tests into hemispheric and lobal sections Chi-square data analysis was performed.

Table 4.6: Division of tests into lobal and hemispheric sub-groupings

Left Hemisphere Tests	**Right Hemisphere Tests**	**Frontal lobe/ executive Tests**	**Lateralising focal lesion Tests**
WMS-III logical memory immediate	Bender Gestalt test	Austin Maze	Line Bisection test
WMS-III logical memory delayed	RCFT (all sub-tests)	WCST	SDSS
Stroop test	Facial Recognition test	Stroop test	Skin Writing test
COWA test (all sub-tests)	VOT	COWA test (all sub-tests)	
Facial Recognition test	WMS-III visual immediate memory		
	WMS-III visual delayed memory		

4.5.5 Notable qualitative components

Lastly in various test (such as PANSS, MMPI-III and RCFT) certain qualitative phenomena within the test may be described in a qualitative assessment section within the data analysis. This section is important in describing non-quantifiable phenomena within the research data which may contribute to the understanding of the structure, functioning and dysfunction of the participants' cognition (Blanchard & Neale, 1994; Shallice et al., 1991; Shallice, 2004).

CHAPTER FIVE

RESULTS

5.1 Case History

Abbey and Gail (CVA) are monozygotic twins, concordant for schizophrenia (diagnosed at 15 years and 4 months and 15 years and 10 months respectively) and discordant for a right hemisphere frontal anterior cerebral artery CVA (when both twins were 37 years 2 months). The family history is negative for psychiatric illness, neurological or coronary disease.

5.1.1 Pregnancy and birth

The twins were the result of an unplanned but wanted pregnancy to a 27-year-old mother and 29-year-old father. The specialist obstetrician confirmed the presence of monzygotic twins (sharing a placenta and chorion) in the 32nd week of the pregnancy. The pregnancy progressed without significant event, and culminated in the twins-birth through spontaneous vaginal delivery three days prior to their estimated due date. Gail (CVA) weighed 2.5 kilograms at birth, with Abbey weighing 2.6 kilograms. Eleven months after the birth of the twins a younger brother was born. Both twins were breast-fed until six months old.

5.1.2 Early development

According to familial report, all motor and speech developmental milestones (including rolling, sitting, crawling, walking, word and sentence formation, and toilet-training) were reached

appropriately. Both twins are right handed. As infants and young children the twins were social and cheerful, but were described as living in 'a world of their own' often communicating with one another through terms and words their family did not understand.

5.1.3 Pre- and primary schooling

The family remained fairly insular and home-schooled the twins through pre-school. The twins entered a public school from grade R (seven years old) onward, and completed grade R through 7 with no reported problems. Both Abbey and Gail (CVA) remained in the same home class through this period. From school progress reports, the twins' academic achievements were matched almost identically with high scores being consistently achieved. The twins were popular in both the social and sporting arenas and socialised together. At this stage Gail (CVA) was described as more 'girly' while Abbey was said to have developed into a 'tomboy'. With the exception of single bouts of childhood chickenpox and mumps, both twins' medical histories were unremarkable.

5.1.4 Secondary schooling

Entering high school for grade eight became increasingly stressful for both twins as they were separated into different classes for the first time in their schooling careers. Although both twins continued to progress in academic and sporting arenas their social relationships became strained. Increasingly unusual behaviour was noted from both twins who developed unfounded paranoid concerns. From parental reports Abbey, particularly, became increasingly fearful with escalating paranoid concerns for her life, withdrawing from social interaction with affective changes (developing a negative mood) and decreased motivation. Following a family disagreement when

the twins were in grade nine (O-levels) Abbey's behaviour became of greater concern to the family and she was admitted to a general medical hospital. Following a full assessment with a consultant psychiatrist at the hospital Abbey was diagnosed with Undifferentiated Schizophrenia, medicated with a low potency antipsychotic (thioridazine, or trade name *Melleril)* and discharged. The total duration of the hospital stay was three weeks. During this period parental reports indicated that Gail's (CVA) paranoid concerns seemed to improve slightly, and she was extremely concerned for her twin.

Abbey remained at home for a period of four months, later returning to grade nine (C-stream). Gail's (CVA) mental state declined during this period and six months after Abbey was admitted to hospital, Gail (CVA) was admitted with paranoid concerns, social withdrawal and affective changes (from parental report). The duration and procedure followed during Gail's (CVA) admission was similar to that of her sister and she was released two weeks after admission on the same dosage of thioridazine as Abbey. Gail (CVA) returned to public school grade 10 (C-stream) the following year after completing her grade 9 O-levels through home schooling. Both Abbey and Gail (CVA) continued their (public) schooling and completed their M-levels (grade 12 equivalent), however, both twins suffered a number of relapses due to medication non-compliance. During this period Abbey and Gail's (CVA) family were reportedly supportive of the twins and were involved with their rehabilitation.

5.1.5 Occupational history

Following completion of M-levels Abbey pursued a typing course while Gail (CVA) chose a secretarial course. During this period both twins remained living at home and on their medication (thioridazine), with residual positive and negative symptoms (from psychiatric case

file). Their psychiatric care was provided by provincial mental health facilities. Both twins developed strong artistic flare and humanitarian interests while doing art courses and volunteering at a home for the physically disabled. Although the twins were increasingly individuated during this period, making separate groups of friends, they remained relatively close. The twins developed an interest in the opposite gender however, had no suitors, but many male friends. Both twins completed their selected courses.

Gail (CVA) started secretarial work in a large bank while Abbey began work in a typing pool. However, both twins found the demands of working life increasingly stressful and both lost their jobs. After trial periods in various other jobs over a number of years both twins struggled to cope with the pressures placed upon them and eventually entered into a sheltered employment scheme in their late twenties. During this period the twins' medication was changed to sulpiride (trade name *Eglonyt)* due to negative side effects. Later, in order to better stabilise the twins negative symptoms and decrease side effects their medication was changed to flupenthixol (or trade name *Fluanxol),* clozapine (25 mg tablets) and carbamazepine (200 mg), on which they currently remain.

After receiving a Disability Grant both twins decided to leave the sheltered employment work to pursue their hobbies at home, and progressed uneventfully over a period of years. During this time the twins' positive symptoms were largely stable with their negative symptoms becoming more pronounced with gradually decreasing interest in many of their preferred hobbies, additionally their symptom profile shifted to that of Residual Schizophrenia.

5.1.6 CVA

Roughly six months prior to Gail's CVA her mood reportedly changed with Gail (CVA) becoming increasingly irritable and 'tense'. Consultation with the family physician revealed no increase in blood pressure or other physical anomaly. However, in 2002 Gail (CVA) was rushed to the emergency room by her family suffering from left sided hemiplegia, hemisensory loss and confusion. Neurological screening investigations at a tertiary level hospital were negative for cardiac embolism and coagulation. From medical reports (no imaging data available) CT and MRI imaging revealed a right hemispheric prefrontal and premotor cortex anterior cerebral artery arterial dissection resulting in an intramural hematoma and subsequent cerebral haemorrhage. Gail's (CVA) condition began to gradually improve after several days. Upon discharge from hospital after two weeks Gail (CVA) was referred to a specialist tertiary hospital for combined neurological and psychiatric care following the occurrence of post-CVA seizures.

Besides the post-CVA seizures (which remitted within a number of months post-CVA) and residual left-sided hemiplegia, Gail's (CVA) family described her emotional improvement as astounding with one family member stating "it was like overnight she was back to my old Gail (CVA), like before she was even diagnosed (with schizophrenia)". Gail's (CVA) condition continued to improve, and although her family noted several neuropsychological dysfunctions resulting from the CVA (left-sided hemiplegia, hemisensory loss and tone-deafness amongst others), they were pleased overall with Gail's (CVA) improvements as she became increasingly sociable, motivated to participate in several of her prior hobbies and help where she could around the house. Significantly the family noted Gail's (CVA) new found (or re-found) ability to initiate conversations and sustain active conversations beyond monosyllabic answers as well as display a range of emotions (from happiness and anger to sadness). This was in contrast to

Abbey whose symptoms remained stable. Additionally, Abbey seems to have taken little notice of Gail's (CVA) changes in social and affective functioning.

Currently both Abbey and Gail (CVA) remain on the same medications as previously (fiupenthixol, and clozapine [25 mg] and carbamazepine [200 mg]) with no break or shift in their treatment (both participants were on this medication during the assessment process). Gail's (CVA) medical condition has stabilised and she continues her bi-weekly physical therapy. Additionally, Gail's (CVA) improved affect, social functioning and motivation has remained and her improved overall functioning has continued, while Abbey's condition has remained unchanged.

5.2 Z-score data descriptive analysis

All tests were scored according to manual instructions and were converted into z-scores as per convention (see Chapter 4, Tables 4.3 and 4.4) (Howell, 2002; Lezak, 2004). The data was then explored via descriptive statistics as a means of gaining a fuller understanding of the data set. The descriptive data was used to explore whether the participants' pattern of neuropsychological functioning was comparable to the existing literature (see Chapter 3, research question 3).

Table 5.1: Sub-division of data points amd z-scores for both participants

Test	**Sub-test/s**	**Abbey Z-scores**	**Gail (CVA) Z-scores**
1-2. SDMT	SDMT - Written	-2.20	-4.20
	SDMT - Oral	-2.30	-3.30
3-4. TMT	TMT-A	-1.90	-2.40
	TMT-B	-5.50	-2.70
5. Stroop test	-	-3.20	-2.20
6. PANSS	-	-3.00	-1.50
7. VOT	-	-0.50	-3.50
8. Skin Writing test	-	0.00	-2.00
9. SDSS	-	0.00	-2.20
10. Line Bisection test	-	-1.00	-2.50
11. Facial Recognition test	-	-2.00	-1.10
12. WCST	-	-1.50	-0.90
13. Austin Maze	-	-1.60	-1.00
14-16. COWA test	COWA test C	-2.50	-2.00
	COWA test F	-3.00	-2.10
	COWA test L	-1.30	-1.70
17. Bender Gestalt test	-	-2.00	-2.50
18-34. WAIS-III	WAIS-III FIQ	-1.60	-1.80
	WAIS-III VIQ	-1.90	-1.20
	WAIS-III PIQ	-1.10	-2.00
	WAIS-III Picture completion	-2.50	-3.00
	WAIS-III Vocabulary	-1.70	-1.80
	WAIS-III Digit Symbol	-2.30	-3.00
	WAIS-III Similarities	-1.50	-1.50
	WAIS-III Block design	-1.00	-2.00
	WAIS-III Arithmetic	-4.00	-4.00
	WAIS-III Matrix reasoning	-2.00	-2.00
	WAIS-III Digit span	-1.70	-2.30
	WAIS-III Information	-2.00	-2.00
	WAIS-III Picture arrangement	-4.00	-4.00
	WAIS-III Comprehension	-1.50	-2.50
	WAIS-III Symbol search	-1.50	-1.50
	WAIS-IU Letter-number sequencing	-1.50	-2.00
	WAIS-III Object assembly	-1.00	-1.50
35-42. WMS-III	WMS-III Auditory immediate	-0.40	-0.10
	WMS-III Auditory delayed	-0.50	-1.30
	WMS-III Visual immediate	-2.60	-2.90
	WMS-III Visual delayed	-2.30	-3.10
	WMS-III Immediate memory	-1.70	-1.60
	WMS-III Auditory recognition delayed	-2.30	-3.00
	WMS-III General memory	-1.90	-2.90
	WMS-III Working memory	-1.70	-2.10
43-46. RAVLT	RAVLT List A total	-3.50	-3.40
	RAVLT List B total	-1.70	-1.70
	RAVLT Recall	-1.40	-2.10
	RAVLT Recognition	-3.00	-4.00
47-50. RCFT	RCFT Copy	-1.60	-4.00
	RCFT 3-minute immediate recall	-2.50	-3.30
	RCFT 30-minute delayed recall	-1.90	-3.30
	RCFT Recognition	-1.90	-4.00

Table 5.2: Descriptive statistics of z-score neuropsychological test data

		Abbey Non-CVA	Gail CVA
N	Valid	50	50
	Missing	0	0
Mean Z-score		-1.9440	-2.3740
Std. Error of Mean		.14320	.13361
Median Z-score		-1.9000	-2.1500
Std. Deviation		1.01261	.94476
Variance		1.02537	.89258
Skewness		-.902	-.173
Std. Error of Skewness		.337	.337
Minimum Z-score		-5.50	-4.20
Maximum Z-score		.00	-.10
Percentiles	25	-2.3500	-3.0250
	50	-1.9000	-2.1500
	75	-1.5000	-1.7000

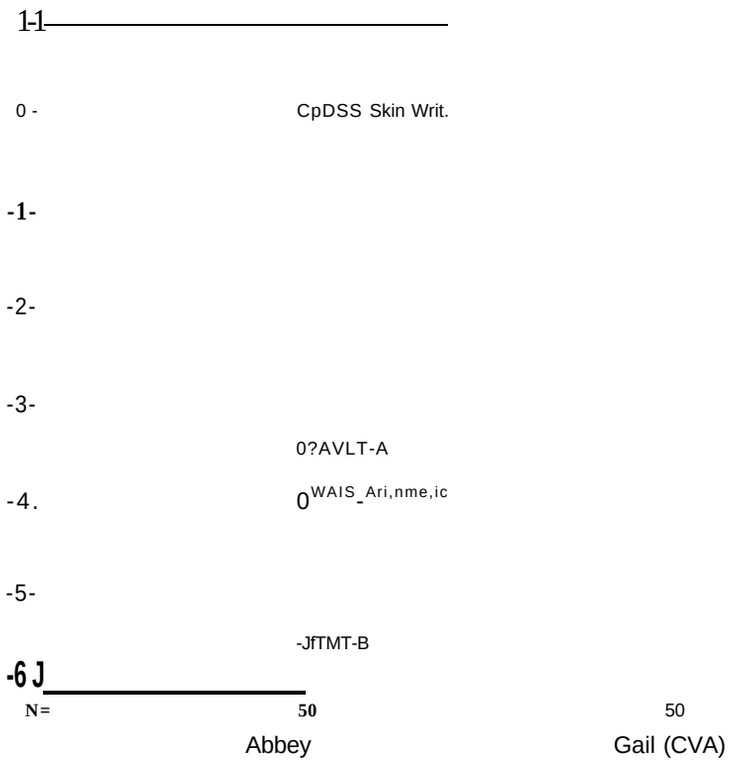


Figure 5.1: Boxplot for z-scores for all neuropsychological tests for both participants

5.3 Parametric and non-parametric inferential analysis

5.3.1 Chi-square test

The Chi-square test for significance was used to analyse for differences between the participants (Howell, 2002; Morgan et al., 2002). This section addressed the research question of difference in neuropsychological functioning between the participants (see Chapter 3, research question 4). Two assumption of the chi-square test (total number of observations should be greater than the number of cells and no cell frequency should be less than one) were violated in the data analysis (Howell, 2003). However, Howell (2003) states that despite violation of these assumptions the analysis remains valid for large frequency tables.

Table 5.3: A 2 x 4 Chi-square contingency table for participants by z-score category

			COLUMN				Total
			Defective	Borderline	Low Average	Average	
ROW	Abbey Non-CVA	Count	15	25	8	2	50
		Expected	21.5	20.5	7.0	1.0	50.0
		ROW	30.0%	50.0%	16.0%	4.0%	100.0%
		COLUMN	34.9%	61.0%	57.1%	100.0%	50.0%
		% of Total	15.0%	25.0%	8.0%	2.0%	50.0%
	Gail CVA	Count	28	16	6	0	50
		Expected	21.5	20.5	7.0	1.0	50.0
		ROW	56.0%	32.0%	12.0%	.0%	100.0%
		COLUMN	65.1%	39.0%	42.9%	.0%	50.0%
		% of Total	28.0%	16.0%	6.0%	.0%	50.0%
Total		Count	43	41	14	2	100
		Expected	43.0	41.0	14.0	2.0	100.0
		ROW	43.0%	41.0%	14.0%	2.0%	100.0%
		COLUMN	100.0%	100.0%	100.0%	100.0%	100.0%
		% of Total	43.0%	41.0%	14.0%	2.0%	100.0%

Note: Chi-square (3, N = 100) = 8.192, p = 0.04, Cramer's V = 0.042.

The relationship between participant and z-score category of neuropsychological test score was significant, Chi-square (3, N = 100) = 8.192, p = 0.04, Cramer's V = 0.042 indicating a deviation in the distribution of scores across the different categories from that expected by chance. When test score category was considered as a continuous variable, the strength of the relationship between test score category and the dichotomous independent variable (participant: Abbey Non-CVA/ Gail CVA) was fair Eta = 0.286, with Eta representing the strength of the association between a nominal and interval variable (Eta squared = 0.082).

5.3.2 The Wilcoxon rank sum test

The Wilcoxon rank sum test was used to examine differences in central tendencies between the participants in the total data set.

Table 5.4: Wilcoxon rank sum test for participant and z-score category

	ROW	N	Mean Rank	Sum of Ranks
COUNT	Abbey Non-CVA	50	39.26	1963.00
	Gail CVA	50	61.74	3087.00
	Total	100		

Note: z = -3.966, p = 0.004.

The Wilcoxon rank sum test revealed that the mean ranks between participant and neuropsychological test score (1963 for participant A; 3087 for participant G, with $n = 50$) were significantly different, z (100) = -3.966, $p = 0.004$. This result indicates that the participants' neuropsychological test z-score were significantly different from one another.

5.3.3 The Sign test

After establishing that there is a statistically significant difference between the participants (above) the Sign test was use to determine the direction of the difference (Howell, 2002).

Table 5.5: The Sign test for direction of differences in neuropsychological test scores

		N
Gail CVA - Abbey NonCVA	Negative Differences(a)	31
	Positive Differences(b)	12
	Ties(c)	7
	Total	50

a (G) SCORE < (A)SCORE
b (G) SCORE > (A) SCORE
c (G) SCORE = (A) SCORE
Note: Z = -2.745, p = 0.009.

From the Sign test Gail (CVA) achieved significantly more negative scores than Abbey (Z = -2.745, p = 0.009).

5.4 Cognitive domain analysis

As results indicated a significant difference between the participants an investigation into where these differences may lie was pertinent to this study. Therefore, the data was divided into test sub-groupings and patterns of differences in the neuropsychological test scores was investigated (see Chapter 3, research question 5).

Table 5.6: Division of tests into sub-groupings and Chi-square data analysis

Attention & Tracking	**Perception & Visual Reasoning**	**Memory & Learning**	**Verbal Functions & Language skills**	**Construction**	**Executive Function**
Stroop test	WAIS Picture Completion	RAVLT (all sub-tests)	CO WA test (all sub-tests)	Bender Gestalt test	WCST
SDMT	Facial Recognition test	WMS-III (all sub-tests)	WAIS Vocabulary	VOT	WAIS Comprehension
TMT	VOT	RCFT (all sub-tests)	WAIS Information	RCFT (all sub-tests)	WAIS Arithmetic
WAIS Digit Span	SDSS			WAIS Block Design	WAIS Picture Completion
WAIS Arithmetic	Skin Writing test				WAIS Picture Arrangement
WAIS Digit Symbol	WAIS Picture Arrangement				WAIS Similarities
Line bisection test					Austin Maze
Chi-square (1,N = 12) = 2.286,/? = 0.09 Not significant	Chi-square (3,N=14) = 7.778, /? = 0.052; Approaching significance	Chi-square (2, N = 32) = 4.399, *p* = 0.50 Not significant	Chi-square (2,N=10) = 2.000, *p* = 0.10 Not significant	Chi-square (2,N = 14) = 7.371,/? = 0.03 Significant	Chi-square (2,N = 14) = 6.000,/? = 0.05 Significant

$p < 0.05$

From the analysis significant differences were found within the construction (Chi-square [2, N = 14] = 7.371,/? = 0.03) as well as the executive function (Chi-square (2, N = 14) = 6.000, p = 0.05) sub-groupings. The perception sub-grouping approached significance (Chi-square [3, N = 14] = 7.778, p = 0.052). Other sub-groupings revealed no significant differences between the participants.

Following these findings the Sign test was used to examine directions of differences between the statistically significantly difference areas cited above.

Table 5.7: The Sign test for direction of difference in construction ability

		N
Gail CVA - Abbey NonCVA	Negative Differences(a)	7
	Positive Differences(b)	0
	Ties(c)	0
	Total	7

a (G) SCORE < (A) SCORE
b (G) SCORE > (A) SCORE
c (G) SCORE = (A) SCORE
Note: Z = -2.415, p = 0.01.

From the Sign test Gail (CVA) has statistically significantly more negative scores than Abbey (Z = -2.415, p = 0.01).

Table 5.8: The Sign test for direction of difference in executive functioning

		N
GaU CVA - Abbey NonCVA	Negative Differences(a)	2
	Positive Differences(b)	3
	Ties(c)	2
	Total	7

a (G) SCORE < (A) SCORE
b (G) SCORE > (A) SCORE
c (G) SCORE = (A) SCORE
Note: Z = -2.200, p = 0.02.

From the Sign test Abbey has statistically significantly more negative scores than Gail (CVA) (Z = - 2.200, p = 0.02).

5.5 Lobal and hemispheric domain analysis

Although the participants displayed significantly different cognitive functioning in the areas of construction and executive functioning an investigation into specific lobal and hemispheric functioning was deemed useful to questions around the pattern of differences between the twins contributing meaningful data to hemispheric theories (see Chapter 3, research question 6).

Following the division of tests into hemispheric and lobal sections Chi-square data analysis was performed. Despite test assumption violation, again Howell's (2003) assertion that the test remain viable was considered.

Table 5.9: Division of tests into lobal and hemispheric sub-groupings and Chi-square analysis

Left Hemisphere Tests	**Right Hemisphere Tests**	**Frontal lobe/ Executive Tests**	**Lateralising for focal lesion Tests**
WMS logical memory immediate	Bender Gestalt test	Austin Maze	Line Bisection test
WMS logical memory delayed	RCFT (all sub-tests)	WCST	SDSS
Stroop test	Facial Recognition test	Stroop test	Skin Writing test
COWA test (all sub-tests)	VOT	COWA test (all sub-tests)	
Facial Recognition test	WMS visual immediate memory		
	WMS visual delayed memory		
Chi-square (3, 4) = 2.533,/? = 0.08 Not significant	Chi-square (3,N = 18) = 6.923, *p > 0.05, p* = 0.061 Approaching significance	Chi-square (2,N = 12) = 3.600,p = 0.077 Not significant	Chi-square (3,N = 6) = 8.000,p = 0.03 Significant

Categories adapted from Blanchard and Neale (1994). $P < 0.05$

From the Chi-square analysis the lateralising data was significantly different between the participants (Chi-square [3, N = 6] = 8.000, $p = 0.03$) with the right hemisphere data approaching significance (Chi-square [3, N = 12] = 6.923,/? > 0.05, $p = 0.061$). Other divisions revealed no significant differences between the groups.

Following these results the Sign test was utilised in order to determine the direction of the differences in the statistically significantly different areas of lobal and hemispheric functioning.

Table 5.10: The Sign test for direction of difference in lateralisation

		N
Gail CVA - Abbey NonCVA	Negative Differences(a)	3
	Positive Differences(b)	0
	Ties(c)	0
	Total	3

a (G) SCORE < (A) SCORE
b (G) SCORE > (A) SCORE
c (G) SCORE = (A) SCORE
Note: Z = -.002, $p = 0.09$

From the Sign test neither Gail (CVA) nor Abbey have directionally different lateralisation scores (Z =-.002,^ = 0.09).

Table 5.11: The Sign test for the direction of difference in right hemispheric functioning

		N
Gail CVA - Abbey NonCVA	Negative Differences(a)	8
	Positive Differences(b)	0
	Ties(c)	0
	Total	8

a (G) SCORE < (A) SCORE
b (G) SCORE > (A) SCORE
c (G) SCORE = (A) SCORE

Note: Z =-2.899. p = 0.045.

From the Sign test Gail (CV A) has statistically significantly more negative scores than Abbey (Z = -2.899,/? = 0.045).

In summary, from the results presented above the twins' overall pattern of neuropsychological functioning was found to be significantly different (from Chi-square and Wilcoxon rank sum tests). The main differences between the twins' functioning lay in constructional and executive function abilities. Further, lateralisation functioning was found to be significantly different between the twins with a difference in right hemisphere functioning approaching significance. From the Sign tests of direction the differences between the participants were as follows: executive functioning more negative scores for Abbey, construction ability more negative score for Gail (CVA), right hemisphere functioning more negative scores for Gail (CVA). Inconclusive directionality of the lateralising tests was revealed.

5.6 Notable qualitative components of the test data

Although both participants attempted a best performance throughout the testing Gail (CVA) was noticeably more anxious and was aware when she was doing poorly. However, Abbey appeared oblivious to whether her performance was average or not and exhibited little anxiety throughout the entire assessment proceedings. This may be attributed to Abbey's overall more poor executive functioning (as shown above) with poor self-regulation and self-monitoring. Abbey may be suffering from Anosonagnosia (the inability to recognise or acknowledge illness or bodily defect) consistent with right hemispheric dysfunction (Kolb & Whishaw, 2003).

Both the PANSS and the MMPI-II indicate that the participants have a significantly different profile of schizophrenia symptomatology. From the PANSS Abbey's overall negative symptoms fall into the z-score 'defective' range, while Gail's (CVA) symptoms were markedly less severe, overall falling into the z-score 'low average' range. Abbey's MMPI-II profile showed a significant elevations on the schizophrenia scale (T = 83), social introversion scale (T = 84) and psychasthenia scale (T = 86). Gail's (CVA) MMPI-II profile showed significant elevation on the depression scale (T = 71), with sub-threshold clinical scores on both the schizophrenia and social introversion scales (see chapter 3, research question 1).

From observation Gail (CVA affected) exhibited some rotation and perseveration in her Bender Gestalt test. Both Gail's (CVA) RCFT 3-minute and 30-minute recall tests were extremely poor with some internal details remembered, however, the overall gestalt of the drawing was missing (see Appendix A).

From observation Abbey (non-CV A affected) exhibited some rotation and perseveration in her Bender Gestalt test, as well as over-working of the lines. In the RCFT Abbey's drawings were overworked and her 3-minute and 30-minute recall drawing exhibited some of the original overall structure however, was lacking in internal detail. From the VOT Abbey showed some bizarre responding common to individuals with schizophrenia with responses such as membrane (picture 17), blood pressure monitor (picture 27) and pepper (picture 30).

CHAPTER SIX

DISCUSSION AND CONCLUSION

6.1 Neuropsychological findings

When considering the results a comparison of the participants' performance to the literature was essential (as outlined in Chapter 3). However, due to the lack of directly corresponding literature, the participants' results had to be compared to the general literature in the areas of schizophrenia, CVA and general neuropsychological principles of lobal and hemispheric functioning.

6.1.1 Research question 1; Differing negative symptoms

From the PANSS the participants have a significantly different profile of schizophrenia symptomatology, with Abbey's symptoms including moderately flat affect, moderate global ratings of alogia and avolition and a marked global rating of anhedonia. Gail's (CVA) symptoms were markedly less severe with mild ratings of alogia and affective flattening. Additionally, the MMPI-II indicates that while Abbey has a profile congruent to that expected of individuals with schizophrenia Gail's (CVA) profile lacked significant elevations in both the schizophrenia and social introversion scales (Butcher et al., 2001). This clinical picture is congruent with collateral accounts and psychiatric records of the participants' current symptomatology.

This finding pertaining to the first research question supports the assumption that there are differences in the participants' current negative symptom presentation.

6.1.2 Research question 2: Decline of cognitive functioning

Both participants' WAIS-III full scale IQ scores were in the upper borderline range and there were significant differences between verbal and performance indices. Gail's (CVA) verbal IQ was 13 scaled score points above her performance IQ score, falling in the low average range, while Abbey's verbal IQ was 12 points below her performance IQ score, falling into the lower borderline range.

Given the fact that both were able to finish secondary schooling it would be reasonable to assume that their pre-morbid intellectual ability was in the average range. It thus appears that there has been some decline in these indices, and this is likely attributable to mental illness or CVA. The finding of mild cognitive decline in early onset schizophrenia is well established in the literature (Blanchard, Horan & Collins, 2005; Bradshaw & Mattingley, 1999; Chan, 2004; Chan et al., 2004; Kolb & Whishaw, 2003; Lewis, 2003), and the cases under investigation seem to conform to this pattern. Further, literature indicates that post-CVA cognitive decline is common and may account for the variance between Gail's (CVA) verbal and performance scores (Kolb & Whishaw, 2003; Lewis, 2003).

Additionally the participants' below average scores in other areas of cognitive functioning (memory, attention, perceptual and executive functioning) indicate some level of cognitive decline in comparison to pre-morbid functioning, and functioning during the early stages of the disorder. These areas of decline are consistent with the literature of the cognitive profile of individuals with schizophrenia (Bradshaw & Mattingly, 1999; Chan et al., 2004; Heinrichs, 2005; Lewis, 2003; Roth et al., 2004).

This finding relating to the second research question seems to support the literature's findings of the presence of some measure of cognitive decline in individuals with early-onset schizophrenia.

6.1.3 Research question 3: Overall cognitive functioning

The literature's cognitive profile of individuals with schizophrenia (being low average to borderline intellectual functioning, low average memory functioning, borderline working memory, low average attention, borderline perceptual functioning and borderline executive functioning, see chapter 2, section 2.5) was compared to the participants' overall neuropsychological performance (Bradshaw & Mattingley, 1999; Chan, 2004; Chan et al., 2004; Lewis, 2003; Roth et al., 2004).

From the descriptive statistics the participants fell into the borderline range for full scale 1Q, with scores ranging from low average to defective on all other tests with the exception of the Skin writing test and SDSS. On these tests Abbey achieved an average score. Besides these scores no average, high average, superior or very superior scores were obtained by either participant.

From this profile the participants' overall neuropsychological functioning fits the general pattern of dysfunction common to individuals with schizophrenia described in the literature (Bradshaw & Mattingly, 1999; Chan, 2004; Chan et al., 2004; Lewis, 2003; Roth et al., 2004). Considering research question 3 this finding supports the assumption that the current cases under investigation have a cognitive profile similar to that expected for individuals with schizophrenia.

6.1.4 Research question 4: Differences between participants

From the Chi-square and Wilcoxon rank sum tests the participants' neuropsychological functioning was found to be statistically significantly different from one another. Both participants exhibited deficits in almost all areas of functioning (with 2 average scores achieved by Abbey only).

Abbey's largest deficits (with defective scores) were in the TMT, Stroop test, WA1S-III digit span, COWA test, WCST and Austin maze. Abbey had specific strengths in the Skin writing test, SDSS and WMS-III visual delayed recall tests. These scores are consistent with the expected performance as outlined by the literature (Bradshaw & Mattingly, 1999).

Gail's (CVA) largest deficits (defective scores) were in the WAIS-III arithmetic, SMDT (both written and oral), Skin writing test, SDSS, WAIS-III picture arrangement, WAIS-III picture completion, WMS-III auditory and visual delayed memory, WMS-III general memory, RCFT, Bender gestalt test, RAVLT and Hooper VOT. Gail (CVA) showed specific strengths (relative to her overall scores) in the WCST, Austin maze, WMS-III auditory immediate memory and PANSS. This performance seems consistent with Gails CVA, as well as deficits expected due to her psychiatric diagnosis (Lewis, 2003; Lezak, 2004).

On overall cognitive profile, from the Sign test, Gail (CVA) presented with a more deficient neuropsychological picture in comparison to her twin Abbey, with significantly more negative scores than Abbey. In relation to research question 4, this finding supports the assumption that

there are statistically significant differences between the participants' neuropsychological performance.

6.1.5 Research question 5: Between participants - cognitive domain analysis

Research question 5 queried patterns of differences between the participants. From the Chi-square analysis specific domains of neuropsychological functioning (see Chapter 4, Table 4.5) were statistically significantly different between the participants. The significant areas of difference were executive functioning and construction ability. Perception and reasoning differences approached significance. No other groupings of neuropsychological functioning were found to be statistically significantly different. These differences seem consistent with known deficits for right-hemispheric CVA (Kolb & Whishaw, 2003; Lezak, 2004) however, the more positive executive functioning score by Gail (CVA) seems unusual given her right-hemispheric prefrontal area CVA.

6.1.5.1 Attention, tracking and concentration

From the Chi-square analysis there was no statistically significant difference in attention, tracking and concentration ability between the participants. Both participants have significant attention difficulties.

6.1.5.2 Perception and reasoning

No statistically significant differences in perceptual ability were detected between the participants, however, Chi-square value did approach significance suggesting that there may be

some subtle differences in perceptual ability between the participants. This lack of specificity may have resulted from the grouping together of the visual perception and tactile perception tests. From eye-ball analysis there seemed to be a clear difference between the participants tactile perceptual abilities with Abbey scoring in the average range for both the SDSS and Skin writing test and Gail (CVA) scoring in the defective range for both of these tests. This difference may be linked to differences in the medial prefrontal and premotor areas between the twins (Lezak, 2004), and is consistent with the location of Gail's CVA.

6.1.5.3 Memory and learning

From the Chi-square analysis no statistically significant differences between the participants were found on this sub-grouping. However, a lack of differences between the participants does not necessarily imply similar functioning. Although not statistically significant, differences between the participants within the WMS-III alone were revealed. Abbey's delayed memory abilities scored consistently better than Gail's (CVA). Additionally, Abbey scored poorer in immediate memory tests.

6.1.5.4 Verbal functions and language skills

From the Chi-square analysis there was no statistically significant differences between the participants on verbal functions and language skills.

6.1.5.5 Construction

From Chi-square analysis the participants had a statistically significant different performance on the construction tests. From the Sign test Gail (CVA) had significantly more negative scores indicating that she did significantly worse than Abbey on these tests. These results suggest better perceptual, motor and spatial abilities in Abbey, and support the notion that her right hemisphere functions are more intact than those of Gail (CVA) as many of the tests in this sub-grouping were sensitive to right (particularly frontal) dysfunction. Generally this pattern of differential findings seems consistent with *a priori* predictions of deficits which would be associated with a right hemisphere CVA.

6.1.5.6 Executive functions and concept formation

From the Chi-square analysis there was a statistically significant difference between the participants' executive function and concept formation abilities. From this Sign test Abbey scored significantly more negative scores indicating a poorer performance than Gail (CVA) on this sub-grouping. As many of the tests used in this sub-grouping are sensitive to frontal functioning this may indicate better frontal functioning in Gail (CVA) compared to Abbey. However, considering Davidson's (1998; 2001; 2002; 2004) theories of right-sided BIS, a possible disruption (due to infarct) in the hyperactivation of this system (due to schizophrenia) may have led to decreased avoidance and dysinhibition, and increased spontaneity and self-regulation.

6.1.6 Research question 6: Between participants - lobal and hemispheric functioning

Research question 6 queried lobal and hemispheric differences between the participants. From the Chi-square analysis specific domains of neuropsychological functioning (see Chapter 4, Table 4.6) were statistically significantly different between the participants. The significant areas of difference were in lateralising tests, with 'right hemisphere' tests approaching significant. No other subgroupings were found to be approaching significance.

6.1.6.1 'Left hemispheric' tests

Chi-square analysis revealed no statistically significant differences between the participants' performance on the left hemispheric tests.

6.1.6.2 'Right hemispheric' tests

From Chi-square analysis a difference between the participants' right hemispheric functioning approached significance. The Sign test revealed significantly more negative right hemispheric scores for Gail (CVA) whose performance on these tests was worse than Abbey's. These results are consistent with Gail's CVA (Lezak, 2004). Additionally, the results seem to lend support to the extension of Davidson's (2002; 2004) theories to individuals with schizophrenia.

6.1.6.3 Frontal/ executive function tests

Chi-square analysis revealed no statistically significant differences between the participants on frontal lobe performance. This is contrary to cognitive domain findings where significant differences between executive functioning and concept formation alluded to differences in frontal functioning. From Davidson's (1998; 2000; 2004) theories both left and right sided dysfunctions were predicted in both participants, with additional difficulties for Gail (CVA). Therefore, this lack of significant difference in frontal functioning may be due to limited specificity and differentiation capabilities within the tests to discern between these deficits, a nuanced difficulty pointed out by Lezak (2004).

6.1.6.4 Lateralising tests

A statistically significant difference on Chi-square analysis of the participants' lateralising test scores was found. This finding is consistent with right hemispheric CVA findings (Lezak, 2004; Rey, 1964). However, from Sign test analysis no conclusive direction of positive versus negative function could be found.

6.1.7 General discussion

Overall PANNS, MMPI-II and the qualitative test data findings indicate that Gail (CVA) currently presents with significantly fewer negative symptoms in comparison with Abbey's current symptom presentation. Additionally, it seems that some cognitive decline, possibly related to their diagnosis of early-onset schizophrenic, is present in both twins. Furthermore the twins present with a pattern of neuropsychological deficits consistent with their diagnosis.

Significant differences between the twins' neuropsychological functioning exists. Abbey presented with a fairly constant picture of deficits (consistent with the literature). Gail (CVA) presented with global deficits as well as likely lesion specific deficits (seen in the right hemispheric and lateralising tests). Overall Abbey has a more positive neuropsychological profile, with Gail (CVA) presenting with global and lesion specific deficits.

From specific domain analysis, including construction and right hemispheric tests, Gail (CVA) presents specifically with greater right hemispheric deficits, including construction difficulties relating to right hemispheric frontal motor and premotor deficits (Kolb & Whishaw, 2003; Lezak, 2004), consistent with her CVA. This seems somewhat of a paradox considering her improved negative symptoms and significantly better executive function and concept formation in comparison with Abbey. These differences were specifically on the Austin maze and WCST. These indicate that Gail's (CVA) conceptual shifting, self-regulation and inhibition, planning, and concept formation abilities were significantly better than Abbey's. The better executive function and concept formation performance of Gail (CVA) seems consistent with improvements described in collateral accounts, and may be associated with changes in functioning of the executive system. As discussed above these may relate to a change in Gail's (CVA) hyperactive right-sided BIS as hypothesised by Davidson (1998; 2000; 2002; 2004).

6.2 Implications of the findings

The findings lend credence to Carpenter and Buchanan's (1994) classification model which includes a cognitive deficit domain. Additionally, the findings support the specific profile of cognitive deficits as suggested by Lewis (2003) and Heinrichs (2005). Further the findings

highlight the complexity inherent to the disorder, which should be reflected in the classification as well as complex biopsychosocial aetiological models (Hultman & Ohmna, 1998; Ishiguro et al., 2000; Rabkin, 1982; Zubin & Steinhauer, 1981).

Based on specific neurophysiological, neuropsychological and neuroscience theories (Beebe, 2003; Bradshaw & Mattingley, 1995; Cutting, 1994; Davidson, 1998; 2000; 2001; 2004; Heinrichs, 2005; Rector et al., 2005) a model of left frontal hypo functioning and right frontal (particularly medial prefrontal) hyperfunctioning, possibly related to anatomical or metabolic anomalies, was hypothesised for both participants. Additionally, a right premotor/prefrontal lesion in Gail (CVA) was hypothesised to lead to further right frontal dysfunction and possibly some measure of disconnection between various functionally related systems, relating to improved negative symptoms.

Despite the relatively poorer performance in tests thought to be associated with right hemisphere functions, it seems that the paradoxical improvement in negative symptoms is related to changes in frontal right hemispheric functions. Given the site of lesion, the right hemisphere executive system seems to be a likely candidate for the improvement in affective and motivational (inhibition) deficits (Davidson, 1998; 2000). Thus, it seems possible to infer that the right hemisphere executive system might contribute to negative symptom patterns in schizophrenia. Hence, when there is anterior right hemisphere damage, there is improvement in negative symptoms, but poorer performance in cognitive processing presumably associated with this area.

From the literature one can speculate as to what functional systems have been disrupted in order to explain Gail's (CVA) changes. Cortically the right ventral and medial prefrontal areas,

involved in social behaviour and affect mediation (as described by Bradshaw & Mattingley, 1995; Kolb & Whishaw, 2003; Lezak, 2004) may have been dysinhibited by the CVA. These areas have sub-cortical projections to the amygdala and tegmentum with reciprocal metabolism noted (Davidson, 1998, 2001; Kolb & Whishaw, 2003; Roth et al., 2004). Therefore, these sub-cortical structures may have been disrupted or disconnected decreasing negative affect and withdrawal (as described by Davidson, 2000, 2004) and increasing the setting of emotional tone, particularly to social cues (as outlined by Chan et al., 2004). Other cortico-cortical projections possibly affected by the CVA include pallidum and thalamus possibly resulting in further dysinhibition. However, the current neuropsychological investigation lacked the high degree of precision necessary to test more elaborate hypotheses or double dissociations.

6.3 Limitations of the research

As outlined in the methodology section above various methodological difficulties are inherent to the research of individuals with schizophrenia. Although the methodology of the current research was carefully considered to yield valuable research data as well as respect the participants' limitations and abilities, there are clear limitations to this research.

6.3.1 Methodological limitations

From a methodological viewpoint it is important to stress the problems one would face in attempting to generalise the findings.

First, although this study included in-depth neuropsychological data collection, data such as neuroimaging, may have been useful for the various neuro-anatomical and functional

perspectives they provide. Additionally, without neuroimaging data the assertion of more concrete causal hypotheses regarding exact CVA location and neuro-chemistry are extremely difficult.

Second, as outlined in the methodology section, research on this special population itself presents inherent difficulties. One must consider the very nature of the individual's symptoms being studied (negative symptoms). As such, involving these individuals in in-depth research may be problematic given their levels of social functioning and ability to tolerate challenges and frustration.

Third, one must consider the use of neuropsychological tests created, normed and standardised on foreign populations, on a South African population. Although these participants were deemed satisfactory for the neuropsychological tests, these participants are not the ideal population group on whom the tests were normed and standardised. As such, various test artefacts may have created nuisance variables which could have impacted on the research findings.

Fourth, the difficulty and relative artificiality of the various sub-groupings and hemispheric groupings constructed by this research, in line with common neuropsychological practice, should be considered. Although this research does lend itself to the division of functioning into sub-groups due to the number of tests employed, Lezak (2004) points out that, despite various areas of neuropsychological functioning being amenable to sub-grouping, it is impossible to completely isolate various functions. Not only is the current knowledge of the exact locations of various functions still being established (in this research, but additionally within Cognitive Neuropsychology as a discipline), but it is known that many functions employ various brain

structures in different and sometimes contralateral areas. Therefore, these cannot be simply localised and divided into specific areas.

Additionally, the investigation of separate hemispheres and their functioning is difficult as the exchange and interplay between the various structures and hemispheres within the human brain is continuous (Lezak, 2004). Despite the sub-groupings of functioning being a common neuropsychological practice it is largely an artefact of modern classification systems within neuropsychology and may lead to other, more subtle, differences between participants being missed. Although these systems are currently widely used within the discipline, future re-classifications and research may reveal important differences that, although not new, are being exposed and explored for the first time.

Finally left hemispheric functioning was not as deeply explored as right hemispheric functioning by this research. The reasons for this include, firstly, the participants current psychiatric diagnosis, namely that of Residual schizophrenia. By definition this diagnosis involves no or few positive symptoms (which are largely located in the left hemisphere by the literature), but with residual negative symptoms remaining (APA, 2000). As such, researching left hemispheric involvement in positive symptoms was considered limited for the current study. Secondly the literature has focused more clearly on right hemispheric functioning. Not only has much of the previous literature supported a greater right hemispheric dysfunction compared to left, but given the effectiveness of modern medication with treating positive symptoms, a focus on negative symptom aetiology and treatment has come to the fore.

6.3.2 Other variable contributions to limitations

Despite taking into account methodological variables, one must take into account other variables which may have had an impact on the participants' performance. First, despite Phillips et al.'s (1997) assertion that neuroleptic medication makes little contribution to outcomes on neuropsychological tests, one must take into account that chronic exposure to such medication (in this case over a roughly 26 year period) and its effects on neuropsychological test results, have not been fully researched. However, it is hoped that any confounding effects that such exposure could create may be controlled for by the participants' medications and dosages being fairly closely matched, hopefully matching their exposure to such effects.

Second, without baseline pre-CVA data it is impossible to say whether there was some significant difference between the participants' neuropsychological functioning, specifically frontal lobe or right hemispheric functioning, prior to the CVA (although assumed not to be so by this research). Pre-CVA neuroimaging data may have contributed to a fuller understanding of differences between the participants, as well as offered information as to why one twin was more vulnerable to the CVA at that point in her life.

Third, the neuropsychological and psychological changes are assumed to be related to the CVA in terms of the changes in neuro-physiology. However, variables such as pre-existing neuro-developmental differences, increased attention and care, and a new-found position of importance in the family, may have contributed to Gail's (CVA) improved symptomatology.

Fourth, despite findings of difference in negative symptomatology, improved negative symptoms in Gail (CVA) assumed from collateral reports as well as psychiatric information, however, as

base-line pre-CV A psychometric data could not gained. Therefore, it is possible that the difference in negative symptomatology between the participants seen in this research is not as significantly large as assumed, with a difference in pre-CV A negative symptoms between the participants being possible.

Lastly, one must consider the researcher's prior relationship with participants. Although this relationship was at a 'professional' helper-helpee level, these contributions should not be discounted. However, it is hoped that these contributions were positive rather than negative and a best-possible performance was elicited from the participants because of the prior relationship. Whereas in other circumstances the participants could have been slow to warm and build rapport and may have shied away from challenging or difficult tests (like many neuropsychological tests!).

6.4 Implications for theories of schizophrenia and schizophrenia aetiology

Theories such as Cutting (1994) and Robinson (1998) which highlight the right hemispheric functioning for the negative symptoms of schizophrenia have not been discounted by this research. This research has outlined how neuro-anatomical and neuro-chemical changes in this hemisphere do seem to be related to a change in negative symptomatology.

Although overall right hemispheric functioning does seem to play an important role, it is however, rather specific regions within the right hemisphere (namely the medial prefrontal and amygdala regions) that seem essential to these negative symptomatology. From this research, and in line with Barnett et al.'s (2005) recent suggestions, it is hypothesised that global right

hemispheric theories may need to be refined into more specific right hemispheric-lobal or structural theories.

This research clearly implicates frontal (ventral and medial prefrontal cortex) involvement. With the ventral and medial prefrontal cortex region's connections to both auditory and visual regions in the temporal lobe as well as sub-cortical connections to the amygdala (which affect the addition of affective tone to sensory input and memories), changes in these areas may lead to a change in negative symptomatology. Although the research is not advocating purposeful lesioning of the right frontal areas as treatment, this area may be further investigated as a site for future treatment strategies.

Unlike other research which has favoured a reductionist approach, this research highlights the complexities inherent in the neuropsychological research in the area of schizophrenia. Additionally, as many areas and structures seem to have been implicated in the neuropsychological functioning differences between the participants a simple claim of right hemisphere hyperfunctioning and left hemisphere hypofunctioning seems to be an overly simplistic explanation for more complex and inter-woven functions.

6.5 Special considerations

6.5.1 The unique nature of this research

This research, besides making a contribution to research in the area of negative symptoms and hemispheric functioning, seemed to be a positive experience for the participants and their family. As a research opportunity this case offered a unique perspective on monozygotic twin study

research and schizophrenia, but was however, a challenging exercise for the participants. Despite this both the participants and their family reported their involvement in the research to be a positive experience. The participants and their family reported the feedback given to them (with participants' consent) as being beneficial in terms of an understanding of the participants' various deficits. Additionally, the participants and their family found the experience a validating one concerning their management of the mental illness both personally and as a family. Having not been exposed to the discipline of psychology prior to the research, both participants reported it to be a pleasant and affirming experience. Since her exposure to psychology Gail (CVA) has considered entering into psychotherapy to discuss some of the issues which concern her. Overall the participants and their family reported being involved in the research as a positive and affirming experience.

Additionally, research of this nature was a unique opportunity with limited twin studies available in the area of the neuropsychology of schizophrenia, especially with a hemispheric focus. Despite the methodological difficulties of twin studies, Joseph (2001) does concede that they offer important research opportunities regarding neuropsychological and neuro-anatomical differences or similarities between various expressions of schizophrenia. Future monozygotic twin study research could focus on twins with similar symptomatology, investigating neuropsychological and neurimagrng differences, as well as similarities and differences in discordant twins, among others areas of focus.

6.5.2 Schizophrenia research in the South African context

Schizophrenia is a vastly under-researched area in South Africa with reliable statistics difficult to ascertain. Although formal research into the area of negative symptoms is minimal within South

Africa, limited psychiatric and psychological resources (which limit psychoeducation and psychotherapeutic programmes) lead one to believe that although positive symptom relief may be effective for many South African individuals through antipsychotic medications, it is possible that many individuals' negative symptoms are not addressed. Additionally, research indicates that, as schizophrenia symptomatology is heterogeneous, the expression of schizophrenia symptoms within the multi-cultural South African population may be vastly heterogeneous and diverse (Maslowski & Oosfhuizen, 1993).

Research regarding schizophrenia prevalence, symptom expression, and neuropsychological effects within South Africa is limited. A factor impacting on the limitations of such research involves the use of neuropsychological tests. Neuropsychological tests are normed and standardised on foreign populations and are neither culturally fair nor applicable to many South African populations. Additionally, many South Africans are not English-first language speakers while almost all of the neuropsychological tests are in English only. Further both neuropsychological testing and neuroimaging are time and resource intensive, both of which are generally lacking within the South African mental health systems.

However, despite these difficulties, research is essential to the enhancement of mental health services within South Africa. Additionally, as there are no reliable statistics on the prevalence and incidence of schizophrenia within South Africa a false assumption of minimal impacts of the illness should not be made. Further the unique multi-cultural context within South Africa offers a diverse and rich setting within which research of this nature may yield a multi-layered perspective on causal aetiologies and symptom expression.

6.6 Implications for future research

The consolidation of the literature's major aetiological findings, as well as the current research findings, has clearly brought to the fore the need for additional research in this area. Although at first glance there seems to be a proliferation of research in the area of schizophrenia, distillation of these reveal that refinement of theories around aetiology and treatment is taking place (Sawa & Snyder, 2002; Sadock & Sadock, 2000).

This research highlights the importance of the right medial and inferior prefrontal regions in the negative symptoms of schizophrenia as well as aiding in information on right hemisphere functioning in individuals with schizophrenia. Additionally, this research has attempted to highlight the need for more consistent theories of both aetiology and treatment of schizophrenia. However, the limitations of Cognitive Neuropsychological methodology for furthering any findings from this research have been outlined. Harley (2004) suggests that computational cognitive neuropsychological modelling may be useful in future research as processes involved are made explicit and hypotheses are testable in a computerised model.

Future steps suggested for research in this area include higher power computational Cognitive Neuropsychological modelling, functional and static neuroimaging addressing anatomical issues, as well as in-depth neuro-chemical research, focusing on right frontal functioning. Additionally, locating select samples of both concordant and discordant monozygotic twins, individuals with schizophrenia with commissurotomy or hemispheric disconnection syndromes as well as other individuals with both schizophrenia and CVA may provide useful data on hemispheric and frontal implications for negative symptoms.

6.7 Conclusions

This research reinforces recent trends in schizophrenia literature, namely the need for more cohesive aetiological models, the need for more connection between aetiological and treatment models, and the need for more research into the understanding and treatment of negative symptoms of schizophrenia (Barnett et al., 2005; Blanchard, Horan & Collins, 2005; Moller, 2003; Roth, Flashman, Saykin, McAllister & Vidaver, 2004).

Overall, this research has partially answered some of the research questions asked, but has raised many more questions around the role of the right hemisphere and the role of the frontal regions, with regard to negative symptoms of schizophrenia. However, despite raising new questions this research has attempted to contribute to the development of new working hypotheses which could inform future research. As such, the research seems to have fulfilled its primary aim. However, the usefulness of this research now seems to rest on the commitment of future research to more fully address many of the questions raised here. Only in so doing will the long-term goal of unpacking negative symptom aetiology and treatment show benefits for those individuals who struggle with these life altering symptoms.

REFERENCES

American Psychological Association. (2000). *Diagnostic and Statistical Manual (5m ed.) - Text revised.* Washington D.C: Author.

Anderson, R.M. (1994). *Practitioner's Guide to Clinical Neuropsychology.* New York: Plenum Press.

Barnett, K., Kirk, I., & Corballis, M. (2005). Right hemisphere dysfunction in schizophrenia. *Laterality, 10(\),* 29-36.

Beebe, L.H. (2003). Theory-based research in schizophrenia *Perspectives in Psychiatric Care, 39(2),* 67 - 74.

Bender, L. (1938). *A Visual Motor Gestalt Test and its Clinical Use.* New York: American Orthopsychiatric Association.

Bird, CM., Papadopoulou, K., Ricciardelli, P., Rossor, M. N., & Cipolotti, L. (2004). Monitoring cognitive changes: Psychometric properties of six cognitive tests. *British Journal of Clinical Psychology, 43,* 197-210.

Blanchard, J.J., Horan, W.P., & Collins, L.M. (2005). Examining the latent structure of negative symptoms: Is there a distinct subtype of negative symptom schizophrenia? *Schizophrenia Research, 77,* 151-165.

Blanchard, J.J., & Neale, J.M. (1994). The neuropsychological signature of schizophrenia: Generalised or Differential Deficit? *American Journal of Psychiatry, 151* (1), 40-48.

Bowden, S.C., Fowler, K.S., Bell, R.C., Whelan, G., Clifford, C.C., Ritter, A.J., & Long, CM. (1998). The reliability and internal validity of the Wisconsin Card Sorting Test.^*Neuropsychological Rehabilitation, 8(3),* 243 - 254.

Bradshaw, J.L., & Mattingley. J.B. (1995). *Clinical neuropsychology: Behavioural and Brain Science.* San Diego: Academic Press.

Butcher, J.N., Graham, J.R., Ben-Porath, Y.S., Tellegen, A., Dahlstrom, W.G., & Kaemmer, B. (2001J. *MMPI-2 Manual for Administration, Scoring and Interpretation (Revised ed).* Minneapolis: University of Minnesota Press.

Carfagno, M.L., Hoskins, L.A., Pinto, M.E., Yeh, J.C., & Raffa, R.B. (2000). Indirect modulation of dopamine D2 receptors as potential pharmacotherapy for schizophrenia: II-glutamate (ant)agonists. *Annals of Pharmacotherapy, 3,* 788-797.

Carpenter, W.T., & Buchanan, R.W. (1994). Schizophrenia. *The New England Journal of Medicine, 330,* 681 - 689.

Carpenter, W.T., Conley, R., & Kirkpatrick, B. (2000). On Schizophrenia and new generation drugs. *Neuropsychopharmacology, 22,* 6 1 - 2.

Centofanti, C.C., & Smith, A. (1986). *The Single and Double Simultaneous (face-hand) Stimulation Test (SDSS) Manual.* California: Western Psychological Services.

Chan, R.C.K. (2004). Executive dysfunctions in schizophrenia: Relationships to clinical manifestation. *European Archives of Psychiatry & Clinical Neuroscience, 254,* 256 - 262.

Chan, R.C.K., Chen, E.Y.H., Cheung, R.F.C., Chen, R.Y.L., & Cheung, H.K. (2004). Problem-solving ability in chronic schizophrenia: A comparison study of patients with traumatic brain injury. *European Archives of Psychiatry & Clinical Neuroscience, 254,* 236-241.

Coffey, M. (1998). Schizophrenia: A review of current research and thinking. *Journal of Clinical Nursing, 7,* 489 - 498.

Cohen, S.N. (Ed.). (2000). *Management of Ischemic Stroke.* New York: McGraw-Hill.

Crawford, J.R., & Garthwaite, P.H. (2002). Investigation of a single case study in neuropsychology: Confidence limits on the abnormality of test scores and test scores differences. *Neuropsychologia, 40,* 1196 - 1208.

Crawford, J.R., Garthwaite, P.H., Howell, D.C., & Gray, CD. (2004). Inferential methods for comparing a single case with a control sample: Modified t-tests versus

Mycroft et al.'s (2002) modified ANOVA. *Cognitive Neuropsychology, 21(1),* 750 - 755.

Crawford, J.R., Garthwaite, P.H., Azzalini, A., Howell, D.C., & Laws, K.R. (2006). Testing for a deficit in single case studies: Effects of departures from normality. *Neuropsychologia, 44,* 666 - 677.

Crow, T.J. (1985). Positive and negative schizophrenic symptoms and the role of dopamine. *British Journal of Psychiatry, 137,* 383-386.

Cutting, J. (1994). Evidence for right hemisphere dysfunction in schizophrenia. In Cutting, J.C., & David, A.S. (Eds.). *The Neuropsychology of Schizophrenia (p. 231 - 242).* New York: Lawrence Erlbaum Associates.

Davidson, R.J. (1998). Affective style and affective disorders: Perspectives from affective neurosciences. *Cognition and Emotion, 12(3),* 307 - 330.

Davidson, R.J. (2000). Affective neuroscience and psychophysiology: Toward a synthesis. *Psychophysiology, 40,* 655 - 665.

Davidson, R.J. (2001). The neural circuitry of emotion and affective style: Prefrontal cortex and amygdala contributions. *Social Science Information, 40(\),* 11 - 37.

Davidson, R.J. (2002). Anxiety and affective style: Role of prefrontal cortex and amygdala. *Society of Biological Psychiatry, 51,* 68 - 80.

Davidson, R.J. (2004). What does the prefrontal cortex 'do' in affect: Perspectives on frontal EEG asymmetry research. *Biological Psychology, 67,* 219 - 233.

Davidson, R.J., Shackman, A.J., & Maxwell, J.S. (2004). Asymmetries in face and brain related to emotion. *Trends in Cognitive Sciences, 8(9),* 389 - 391.

Deckersbach, T., Savage, C.R., Henin, A., Mataix-Cols, D., Otto, M.W., Wilehlm, S., Rauch, S.L., Baer, L., & Jenike, M.A. (2000). Reliability and validity of a scoring system for measuring organisational approach in a complex figure test. *Journal of Clinical and Experimental Neuropsychology, 22(5),* 640 - 648.

Ferber, S., & Karnath, H.O. (2001). How to assess spatial neglect - line bisection or cancellation tasks? *Journal of Clinical and Experimental Neuropsychology, 23(5),* 599 - 607.

Fiez, J.A. (2001). Bridging the gap between neuroimaging and neuropsychology: Using working memory as a case study. *Journal of Clinical and Experimental Neuropsychology,* 23(1), 19-31.

Foxcroft, C, & Roodt, G. (2001). *An Introduction to Psychological Assessment in the South African Context.* Cape Town: Oxford University Press.

Gabrovska-Johnson, V.S., Scott, M., Jeffries, S., Thacker, N., Baldwin, R.C., Burns, A., Lewis, S.W., & Deakin, J.F.W. (2003). Right-hemisphere encephalopathy in elderly

subjects with schizophrenia: Evidence from neuropsychological and brain imaging studies. *Psychopharmacology, 169,* 367 - 375.

Grant, I., & Adams, K.M. (1996). *Neuropsychological Assessment of Neuropsychiatric Disorders.* New York: Oxford University Press.

Harley, T.A. (2004). Does cognitive neuropsychology have a future? *Cognitive Neuropsychology,* 27(1), 3 - 16.

Hawkins, K.A., Dean, D., & Pearlson, G.D. (2004). Alternative forms of the Rey auditory verbal learning test: A review. *Behavioural Neurology, 15,* 99 - 107.

Heinrichs, R.W. (2005). The primacy of cognition in schizophrenia. *American Psychologist, 60(3),* 229 - 242.

Higashima, M., Nagasawa, T., Oka, T., Tsukada, T., Okamoto, T., Komai, Y., Kawasaki, Y., & Koshino, Y. (2005). Neuropsychological correlates of an attention-related negative component elicited in an auditory oddball paradigm in schizophrenia. *Neuropsychobiology, 51,* 177 - 182.

Hobart, M.P., Goldberg, R., Bartko, J.J., & Gold, J.M. (1999). Repeatable battery for the assessment of neuropsychological status as a screening test in schizophrenia: Convergent/ discriminant validity and diagnostic group comparisons. *American Journal of Psychiatry,* 756(12), 1951-1957.

Hooper, H.E. (1958). *The Hooper Visual Organisation Test Manual.* California: Western Psychological Services.

Howell, D.C. (2002). *Statistics for Psychology (5th ed).* Pacific Grove, California: Duxbury Thomson Learning.

Hultman, CM., & Ohman, A. (1998). Perinatal characteristics and schizophrenia: Electrodermal activity as a mediating link in a vulnerability-stress perspective. *International Journal of Developmental Neuroscience, 16,* 307 - 316.

Hutt, M.L. (1985). *The Hutt adaptation of the Bender-Gestalt Test* (4th Edition). Orlando: Grune and Stratton.

Ishiguro, H., Okuyama, Y., Toru, M., & Arinami, T. (2000). Mutation and association analysis of the 5' region of the dopamine D3 receptor gene in schizophrenia patients: Identification of the Ala38Thr polymorphism and suggested association between DRD3 haplotypes and schizophrenia. *Molecular Psychiatry, 5,* 33 - 38.

Jackson, D.C, Mueller, C.J., Dolski, I., Dalton, K.M., Nitschke, J.B., Urry, H.L., Rosenkranz, M.A., Ryff, CD., Singer, B.H., & Davidson, R.J. (2003). Now you feel it, not you don't: Frontal brain electrical asymmetry and individual differences in emotion regulation. *Psychological Science, 14(6),* 612-617.

Jones, J.J.S., van Schaik, P., & Witts, P. (2006). A factor analysis of the Weschler Adult Intelligence Scale 3m Edition (WAIS-III) in a low IQ sample. *British Psychological Society, 45,* 145 - 152.

Joseph, J. (2001). Don Jackson's 'A critique of the literature on the genetics of schizophrenia': A reappraisal after 40 years. *Genetic, Social & General Psychology Monographs,* 727(1), 27 - 58.

Joseph, J. (2002). Twin studies in psychiatry and psychology: Science or pseudoscience? *Psychiatric Quarterly,* 73(1), 71 - 82.

Josman, N., & Katz, N. (2006). Relationships of categorization on tests and daily tasks in patients with schizophrenia, post-stroke patients and healthy controls. *Psychiatric Research,* 747(1), 15-28.

Kalat, J. W. (1998). *Biological Psychology (6th ed).* Pacific Grove, CA: Brooks/Cole.

Kay, S.R., Fizbein, A., & Opler, L.A. (1987). The Positive and Negative Syndrome Scale (PANSS) for schizophrenia *Schizophrenia Bulletin, 2,* 261 - 276.

Kolb, B., & Whishaw, I.Q. (2003). *Fundamentals of Human Neuropsychology (5th ed.)* New York: W.H Freeman and Company.

Lancon, C, Auquier, P., Nayt, G., & Reine, G. (2000). Stability of the five-factor structure of the Positive and Negative Syndrome Scale (PANSS). *Schizophrenia Research, 42,* 231 -239.

Lewis, R. (2003). Should cognitive deficit be a diagnostic criterion for schizophrenia? *Journal of Psychiatry Neuroscience, 29(2),* 102 - 113.

Lezak, M.D. (2004). *Neuropsychological Assessment (4^{m} ed.)* New York: Oxford University Press.

Mansfield, D. J. (2002). *Neuropsychological Assessment: A practice reference.* (Unpublished booklet).

Maslowski, J., & Oosthuizen ,C. (1993). Transcultural aspects of schizophrenia: A comparative study in South Africa and in Namibia. A preliminary report. *Bulletin of the Institute of Maritime and Tropical Medicine in Gdynia, 45(4),* 95-101.

Meaney, M.J. (2001). Nature, nurture and the disunity of knowledge. *Annals of New York Academy of Sciences, 395,* 50-61.

Meehl, P.E. (1962). Schizotaxia, schizotypy, schizophrenia. *American Psychologist, 17,* 827 - 838.

Merten, T., & Beal, C. (2000). An analysis of the Hooper visual organisation test with neurological patients. *The Clinical Neuropsychologist, 14(4),* 521 - 529.

Meyers, J.E., & Meyers, K.R. (1995). *Rey Complex Figure Test and Recognition Trial.* Pacific Grove, USA: Psychological Association Resources Inc.

Moller, H.J. (2003). Management of the negative symptoms of schizophrenia. *CNS Drugs,* 77(11), 793-824.

Morgan, S.E., Reichert, T., & Harrison, T.R. (2002). *From Numbers to Words: Reporting Statistical Results for the Social Sciences.* Boston: Allyn & Bacon.

Nell, V. (1999). Standardising the WAIS-III and the WMS-III for the South Africa: Legislative, psychometric and policy issues. *South African Journal of Psychology, 29(3),* 128 - 138.

Neurosciences Unit. (1983). *Hooper Visual Organisation Test (VOT) Manual (1983 ED.)* California: Western Psychological Services.

Niethammer, R., & Weisbrod, M. (2000). Genetic influence on laterality in schizophrenia? A twin study of neurological soft signs. *American Journal of Psychiatry,* 757(2), 272 - 275.

Olie, J.P. (2006). Ziprasidone and amisulpride effectively treat negative symptoms of schizophrenia: Results of a 12-week, double-blind study. *International Clinical Psychopharmacology,* 27(3), 143 - 151.

Phillips, M.L., Howard, R., & David, A.S. (1997). A cognitive neuropsychological approach to the study of delusions in late-onset schizophrenia. *International Journal of Geriatric Psychiatry, 12,* 892 - 901.

Rabkin, J.G. (1982). Stress and psychiatric disorders. In L. Goldberger & S. Breznitz (Eds.), *Handbook of Stress, Theoretical and Clinical Aspects* (pp. 566-577). New York: Macmillan.

Rector, N.A., Beck, AT., & Stolar, N. (2005). The negative symptoms of schizophrenia: A cognitive perspective. *Canadian Journal of Psychiatry, 50,* 247 - 257.

Rey, A. (1964). L'Examen Clinique en Psychologic As cited in Lezak, M.D. (2004). *Neuropsychological Assessment (4th ed.)* (pp. 569). New York: Oxford University Press.

Robinson, R.G. (1998). *The Clinical Neuropsychiatry of Stroke.* Cambridge: Cambridge University Press.

Rotenberg, V. S. (1994). An integrative psychophysiological approach to brain hemisphere functions in schizophrenia. *Neuroscience and Biobehavioural Review, 18(4),* 487-495.

Roth, R.M., Flashman, L.A., Saykin, A.J., McAllister, T.W., & Vidaver, R. (2004). Apathy in schizophrenia: Reduced frontal lobe volume and neuropsychological deficits. *American Journal of Psychiatry, 161(\),* 157 - 159.

Sadock, B.J. & Sadock, V.A. (2000). *Kaplan & Sadock's Comprehensive Textbook of Psychiatry (7m ed).* New York: Lippincott Williams & Wilkins.

Savage, R.M., Jackson, W.T. & Sourathathone, CM. (2003). A brief neuropsychological testing battery for evaluating patients with schizophrenia. *Community Mental Health Journal, 39(3),* 253-262.

Sawa, A., & Snyder, S.H. (2002). Schizophrenia: Diverse approaches to a complex disease. *Science, 5568(296),* 692 - 696.

Segalowitz, S.J. (1999). Why twin studies don't really tell us much about human heritability. *Behavioural and Brain sciences, 22(5),* 904 - 905.

Shallice, T. (1988). *From Neuropsychology to Mental Structure.* Cambridge: Cambridge University Press.

Shallice, T. (2004). On Harley on Rapp. *Cognitive Neuropsychology,* 27(1), 41 - 43.

Shallice, T., Burgess, P.W., & Frith, CD. (1991). Can the neuropsychological case-study approach be applied to schizophrenia? *Psychological Medicine, 21(3),* 661 - 673.

Silver, H. (2003). Selective serotonin reuptake inhibitor augmentation in the treatment of negative symptoms of schizophrenia. *International Clinical Psychopharmacology, 18(6),* 305-314.

Singh, S.M., McDonald, P., Murphy, B., & O'Reilly, R. (2004). Incidental neurodevelopmental episodes in the aetiology of schizophrenia: An expanded model involving epigenetics and development. *Clinical Genetics, 65,* 435 - 440.

Smith, A. (1982). *Symbol Digit Modalities Test Manual.* California: Western Psychological Services.

Stratta, P., Donda, P., Rossi, A., & Rossi, A. (2005). Executive function assessment of patients with schizophrenic disorder residual type in olanzapine treatment: An open study. *Human Psychopharmacology, 20,* 401 - 408.

Suslow, T., Roestel, C, & Arolt, V. (2003). Affective priming in schizophrenia with and without affective negative symptoms. *European Archives of Psychiatry and Clinical Neurosciences, 253(6),* 292 - 300.

Sutton, S.K., & Davidson, R.J. (1997). Prefrontal brain asymmetry: A biological substrate of the behavioural approach and inhibition systems. *Psychological Science, 8(3),* 204 - 210.

Tate, R.L., Perdices, M., & Maggiotto, S. (1998). Stability of the Wisconsin card sorting test and the determination of the reliability of change in scores. *The Clinical Neuropsychologist, 12(3),* 348 - 357.

Terre Blanche, M. & Durrheim, K. (1999). *Research in Practice.* Cape Town: University of Cape Town Press.

Tseng, K.Y., & O'Donnell, P. (2004). Dopamine-glutamate interactions controlling prefrontal cortical pyramidal cell excitability involve multiple signalling mechanisms. *The Journal of Neurosciences, 24(22),* 5131 - 5139.

Tsuang, M.T., & Faraone, S.V. (2002). Diagnostic concepts and the prevention of schizophrenia. *Canadian Journal of Psychiatry, 47(6),* 515 - 517.

Tulskey, D.S. (2004). A new look at the WMS-III: New research to guide clinical practice. *Journal of Clinical and Experimental Neuropsychology,* 26(4), 453 - 458.

Van Haren, N.E.M., Picchioni, M.M., McDonald, C, Marshall, N., Davis, N., Ribchester, T., Hulshoff, P.H.E., Sharma, T., Sham, P., Kahn, R.S., & Murray, R. (2004). A controlled study of brain structure in monozygotic twins concordant and discordant for schizophrenia. *Biological Psychiatry, 56(6),* 454 - 461.

Wechsler, D. (1997a). *Wechsler Adult Intelligence Scale (3rd ed.) (WAIS-III).* San Antonio: Psychological Corporation.

Wechsler, D. (1997b). *Wechsler Memory Scales (3rd ed.) (WMS-III).* San Antonio: Psychological Corporation.

Yin, R.K., & Campbell, D.T. (2003). *Case Study Research.* London: Sage Publications.

Zubin, J., & Steinhauer, S. (1981). How to break the logjam in schizophrenia. *Journal of Nervous and Mental Disease,* 769(8), 477-49.

APPENDIX

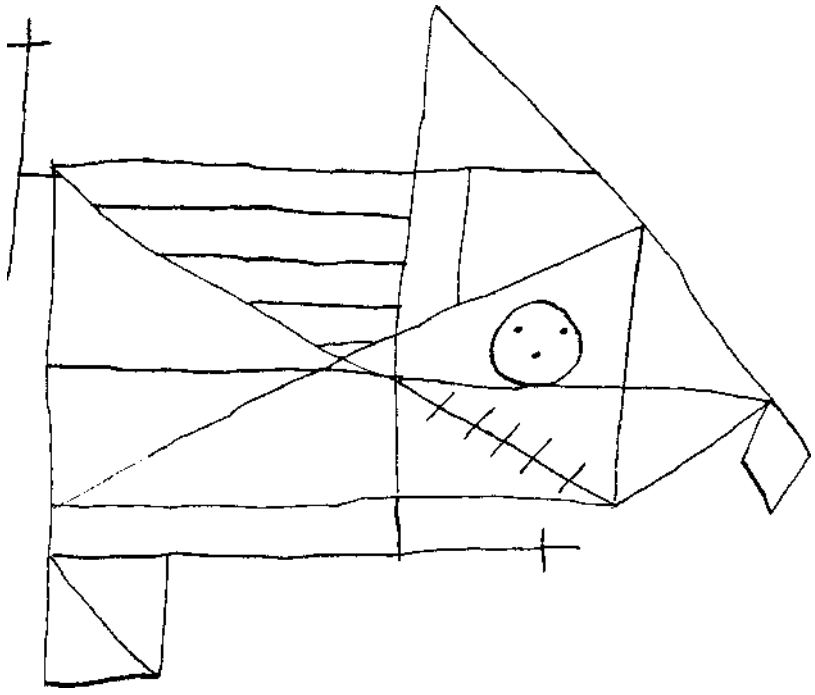


Figure A1: Gail RCFT Copy

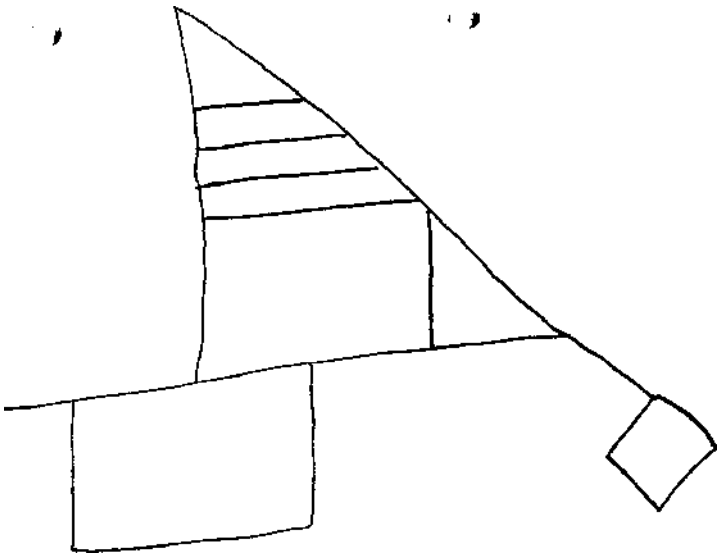


Figure A2: Gail RCFT three minute recall

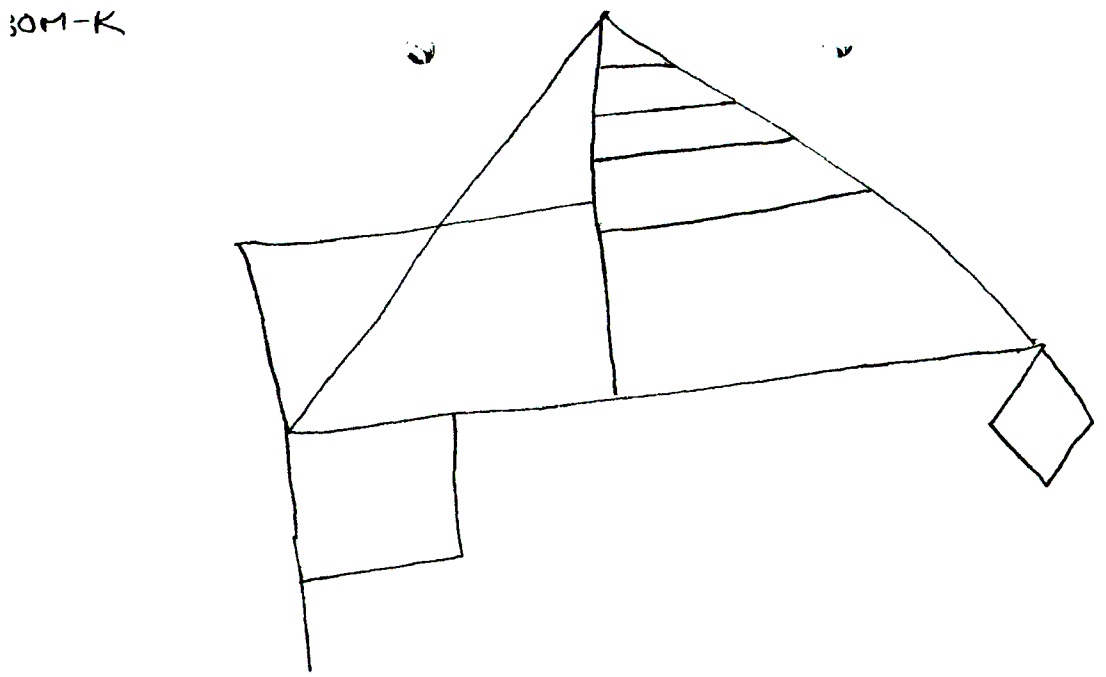
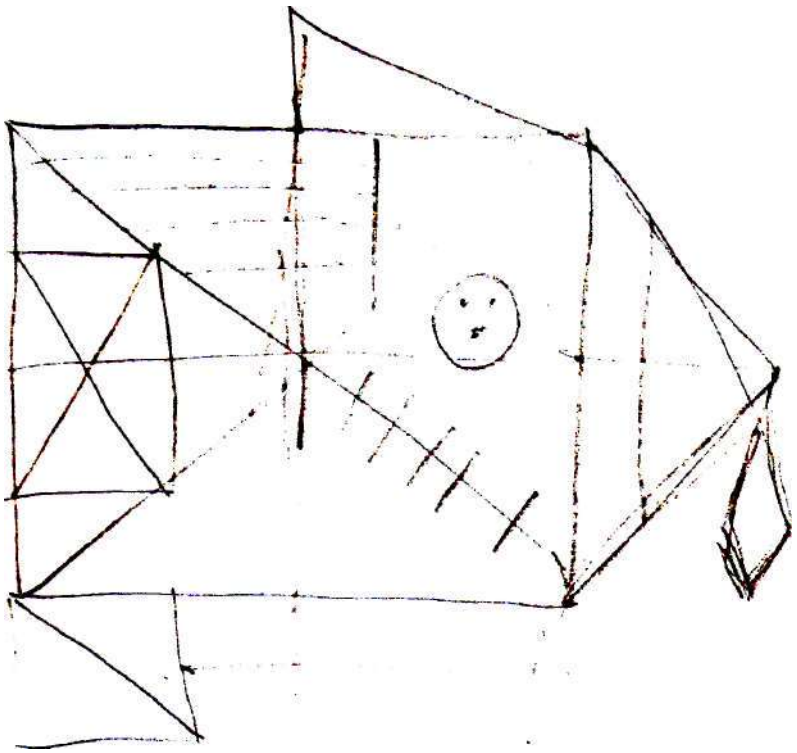


Figure A3: Gail RCFT 30 minute recall



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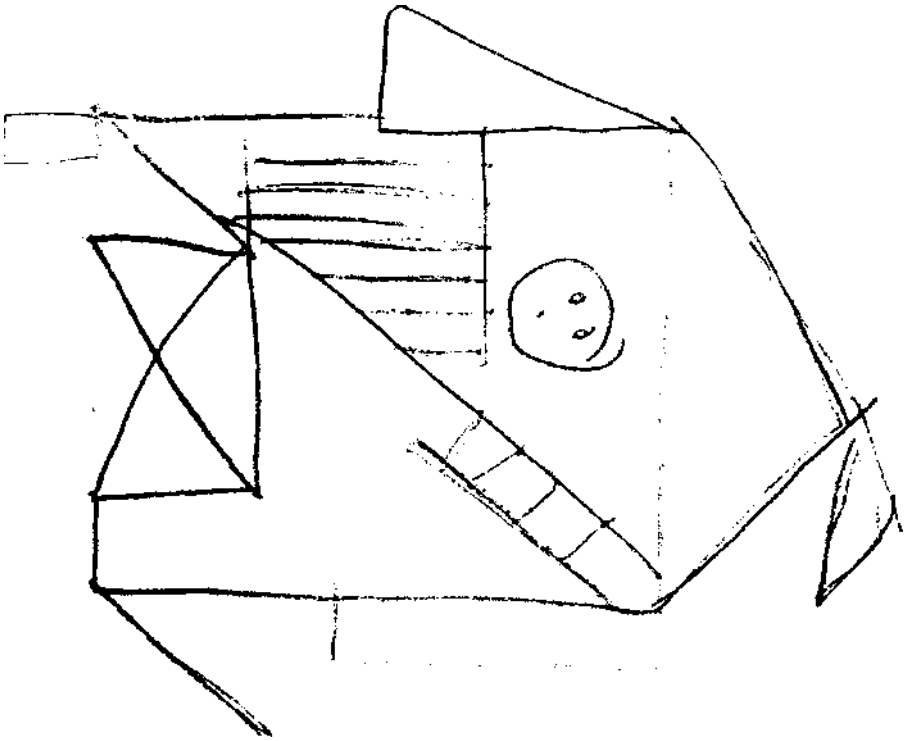

Figure A5: Abbey RCFT three minute recall

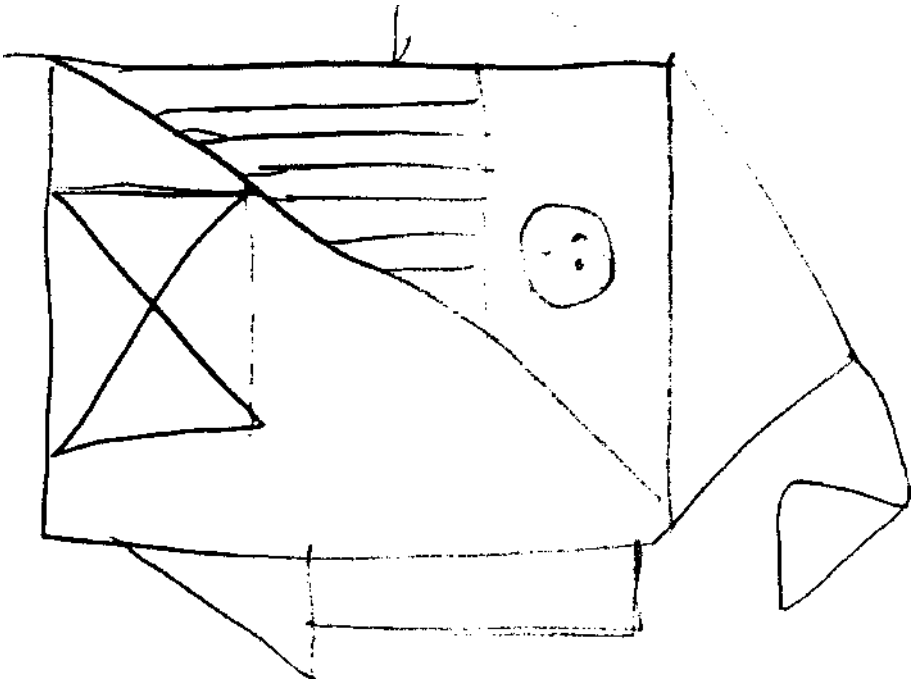

Figure A6: Abbey RCFT 30 minute recall