

CARDIFF UNIVERSITY

# The Role of Cognitive Control in Memory Retrieval

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Applications to Schizotypy and  
Schizophrenia

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**A thesis submitted to Cardiff University for the degree of Doctor of Philosophy in  
Psychology**



## ABSTRACT

Individuals with schizophrenia have memory impairments. The experiments in this thesis were designed to determine whether these impairments arise from failures of cognitive control operations. Specifically, these experiments examined whether differences in target and non-target left-parietal old/new effects – a proposed neural correlate of strategic control over recollection - are predicted by schizotypy and/or schizophrenia symptomology. Correlations between schizotypy measures or symptom scores and how well people exercise control over retrieval of relevant information would point to one locus for memory problems associated with schizophrenia.

Target left-parietal old/new effects were significantly more positive going than non-target left-parietal old/new effects in healthy, young participants indicating these participants could prioritise the recollection of some memory contents over others. Whilst there was no correlation between schizotypy scores and the ERP evidence for the extent of control over retrieval, there was evidence to suggest those higher in schizotypy engage post-retrieval control mechanisms to a greater extent than those lower in schizotypy, as indicated by the positive correlation between the magnitude of the right-frontal old/new effect for imagined items and measures of positive schizotypy in Experiment Two. This pattern of results however did not hold for older, healthy volunteers or patients with schizophrenia. These outcomes suggest age, or an age-related confound such as working memory capacity, is a determinant of the extent to which retrieval control processes are engaged.

Despite the lack of correlations between left-parietal old/new effects and symptomology, several behavioural correlations were identified. Patients higher in negative symptoms had greater difficulty discriminating imagined items from other items. Estimates of recollection for imagined items were also negatively correlated with negative symptoms. This pattern of findings was not present in young or older healthy participants. This could be because assessments of schizotypy are useful for studying deficits associated with schizophrenia only in some cognitive domains.

Taken together, these results indicate that memory processes in patients with schizophrenia are impaired. The extent to which this is a consequence of failures in control operations is not well determined.

## DECLARATION

This work has not previously been accepted in substance for any degree and is not concurrently submitted for candidature for any degree.

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### Statement 1

This thesis is being submitted as partial fulfilment of the requirements for the degree of PhD.

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### Statement 2

This thesis is a result of my own independent work/investigation, except where otherwise stated. Other sources are acknowledged by explicit references.

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## PROLOGUE: THESIS OVERVIEW

There is a growing body of evidence to suggest cognition, particularly memory, is adversely affected in people with schizophrenia (e.g. Green, 1996; Green, Kern, Braff, & Mintz, 2000; Aleman, Hijman, de Haan, & Kahn, 1999; Heinrichs & Zakzanis, 1998). The mechanisms underlying these deficits however, are less well understood. It has been hypothesised that many of the deficits observed in schizophrenia patients arise at least in part due to failures in cognitive control operations (Cohen & Servan-Schreiber, 1992). The principle aim of the experiments reported in this thesis were to better understand whether failures in cognitive control operations contribute to the memory deficits observed in people with schizophrenia.

The introductory chapters of this thesis address the key areas of literature that have been drawn upon in developing the experiments reported in this thesis. The first chapter focuses on schizophrenia. It describes the relationship between schizotypy and schizophrenia and why we can use this dimensional correlate to gain a better understanding of the problems experienced by patients with schizophrenia. Crucially, as well as introducing evidence indicating memory is a core cognitive deficit for patients with schizophrenia, this chapter introduces the idea that a more parsimonious explanation for deficits across multiple cognitive domains would be impaired higher-order functions, such as cognitive control. The second chapter focuses on evidence for deficits of cognitive control in patients with schizophrenia and those high in schizotypy, and introduces a model of cognitive control in relation to memory; providing a basis from which we can investigate cognitive control in relation to memory processes. The third chapter describes the models of memory that have been drawn upon in the development of the experiments reported in this thesis and how behavioural paradigms and Event-Related Potentials (ERP) can be used to better understand the different processes that contribute to memory performance. The fourth and final introductory chapter of this thesis brings together these three topics and introduces studies that have used methods similar to those adopted in the present investigation to research memory processes in patients with schizophrenia. Importantly, the heterogeneity of present investigations limits the strength of conclusions that can be drawn highlighting the need for more specific investigations into the mechanisms underlying deficient memory processes in people with schizophrenia.

This structure is used to build up the argument that deficits in cognitive control may underlie memory problems in people with schizophrenia and ERPs in conjunction with certain behavioural paradigms may provide an appropriate method to investigate this possibility. By investigating this hypothesis in relation to healthy volunteers using schizotypy measures, it is possible to gain further insight into the relationship between this construct and schizophrenia.

The principle hypothesis of all experiments reported in this thesis was that differences in target and non-target left-parietal old/new effects – a proposed neural correlate of strategic control over recollection - are predicted by schizotypy scores and schizophrenia symptomology. Subsidiary hypotheses were that differences in target and non-target late posterior negativity and right frontal old/new effects – proposed neural correlates of strategic control over post-retrieval processes – are predicted by schizotypy scores and schizophrenia symptomology.

In the first two large scale experiments reported in this thesis ERPs were acquired during completion of exclusion tasks, and ERP evidence for control over retrieval was assessed in relation to a range of individual difference measures. The principle difference between these two studies was that in the first experiment, the task was designed to achieve high levels of task performance whereas in the second experiment, parameters were adjusted to increase task difficulty. Critically, this was intended to increase our chance of distinguishing between those high and low in schizotypy on the basis of their differential neurophysiological response [ERPs]. Specifically, it was hypothesised that at higher levels of task difficulty, those higher in schizotypy would be less able to employ compensatory strategies and thus the difficulties experienced would be more easily identified.

These studies are followed by a report of findings in similar paradigms in which neural and behavioural measures from patients with schizophrenia and controls were the variables of interest. Chapter Seven presents data from the participants recruited as controls for the data from patients with schizophrenia. By presenting this data separately, it was possible to examine the generality of patterns of data obtained from university students. Given that university students are highly versed at learning and remembering information and this population is usually associated with a number of protective factors that may minimise the impact of experienced problems (Lenzenweger, 2006), it is important to examine processes in non-university populations.

Chapter Eight presents data from patients with schizophrenia. Considering schizotypy is not simply an analogue of schizophrenia but rather an indicator of liability (Lenzenweger, 2006), results from the previous investigations do not preclude investigations of cognitive control in patients with schizophrenia. Under this view, whilst investigations using measures of schizotypy can provide invaluable insights into factors implicated in the development of schizophrenia, ultimately studies using measures of schizotypy, especially those employing psychometric assessments, will not invariably provide indicators that translate to patients with schizophrenia (Kwapil & Barrantes-Vidal, 2015).

Whilst each experimental chapter presents a brief discussion of the findings which principally provide the rationale for the subsequent experimental chapters, more in depth discussion of the pattern of findings and broader theoretical considerations are reserved for the General Discussion presented as the final chapter of this thesis.

## CHAPTER ONE: SCHIZOPHRENIA

Kraepelin (1919/1971) and Bleuler (1911/1950) were among the first to identify a chronic, deteriorating psychotic state, characterised by onset in late teens to early adulthood and rapid cognitive disintegration. Initially, the condition was termed dementia praecox (Kraepelin, 1919/1971); it was only later generally described as schizophrenia (Bleuler, 1926). Now, schizophrenia is accepted as a common, but heterogenous, psychiatric disorder. It affects approximately 1% of the population (Andreasen, 2000). Individuals who develop schizophrenia experience their own unique combination of symptoms and experiences, including aberrations in perceptions, thoughts, affect and behaviour (NICE, 2014).

### SYMPTOMS

Many researchers have attempted to classify the symptoms of schizophrenia. One of the most influential systems suggests that symptoms are divided into two domains: positive and negative (Andreasen & Olsen, 1982; Crow, 1980; Strauss, Carpenter, & Bartko, 1974). Positive symptoms are considered abnormal by their presence, and include hallucinations, delusions and incoherent speech. Conversely, negative symptoms are considered abnormal by their absence, and include alogia, poverty of speech, and anhedonia, which is loss of pleasure from previously enjoyed activities. There are a number of diagnostic systems that can be used to diagnose schizophrenia, including the International Statistical Classification for Diseases and Health Related Problems (ICD-10; WHO, 2010) and the Diagnostic and Statistical Manual of Mental Disorders (DSM-V; APA, 2013). The patient studies conducted for this thesis used the DSM-V diagnostic criteria to determine diagnoses as this system provides consistent and reliable criteria for researching mental disorders (APA, 2013). According to this system, in order to receive this diagnosis, patients must have experienced at least two of five characteristic symptoms for at least one month, with continuous signs of disturbance for at least six months. Disturbance may include prodromal periods, where symptoms are beginning to develop, or residual periods, where symptoms are no longer prominent following an active episode. At least one of the pre-requisite symptoms must be delusions, hallucinations or disorganised speech. Finally, individuals should have experienced significant social or occupational dysfunction since the onset of disturbance in one or

more major areas: work, interpersonal relations or self-care. The following sections will outline the characteristic symptoms of schizophrenia as they are described in the DSM-V criteria (APA, 2013).

### Hallucinations

Hallucinations are perceptual experiences in the absence of external stimulation, but with the qualities of real perceptions. Larøi and Woodward (2007) proposed there are two important phenomenological dimensions to hallucinations: i) the self-generated vs non-self-generated dimension and ii) the inner vs outer dimension. The first dimension refers to the perceived agent in the cognitive event, whereas the second dimension refers to the spatial location of the cognitive event. Larøi and Woodward (2007) proposed that all hallucinations originate as inner, self-generated cognitive events that are somehow misattributed either in terms of subjective origin or location.

Hallucinations are distinct from dreaming as they occur during conscious wakefulness. Hallucinations are also distinct from illusions, which involve the distortion or misinterpretation of real perceptions. Less intense hallucinations are commonly referred to as sensory distortions, but both distortions and hallucinations can occur in any sensory modality. Auditory hallucinations are most commonly reported by patients with schizophrenia (Chen & Berrios, 1996). These experiences can be classified as simple or complex. Simple auditory hallucinations involve the perception of noises such as white noise or whistling. By contrast, complex auditory hallucinations involve the perception of voices or music, which may be familiar or unfamiliar, and friendly or aggressive. Furthermore, the quality of these experiences can vary. Auditory hallucinations may seem to originate from within the person or from external sources. They may be as vivid as if someone was being addressed directly. Alternatively, they may be muted or unclear.

Command hallucinations are a specific class of auditory hallucinations. As the name suggests, they involve a person perceiving a voice giving instructions to do something. These commands can range from innocuous requests such as “shut the door” to orders to harm the self or others. Importantly, someone experiencing command hallucinations may or may not obey the commands, and there are several factors that contribute to compliance, including beliefs of the benevolence or malevolence of the voice and perceived superiority or inferiority (Fox, Gray, & Lewis, 2004).

Visual hallucinations are also commonly reported by individuals with schizophrenia. As for auditory hallucinations, visual hallucinations can be classified as simple or complex. Simple visual hallucinations are perceptions of non-formed shapes or objects including; lights, colours, geometric shapes and indiscrete objects. Complex hallucinations involve perceiving clearly formed life-like images and scenes. Gustatory and olfactory hallucinations are less commonly reported but when they are experienced, these tend to be unpleasant in nature. Olfactory, gustatory and tactile hallucinations frequently co-occur (Langdon, McGuire, Stevenson, & Catts, 2011). Tactile hallucinations can take the form of pain or touch, and are usually triggered by emotional cues such as guilt, sadness, anger or fear. These latter hallucinations are reported far less frequently than auditory or visual hallucinations.

### Delusions

Delusions are firmly held erroneous beliefs that are inconsistent with the cultural, social and educational background of an individual. These beliefs are highly resistant to contrary evidence and reasoning. There have been several explanations offered for delusions centred around either providing rational interpretations for abnormal events (Ellis & Young, 1990; Maher, 1974) or abnormal reasoning processes (Garety, Hemsley, & Wessely, 1991), although more recent findings are lending support to abnormal information processing accounts (Kaney, Wolfenden, Dewey, & Bentall, 1992; Phillips & David, 1998).

Broadly, delusions can be classified within four domains: persecution, grandeur, reference and control. Delusions of persecution are the most common. Here, individuals believe others are trying to harm, threaten or manipulate them. These delusions can include fears of being watched, followed or poisoned. Individuals are considered to have delusions of grandeur if they have an inflated sense of self. For example, individuals may believe they are very rich and famous or particularly powerful or gifted. Reference delusions are occasionally related to delusions of grandeur. People experiencing reference delusions believe events in the world and the behaviour of others pertain to them. For example, individuals may believe that television programmes or news articles are produced specifically about them. Finally, delusions of control refer to the feeling of being able to control other people or world events. A common variant of this type of



delusion includes believing the thoughts of others can manipulate an individual's own behaviour.

### Grossly Disorganised or Catatonic Behaviour

Psychomotor disturbances are either accelerated or reduced motor activity, including postures, movements and speech. Individuals experiencing high levels of these symptoms may alternate between aimless excessive movements and periods of stupor. This cluster of symptoms incorporates catalepsy, holding unusual positions for an extended period of time. Catalepsy can also be accompanied by waxy flexibility whereby individuals can be re-positioned with relative ease. Other behaviours include stereotypies, the repetitive movement of a single body part; automatism, automatic compliance to commands irrespective of consequences and negativism, a behavioural response in opposition to what was intended.

### Disorganised Speech

When considering this cluster of symptoms it is important to differentiate thought content, such as delusions, from the form of thought disorder. Considering the latter, Andreasen (1982) proposed it is important to establish whether individuals exhibit disordered thought processes or disorganised language and speech. Disordered thought processes can manifest in multiple ways including concrete thinking, the literal interpretation or use of expressions and loosening of associations, moving from topic to topic without coherent progression. This is in contrast to disorganised speech where individuals may produce speech that is inconsistent with grammatical convention resulting in a 'word salad' or the creation of new words (neologisms).

### Negative Symptoms

Three of the most commonly reported emotional disturbances in people with schizophrenia are anhedonia, blunted and inappropriate affect. Anhedonia is reduced feelings of pleasure from previously enjoyed activities. Anhedonia can be divided into social and physical domains; social anhedonia is reduced enjoyment from interacting with friends or family, and physical anhedonia is reduced pleasure from physical items such as food and drink. Blunted affect refers to a reduction in the range or intensity of emotions experienced, including reduced facial expression and vocal intonation. This is

in contrast to inappropriate affect whereby the emotional expression of an individual is inconsistent with the circumstance.

## ASSESSING SYMPTOMS

Several tools exist for assessing the extent and severity of symptoms experienced by individuals with schizophrenia. The positive/negative dichotomous model formalised by Crow (1980) initially appeared promising for understanding variability in the aetiology, treatment and prognosis of schizophrenia. In practice, however, tools based on this framework produced inconsistent results (e.g. Andreasen, 1982; Bell, Lysaker, Beam-Goulet, Milstein, & Lindenmayer, 1994; Lindenmayer, Bernstein-Hyman, & Grochowski, 1994). More recently, factor analyses of symptom ratings have indicated that schizophrenia symptoms cluster along three, rather than two, dimensions (e.g. Arndt, Alliger, & Andreasen, 1991; Liddle, 1987).

Under this three-factor structure, the negative dimension remains essentially the same as in the Crow model (1980), but the dimension of disorganisation (incorporating inappropriate affect and thought disorder) can be distinguished from the symptoms of hallucinations and delusions that formed part of the original positive dimension (Cameron et al., 2002). Since the identification of these three dimensions, the underlying structure of instruments developed to assess positive and negative symptoms (e.g. Positive and Negative Syndrome Scale [PANSS]; Kay, Fiszbein, & Opfer, 1987) has been re-evaluated. The three dimensions of positive, negative and disorganised symptoms have consistently emerged, in spite of differences in samples between studies, including demographic characteristics, illness duration and treatment type (e.g. Bell, Lysaker, Milstein, & Beam-Goulet, 1994; Peralta & Cuesta, 1994). Now, it is commonly accepted that the positive dimension incorporates delusions, hallucinations, grandiosity, suspiciousness and unusual thought content; the negative dimension comprises blunted affect, emotional withdrawal, lack of spontaneity or flow of conversation, motor retardation and active social avoidance; and the disorganised dimension includes conceptual disorganisation, difficulty in abstract thinking, disorientation and poor attention (Cameron et al., 2002).

## SUBTYPES OF SCHIZOPHRENIA

Previously under the DSM-IV diagnostic criteria (APA, 2000) schizophrenia diagnoses were differentiated depending on the most significant and predominant symptoms experienced by the individual. Since symptoms can change over the course of the illness, it was not unusual for individuals with schizophrenia to change diagnostic subtype. Under these criteria the recognised subtypes of schizophrenia were: paranoid, disorganised, catatonic, undifferentiated and residual (APA, 2000).

The paranoid subtype was characterised by hallucinations, most commonly auditory, and delusions primarily of persecution and conspiracy. Disorganised subtype, as the name suggests, was characterised by disorganised thought processes and behaviour, and often co-occurred with emotional impairments and communication difficulties. This subtype tended to onset earlier than other subtypes; usually before mid-twenties (Fenton & McGlashan, 1991). Catatonic subtype was typically characterised by movement disturbances; either vastly reduced or increased voluntary movement. Individuals diagnosed with this subtype may also have exhibited actions that seemed purposeless and were performed repetitively. Alternatively, patients may have demonstrated echolalia or echopraxia, mimicry of another's speech or movements. This subtype often onset suddenly and was more rare than other subtypes. Individuals diagnosed with undifferentiated subtype experienced symptoms of schizophrenia, however these were not sufficiently formed or specific enough to be classified as another subtype. Alternatively, individuals with atypical or fluctuating symptoms may have received this diagnosis. Finally, individuals received a residual subtype diagnosis when they no longer experienced prominent symptoms. Hallucinations, delusions and other symptoms may still have been present but these were of a significantly reduced intensity and frequency compared to acute phases of illness.

During the development of DSM-IV, it was acknowledged that these subtypes had poor reliability and prognostic value (McGlashan & Fenton, 1994), however the decision to continue using these subtypes was retained due to their substantial clinical tradition (Flaum, Andreasen, & Widiger, 1994). Nonetheless, subsequent investigations using cluster analysis, among other approaches, to identify taxonomic subtypes of schizophrenia have consistently failed to identify the DSM-IV clinical subtypes of

schizophrenia (Helmes & Landmark, 2003; Linscott, Allardyce, & van Os, 2010; Lykouras, Oulis, Daskalopoulou, Psarros, & Christodoulou, 2001; Peralta & Cuesta, 2003; Picardi et al., 2012); supporting the findings of previous studies (Carpenter & Stephens, 1979; Carpenter, Strauss, & Muleh, 1973; Strauss, Bartko, & Carpenter, 1973). Consequently, subtypes of schizophrenia were eliminated from the more recent DSM-V diagnostic criteria (APA, 2013) due to limited diagnostic stability, low reliability, poor validity and prognostic value (Cardno et al., 1998; Jablensky, 2006; Korver-Nieberg, Quee, Boos, & Simons, 2011; Peralta & Cuesta, 2007).

## BOUNDARIES OF SCHIZOPHRENIA

The above description of schizophrenia appears to consider this disorder as an “all-or-none” phenomenon whereby individuals either have a diagnosis and receive treatment or are healthy and symptom-free. Whilst this is a convenient way to conceptualise illness, in practice this is more difficult to implement and diagnostic classifications now exist to reflect disorders that share similarities with schizophrenia, but do not fully warrant this diagnosis. The following sections will describe some of these conditions characterised by the DSM-V criteria (APA, 2013).

### Schizophreniform Disorder

According to the DSM-V criteria, this condition precisely reflects the symptomology of schizophrenia but differs in terms of illness duration. Schizophreniform disorder is diagnosed if symptoms are experienced for more than one month but less than six months. This is in contrast to schizophrenia where individuals must have experienced symptoms for more than six months. A further difference is that deterioration in social and occupational functioning is not required for diagnosis of schizophreniform disorder, and is required for a diagnosis of schizophrenia.

### Schizoaffective Disorder

Individuals diagnosed with schizoaffective disorder experience a combination of both psychotic symptoms and mood disorder. Patients must meet criteria for schizophrenia in terms of the number, type and duration of psychotic symptoms experienced, in addition to having at least two active episodes (APA, 2013). Mood symptoms must also

be present for the majority of the illness. Mood symptoms include major depressive episodes, manic episodes or a combination of the two.

A major depressive episode is characterised by experiencing five or more of the following symptoms for at least two weeks, with at least one symptom being either depressed mood or loss of interest or pleasure: i) depressed mood, ii) markedly diminished interest in almost all activities, iii) significant weight loss or gain when not dieting, iv) insomnia or hypersomnia, v) psychomotor agitation or retardation, vi) fatigue or loss of energy, vii) feelings of worthlessness or excessive, inappropriate guilt feelings, viii) reduced ability to concentrate or indecisiveness, ix) recurrent suicidal ideation (APA, 2013). A manic episode is characterised by experiencing abnormal and persistently elevated, expansive or irritable mood for at least one week with at least three or more of the following symptoms being present to a significant degree: i) inflated self-esteem or grandiosity, ii) decreased need for sleep, iii) increased talkativeness, iv) racing thoughts, v) increased distractibility, vi) increase in goal-directed activity or psychomotor agitation, vii) excessive engagement with pleasurable activities with high potential for negative consequences (APA, 2013). Finally, to diagnose both depressive and manic episodes the symptoms experienced should not be attributable to the direct physiological effects of any substance or general medication and the mood disturbance should be sufficiently severe as to disrupt social or occupational functioning.

Importantly, delusions and hallucinations must occur in the absence of mood symptoms for at least two weeks, and use or abuse of substances including medications, recreational drugs and alcohol must be ruled out. Finally, unlike schizophrenia, social or occupational dysfunction is not a pre-requisite for a diagnosis of schizoaffective disorder, though functioning is frequently impaired in individuals with this diagnosis.

### Schizotypal Personality Disorder

This disorder is characterised by eccentric behaviour, odd or magical thinking, reduced interpersonal skills in conjunction with great difficulty in establishing and maintaining close personal relationships. Importantly, to receive this diagnosis, individuals must demonstrate a long-enduring pattern of behaviour. Evidence from heredity studies indicates that there is greater prevalence of this disorder in relatives of schizophrenia patients than in comparison groups (Condray & Steinhauer, 1992; Kendler, Gruenberg,

& Strauss, 1981; Kety et al., 1994). This condition is therefore considered to be part of the genetic spectrum of schizophrenia.

## SCHIZOTYPY

The disorders described above are all recognised by DSM-V (APA, 2013). Some researchers, however, have suggested that schizophrenia-like symptoms and psychological characteristics can be found in non-clinical samples as well as patient populations, albeit to a lesser extent. Collectively these traits are termed schizotypy and they refer to the propensity of an individual to experience schizophrenia-like phenomena. Several models have been developed to describe this concept. The following sections will describe the three principal approaches to schizotypy, and how schizotypy is defined for the work reported in this thesis.

According to the quasi-dimensional, or disease model, schizotypy is considered to be a milder form of schizophrenia (Meehl, 1962; Rado, 1953). This approach is thus firmly rooted in the illness domain. Individuals scoring highly for one or more schizotypy domains show signs of psychological ill-health or partially expressed schizotaxia, which is proposed to be a heritable neurointegrative defect that underlies schizophrenia (Meehl, 1962). Furthermore, this model implies that those scoring highly for schizotypy would be at increased risk or vulnerable to developing fully-characterised schizophrenia. This view is consistent with work by Chapman and colleagues who found that healthy individuals experiencing psychotic-like phenomena or social and physical anhedonia were psychosis-prone (Chapman & Chapman, 1985, 1987; Chapman, Edell, & Chapman, 1980). Under this model, one proposed mechanism for schizotypal individuals transitioning to full diagnosis is sufficient psychological stress; consistent with the stress-vulnerability model (Zubin & Spring, 1977). Despite receiving support from several research groups, this approach to schizotypy was challenged by the findings of McCreery and Claridge (1995) who found that individuals reporting aberrant perceptions or unusual beliefs can consider these experiences to be positive rather than negative or indicative of ill-health.

An alternative approach was proposed by Eysenck (1960) who adopted a personality approach to schizotypy. This approach assumes that all psychotic disorders arise from the trait of psychoticism and that a person experiencing psychosis is positioned towards

the upper limits of a normality-psychosis continuum (Eysenck, 1992; Eysenck & Eysenck, 1975; Eysenck, Eysenck, & Barrett, 1985). In support of this view, Claridge and colleagues have reported elevated psychoticism scores among schizophrenia patients and their first-degree relatives (Claridge, Robinson, & Birchall, 1983, 1985). Despite this support, this approach has been criticised for not qualitatively distinguishing healthy individuals and patient groups (Claridge, 1997).

Claridge (1997) tried to reconcile these approaches by developing a fully-dimensional approach to schizotypy. Claridge (1997) proposed that schizophrenia could be conceptualised as a continuum throughout the general population, rather than a dichotomous psychiatric condition where an individual either does or does not have the disorder. According to this view, schizotypy is a personality trait present to varying degrees throughout the population (Claridge et al., 1996). However, schizophrenia is not simply considered extreme schizotypy. Rather, it incorporates other factors, including genetic and neurodevelopmental changes, which make this disorder pathological (Claridge et al., 1996). In this sense, schizophrenia is viewed on a second continuum, parallel to schizotypy, incorporating clinical states such as schizotypal personality disorder and psychosis (Claridge & Beech, 1995).

The work in this thesis conceptualises schizotypy using the approach proposed by Claridge (1997), where schizotypy represents the propensity of individuals in the general population to experience psychotic-like symptoms, rather than a clinical disorder. The following sections will review the evidence for the presence of psychotic phenomena in the general public.

#### EVIDENCE FOR PSYCHOTIC PHENOMENA IN THE GENERAL POPULATION

Kendler, Gallagher, Abelson, and Kessler (1996) found that based on 5,877 respondents to a National Comorbidity Survey, 28.4% endorsed at least one psychosis screening question. Similarly, Olfson et al. (2002) found that 20.9% of the 1,005 surveyed attendants of a large, urban, university-affiliated general medical practice serving a low income community reported experiencing at least one psychotic-like symptom, most commonly auditory hallucinations.

Rather than broadly assessing the prevalence of psychotic-like experiences, other researchers have chosen to focus on particular symptom types. One of the earliest investigations into hallucinations specifically was conducted by Sidgwick, Johnson, Myers, Podmore, and Sidgwick (1894). 17,000 adults from ten countries were interviewed using a standard interview schedule. Those with obvious physical or psychiatric conditions were excluded from further analysis, but of the remaining participants nearly 8% of men and 12% of women reported experiencing at least one hallucinatory experience in their lifetime. Similar results were obtained in a more recent investigation conducted by Tien (1991). Under the NIMH Epidemiologic Catchment Area Program, 18,572 community residents were interviewed using the Diagnostic Interview Schedule (Robins, Helzer, Croughan, & Ratcliff, 1981). Lifetime prevalence of hallucinations not directly attributable to substances or physical problems was approximately 10% for men and 15% for women, with comparable rates of people endorsing these experiences when differentiated by hallucinatory modality. Importantly, significantly more people reported these experiences did not cause distress or impair functioning compared to those that reported they did. These findings therefore provide further evidence that challenge quasi-dimensional or disease models of schizotypy.

Similar findings have been obtained when investigating delusional beliefs in the general population. Peters, Joseph, and Garety (1999) developed a self-report measure – the Peters Delusional Inventory [PDI] – which, in addition to assessing a wide range of delusional beliefs, also assesses the degree of distress, preoccupation and conviction surrounding the beliefs. When the PDI was administered to 272 healthy adult participants, individual items were endorsed, on average, by 25% of participants. Furthermore, when this measure was completed by 20 inpatients experiencing psychotic symptoms the inpatients had a higher mean score compared to healthy individuals, but the range of scores was comparable across groups. Interestingly, nearly 10% of healthy individuals had mean scores above the mean inpatient score. Taken together, these findings suggest that a proportion of healthy individuals report experiencing a range of schizophrenia-like experiences, supporting descriptions of psychosis on a continuum.

Some researchers have suggested that if psychosis is truly dimensional it would be possible to demonstrate specific symptom dimensions found within schizophrenia in the general population; namely positive, negative and disorganised dimensions.



Confirmatory factor analysis has revealed schizotypy has the same tripartite factor structure that is reported in schizophrenia (Vollema & van den Bosch, 1995), corresponding to various behaviours or beliefs required for a diagnosis of schizophrenia (Bentall, Claridge, & Slade, 1989; Mason, Claridge, & Williams, 1997). This tripartite structure appears invariant across culture, gender, family adversity, religious affiliation and psychopathology (Gruzelier & Doig, 1996; Raine et al., 1994; Reynolds, Raine, Mellinger, Venables, & Mednick, 2000), lending strong support to this conceptualisation of the three-factor model and the dimensionality of psychosis. Nonetheless, it is important to acknowledge that the factor structure obtained from such analyses is dependent on the measures used to collect data on symptom-endorsement. Thus, it is important to consider the factor structure obtained when other measures of schizotypy are employed.

Bentall et al. (1989) developed the Combined Schizotypal Trait Questionnaire [CSTQ] by combining items from the Eysenck Personality Questionnaire (EPQ; Eysenck & Eysenck, 1975), ten other personality scales assessing propensity for schizotypal experiences and four questionnaire scales measuring active psychotic symptomatology (Delusions-Symptoms-State-Inventory [DSSI]; Foulds & Bedford, 1975). Initial factor analyses were conducted using the 14 personality trait scales from 180 healthy adults revealing a three-factor model with factors of positive symptomology, negative symptomology and disorganisation/social anxiety. When data were re-analysed incorporating the DSSI scales, a four-factor model was extracted; three factors were comparable to those previously obtained with the additional factor indicating a social component to schizotypy. Subsequent confirmatory factor analysis conducted using data from over one thousand participants suggested this four-factor model provided the best fit for the data (Mason, 1995).

Overall, these findings suggest that schizotypy is a multidimensional construct. Most studies of both schizophrenia and schizotypy identify three dimensions; positive, negative and disorganised symptomology. Some schizotypy researchers have however identified a fourth factor comprising asocial and disinhibited behaviour and thought processes, which is not found in investigations of the factor structure of schizophrenia. Items assessing these constructs are primarily found in the psychoticism scale of the EPQ and thus it has been proposed that this factor appears only for schizotypy investigations

as scales assessing psychoticism have not been given to individuals with schizophrenia and have therefore not been included in factor analyses for patient investigations (Mason, 1995). Nonetheless, it is important to acknowledge that irrespective of the presence or absence of the fourth factor, the remaining three factors are consistent across schizotypy and schizophrenia investigations, lending support to the presence of positive, negative and disorganised dimensions in both schizotypy and schizophrenia.

Beyond lending support to the comparable dimensions within schizotypy and schizophrenia, other researchers have conducted pharmacological studies investigating schizotypy scores in relation to induced psychotic-like experiences. As previously alluded to, people with a diagnosis of schizophrenia tend to have higher scores on schizotypy dimensions than those without a diagnosis (Nettle, 2006; Peters et al., 1999; page 30). Ketamine, an N-methyl-D-aspartate (NMDA) receptor agonist, has previously been used to produce animal models of schizophrenia (Becker et al., 2003; Newcomer et al., 1999) and has been found to induce transient positive and negative symptoms in healthy human volunteers (Krystal et al., 1994). Curran and Morgan (2000) therefore decided to investigate the effect of ketamine on schizotypy scores. Individuals who reported taking ketamine 30mins before testing had higher schizotypy scores compared to those who had not taken ketamine. Furthermore, individuals who had taken ketamine still exhibited elevated schizotypy scores three days later. Similar results have been obtained in subsequent studies comparing chronic and infrequent ketamine users to control participants, with chronic users exhibiting higher schizotypy scores compared to infrequent users and both exhibiting significantly higher scores compared to control participants (Curran & Monaghan, 2001). Daily, chronic ketamine users also show similar patterns of 'basic symptoms' to individuals prodromal for schizophrenia (Morgan, Muetzelfeldt, & Curran, 2010). Importantly, whilst these findings are suggestive that experiencing psychotic-like phenomena are associated with higher schizotypy scores, the aforementioned investigations do not rule out the residual effects of ketamine or pre-existing differences between participants (Morgan et al., 2010). Thus, further investigations are required to more conclusively associate ketamine-induced psychotic states with elevated schizotypy scores.

Other researchers have focused on investigating cognitive and neural correlates in relation to schizotypy, rather than pharmacological interventions. For example, people

with schizophrenia exhibit attenuated pre-pulse inhibition [PPI] of the startle reflex (Braff et al., 1978; Grillon, Ameli, Charney, Krystal, & Braff, 1992). PPI is the attenuation of a startle response when the startling stimulus (e.g. loud noise) is preceded approximately 30-500ms before onset by a weaker stimulus (Graham, 1975). Non-smoking participants high in cognitive disorganisation exhibit reduced PPI between 50 and 260ms, whereas individuals high in introvertive anhedonia exhibit greater PPI at intervals of 80 and 140ms (Evans, Gray, & Snowden, 2005). Comparably, patients with schizophrenia have poor sensory gating, as indexed by P50 suppression (Boutros, Belger, Campbell, D'Souza, & Krystal, 1999; Clementz, Geyer, & Braff, 1998; Nagamoto, Adler, Waldo, Griffith, & Freedman, 1991). P50 is an Event Related Potential (ERP) index of early pre-attentive processing (Clementz et al., 1998). Evans, Gray, and Snowden (2007) showed that individuals scoring highly in cognitive disorganisation exhibited reduced P50 suppression.

Overall, the proposed similarities between schizotypy and schizophrenia imply that it is possible to investigate the mechanisms underlying symptoms of schizophrenia using non-clinical samples (Claridge, 1997). There are several advantages to using this approach, but most importantly, it is possible to avoid some of the confounds in patient research. Interpreting differences between control and patient groups is inherently difficult due to a number of variables associated with mental illness. For example, the stigma and socialisation surrounding the label of 'patient', the duration of illness, the duration and type of treatment received, and the presence or absence of comorbid diagnoses may all contribute to functioning and performance in patient groups (Lenzenweger, 2011). By examining certain functions in non-clinical groups, it is possible to test theories and highlight important areas to examine in patients with schizophrenia. Furthermore, replicating deficits observed in schizophrenia in non-clinical samples provides evidence that the deficits can be attributed to the condition, rather than to any confounding variables. In light of these advantages, in some of the experiments reported in this thesis, measures of schizotypy have been employed for initial examinations of hypotheses of interest.

## ASSESSING SCHIZOTYPY

As with assessing schizophrenia symptoms, there are several measures for assessing the various dimensions of schizotypy. Some of these measures, such as the Oxford-Liverpool Inventory of Feelings and Emotions (Mason, Claridge, & Jackson, 1995) and the Schizotypal Personality Questionnaire (Raine, 1991) are broad in scope, assessing multiple symptom dimensions. Other measures, such as the PDI (Peters et al., 1999) and Launay-Slade Hallucinatory Scale (Launay & Slade, 1981), focus on more specific symptom domains or experiences. Collectively, these measures tend to be self-reported questionnaires that require individuals to indicate whether or not an item is endorsed. Additionally, some measures, such as the PDI, require individuals to indicate to what extent items are endorsed (e.g. preoccupation and conviction of beliefs). Consequently, broad measures can be considered particularly useful for identifying dimensions of interest. Preliminary investigations using these measures can be valuable in directing subsequent studies using more specific symptom scales (e.g. Evans et al., 2007). By using more specific scales researchers can then more effectively characterise aspects of a symptom dimension that may be pivotal to functioning.

When constructing schizotypy measures, it is important to consider the manner in which items are scored. For example, some scales, such as the Schizotypal Personality Questionnaire (Raine, 1991), result in high scores when individuals provide affirmative answers to items. As a result, these measures are potentially more subject to acquiescence response bias in participants. This is in contrast to measures such as that developed by Mason et al. (1995) – The Oxford Liverpool Inventory of Feelings and Experiences [O-LIFE]. This measure is based on the CSTQ originally developed by Bentall et al. (1989), described in more detail in the previous subsection. However, the CSTQ consists of 420 items and was therefore deemed impractical for experimental research due to the time-consuming, fatiguing and repetitive nature of the measure (Claridge et al., 1996). Consequently, new scales for the four factors identified in the CSTQ were developed. The O-LIFE was designed for use with healthy adult volunteers and consists of items assessing general personality characteristics and only later presents participants with items addressing the different dimensions of schizotypy. Constructing the questionnaire in this way arguably reduces the pathological feel of the measure, increasing the likelihood that participants will respond honestly and producing

reasonable rates of endorsement across items (Mason et al., 1995). Furthermore, although most items in this measure require affirmative responses to produce high scores, some items are reverse scored. This method of scoring avoids the acquiescence response bias that is potentially associated with measures only requiring affirmative answers to produce high scores. Most importantly, the O-LIFE has been found to have both high internal consistency ( $\alpha > 0.77$ ; Mason et al., 1995) and test-retest reliability (Burch, Steel, & Hemsley, 1998). Consequently, this measure is used to assess schizotypy in the first three experiments reported in this thesis, in conjunction with more specific symptom scales.

## COGNITIVE DYSFUNCTION IN SCHIZOPHRENIA

An increasingly accepted domain of dysfunction in schizophrenia is cognition (Green, 1996; Green, Kern, Braff, & Mintz, 2000). It is estimated that cognitive deficits affect 75-85% of patients with schizophrenia (Reichenberg et al., 2006). Mesholam-Gately, Giuliano, Goff, Faraone, and Seidman (2009) conducted a meta-analysis of 47 studies of first-episode (FE) schizophrenia patients compared to healthy control participants. This meta-analysis incorporated 43 different samples, and assessed 156 cognitive test variables, divided into ten cognitive domains: i) general cognitive ability, ii) immediate verbal memory, iii) delayed verbal memory and learning strategies, iv) non-verbal memory, v) attention (processing speed, working memory and vigilance), vi) language function, vii) visuospatial abilities, viii) executive functioning, ix) social skills and x) motor skills. Immediate verbal memory had the largest effect size (Standard Mean difference [SMD]=-1.20), where negative effect sizes represent worse performance by FE patients compared to control participants. These findings are consistent with those in previous meta-analyses using older, chronic schizophrenia patients (e.g. Aleman, Hijman, de Haan, & Kahn, 1999; Heinrichs & Zakzanis, 1998;  $d=-1.22$  and  $d=-1.41$  respectively). Mesholam-Gately et al. (2009) also found the attention-processing speed subdomain and non-verbal memory domain had the second and third largest effect sizes (SMD=-0.96 and -0.91 respectively). The non-verbal memory domain effect size presented in Mesholam-Gately et al. (2009) is intermediate to the values found by Heinrichs and Zakzanis (1998);  $d=-0.74$  and Aleman et al. (1999);  $ds=-1.0$  -  $-1.09$ . Comparisons between the effect sizes for the attention-processing speed subdomain and those of the two aforementioned meta-analyses are not possible as analogous measures were not

incorporated in the previous meta-analyses. However, the main cognitive test variable contributing to the attention-processing speed effect size was the Digit Symbol Substitution Test [DSST] (Wechsler, 1997), where the effect size (SMD=-1.59) is of the same magnitude as that reported by Dickinson, Ramsey, and Gold (2007);  $d=-1.57$  in a meta-analysis of 37 studies.

The consistency between the findings across these studies despite differences in sample characteristics highlights several important issues. First, the cognitive deficits experienced by schizophrenia patients are severe and enduring, despite psychopharmacological treatment. Cognitive deficits not only predict adherence to medication (Burton, 2005), but also treatment programmes more broadly, including psychological therapies (Prouteau et al., 2005). Patients presenting with significant cognitive deficits also show reduced living and social skills (Bowie & Harvey, 2005), as well as an increased tendency for symptom relapse (Chen et al., 2005). Second, memory and attention are the most disrupted in schizophrenia compared to other cognitive domains. Deficits in these domains are also the strongest predictors of functional outcome (Green et al., 2000; Nuechterlein et al., 2011; Puig et al., 2008). These findings highlight alleviating cognitive dysfunction as an important treatment target.

#### RELATIONSHIP OF COGNITIVE DYSFUNCTION TO SYMPTOM DIMENSIONS IN SCHIZOPHRENIA

One approach to understanding the heterogeneity of schizophrenia is to consider symptom clusters in relation to cognitive deficits. In doing so, it may be possible to identify the mechanisms underlying dysfunction (e.g. Strauss et al., 1974). However studies of this kind have yielded inconsistent results. For example, Bell, Lysaker, Milstein, et al. (1994) reported that performance on a variety of cognitive tests including the Wisconsin Card Sorting Task (WCST; a measure of executive function; Grant & Berg, 1948; Heaton, Chelune, Talley, Kay, & Curtiss, 1993), and the DSST (a measure of attention; Wechsler, 1997) predicted more than one third of the variance in PANSS Cognitive Scores. PANSS Cognitive Scores are derived from items assessing difficulty in abstract thinking, poor attention and cognitive disorganisation (Bell, Lysaker, Milstein, et al., 1994), meaning that these cognitive performance scores can be related to the disorganised dimension of schizophrenia.

These findings contrast with others where there have been associations between specific cognitive deficits and negative symptoms. Aleman et al. (1999) conducted a meta-analysis of 70 studies investigating neurocognitive deficits in schizophrenia patients and identified a small but significant negative association between negative symptoms and memory performance ( $Q_B=4.0$ ). Positive symptoms were not associated with memory performance. Partially similar results were found by Nieuwenstein, Aleman, and de Haan (2001). They investigated WCST (Wechsler, 1997) and Continuous Performance Task performance (CPT; a measure of attention; Rosvold, Mirsky, Sarason, Bransome Jr, & Beck, 1956) in relation to the positive, negative and disorganised symptoms of schizophrenia. Negative symptoms were negatively correlated with WCST and CPT performance. Mirroring Aleman et al. (1999), no correlations were identified for positive symptoms. Disorganised symptoms, however, demonstrated a positive correlation with perseveration scores on the WCST, but no associations were found for other measures with this symptom cluster. Despite identifying these correlations, the authors proposed that given the typically weak correlations identified, these findings could be indicative of independent disease processes for psychiatric symptoms and cognitive performance.

Considering these studies together, some consistencies can be identified. First, the cognitive deficits that are particularly pronounced in schizophrenia (e.g. attention and memory), in contrast to other domains, are associated with symptom clusters. Second, the aforementioned studies all provide evidence that disorganised and/or negative, but not positive symptoms are associated with cognitive dysfunction. These conclusions are strengthened by findings indicating that cognitive improvements in schizophrenia are typically accompanied by reductions in negative, but not positive symptoms (e.g. Schuepbach, Keshavan, Kmiec, & Sweeney, 2002). However, the divergence in terms of which symptom cluster is more strongly associated with cognitive deficits, in conjunction with propositions that separable disease processes may operate for psychiatric and cognitive symptoms, highlights the need for more specific investigations of the mechanisms underlying particular cognitive deficits in schizophrenia patients.

## METHODOLOGICAL ISSUES

### Antipsychotic Medications

There are several medications available that alleviate the symptoms associated with schizophrenia. Broadly, these can be divided into two categories: typical or atypical. Typical medications first appeared in the mid-1950s and hence are also referred to as 'first generation' medications. These medications primarily act on dopamine 2 (D<sub>2</sub>) receptors throughout the brain, but therapeutic benefits are associated with the blockade of dopamine transmission in mesolimbic dopamine pathways (Dixon, Lehman, & Levine, 1995). As a result of reducing the action of dopamine, motor disruption or extrapyramidal symptoms are common side effects of this medication. Up to 50% of patients taking these types of medications experience pseudoparkinsonism, akathisia (motor restlessness) or dyskinesia (involuntary muscle contractions resulting in twitching or repetitive movements; Love, 1996). Moreover, whilst these medications are effective for positive symptoms, they are less effective for treating negative symptoms (King, 1998). Finally, typical medications have not been shown to remediate cognitive dysfunction associated with schizophrenia (Sharma, 1999). It is important to acknowledge, though, that performance on tasks assessing cognition may be adversely affected by any motor side effects experienced (Cassens, Inglis, Appelbaum, & Gutheil, 1990).

Some of the shortcomings of these medications were addressed by the introduction of 'second-generation', atypical antipsychotic medications. These medications, in contrast to first-generation products, act on both dopamine and serotonin pathways. The advantage of these dual-action products is a reduction in certain side effects experienced by patients; namely, extrapyramidal symptoms. These medications are more commonly associated with other side effects, though, such as weight gain and sedative effects. Nonetheless, atypical medications were initially marketed as improving both positive and negative symptoms (Kane et al., 2003), and were therefore considered more effective at reducing overall symptoms compared to typical medications. Systematic reviews of this claim, however, have highlighted that this may only be true for certain atypical medications (e.g. amisulpride, clozapine, olanzapine and risperidone; Leucht et al., 2009). Finally, there is evidence to suggest that these medications are more effective



at alleviating some of the cognitive problems experienced by schizophrenia patients (Sharma, 1999), compared to typical medications.

Given the variety of medications available to treat the symptoms of schizophrenia and the potential difference in their efficacy, medications represent an important methodological issue, and will be considered when interpreting the patient data reported in this thesis.

### Smoking Status

Another methodological consideration when interpreting the results reported in this thesis is the smoking status of participants with schizophrenia. The prevalence of smoking in individuals with schizophrenia is dramatically higher compared to other psychiatric patients or control participants across a range of settings; inpatient, outpatient and community (Dalack, Healy, & Meador-Woodruff, 1998). Furthermore, patients with schizophrenia are heavier smokers and extract more nicotine per cigarette compared to the general population (Strand & Nybäck, 2005). There is considerable debate as to the reasons for increased smoking in patients with schizophrenia. One of the more prominent suggestions is self-medication across multiple domains: psychiatric symptoms, antipsychotic-induced side effects and cognitive dysfunction (Kumari & Postma, 2005).

Regarding the reduction of psychiatric symptoms, patient reports indicate that smoking reduces psychiatric symptoms, which become worse during withdrawal (Dalack & Meador-Woodruff, 1996). Whilst there have been few empirical investigations of these claims, Smith, Singh, Infante, Khandat, and Kloos (2002) found that smoking high-nicotine cigarettes, compared to de-nicotinised cigarettes, decreased negative symptoms, but did not affect positive symptoms. However, the relationship between smoking status and symptomology is far from clear. For example, Goff, Henderson, and Amico (1992) found smokers with schizophrenia experienced more positive and negative symptoms compared to non-smokers with schizophrenia, while Patkar et al. (2002) reported negative symptoms to be more prevalent in highly nicotine dependent schizophrenia patients. Despite the mixed results reported here, smoking status in relation to symptom clusters will be considered when interpreting the patient data reported in this thesis.

The administration of nicotine patches has been found to remediate antipsychotic-induced bradykinesia-rigidity in schizophrenia patients (Yang, Nelson, Kamaraju, Wilson, & McEvoy, 2002). Considering the increased prevalence of motor disturbances with certain types of antipsychotic medication, it may be the case that medication type and smoking status interact and this will also be considered when interpreting data.

Sacco et al. (2005) compared 25 smokers with schizophrenia to 25 control smokers on visuospatial working memory (VSWM) and continuous performance test (CPT) scores. Smoking abstinence reduced CPT hit rates in both groups, but VSWM was only impaired in abstaining smokers with schizophrenia. Furthermore, smoking reinstatement reversed abstinence-induced cognitive impairments. Similar cognitive improvements have also been observed in pre-pulse inhibition, smooth pursuit eye movement and anti-saccadic tasks. Studies have reliably shown schizophrenia patients exhibit impaired smooth pursuit eye movements (SPEM) and increased errors in anti-saccadic tasks compared to healthy controls (Ettinger & Kumari, 2003). Furthermore, the deficits observed in patients were ameliorated by the administration of nicotine and the performance of healthy controls was improved (Ettinger & Kumari, 2003). This evidence highlights the importance of considering smoking status when evaluating cognitive performance in both patient and matched control participants.

### Cognitive Deficits

Importantly, much of the evidence for cognitive dysfunction in schizophrenia comes from studies using standardized neuropsychological batteries. Whilst such measures have highlighted that individuals with schizophrenia generally have impaired cognition, utilising standardised measures limits the ability to understand the complexity of the underlying dysfunction, because particular tests may engage multiple cognitive processes (Cho et al., 2005). A good example of this is the DSST (Wechsler, 1997). This measure is typically considered a test of attention and is one of the most reliably documented impairments in the clinical neuropsychology literature for schizophrenia (Dickinson et al., 2007). However, successful performance on this task requires active maintenance of digit-symbol pairings in working memory, psychomotor speed as well as simple visual attention (Lesh, Niendam, Minzenberg, & Carter, 2011). Therefore, interpreting lower performance in patient populations is difficult as poorer performance could be attributed to a deficit in one or all of the aforementioned component processes

and/or deficient integration of these processes (Lesh et al., 2011). Using paradigms that isolate particular cognitive process would facilitate understanding which cognitive processes are deficient in schizophrenia.

In recent years, researchers have increasingly utilised more specialised tests in order to better understand the cognitive deficits experienced by schizophrenia patients. These approaches have revealed deficits in selective attention (e.g. Carter, Robertson, & Nordahl, 1992), working memory (e.g. Glahn, Cannon, Gur, Ragland, & Gur, 2000), episodic memory (e.g. Ranganath et al., 2008), language production (e.g. Barch & Berenbaum, 1996) and comprehension (e.g. Condray, van Kammen, Steinhauer, Kasperek, & Yao, 1995).

Using standardized neuropsychological batteries may have also clouded understanding of the relationship between symptom clusters and cognitive deficits. In contrast to what has been suggested in a previous section, more specific memory assessments have suggested that positive symptoms of schizophrenia are correlated with behavioural performance. For example, in a recognition memory paradigm, patients experiencing hallucinations and delusions were more likely to confuse imagined and perceived pictures (e.g. Brébion et al., 2000). See Chapter Four: Memory and Schizophrenia (page 80) for a more in depth review of this topic. These outcomes suggest that by using more specific cognitive tests, not only would it be possible to improve our understanding of cognitive profiles in patients with schizophrenia, but also gain better insight into the mechanisms underlying such deficits.

## CHAPTER ONE SUMMARY

The preceding sections, and the shortcomings that have been highlighted, provide the backdrop for a key premise for the work in this thesis. The starting point is the observation that whilst it is possible that schizophrenia patients experience deficits across multiple cognitive systems, a more parsimonious explanation is one proposed by Kraepelin (1919/1971), in which these deficits have a common root in impaired higher-order functions, such as cognitive control. The experiments in this thesis are designed to investigate whether deficits in cognitive control contribute to memory problems in people with schizophrenia. The methods employed to achieve this are a combination of behavioural and Event-Related Potential (ERP) measures in both healthy individuals from

whom schizotypy measures are collected and patients with schizophrenia. The following chapter in this thesis will review a model of cognitive control in relation to memory and evidence for cognitive control problems in patients with schizophrenia and those high in schizotypy; introducing the basis from which we can investigate cognitive control in relation to memory processes.

## CHAPTER TWO: COGNITIVE CONTROL

Cognitive control is crucial to everyday life. It enables an individual to manage complex demands by co-ordinating incoming sensory and motor information with higher-level internal or external goals to facilitate appropriate response selection and execution (Lesh et al., 2011). Importantly, cognitive control is not restricted to one particular cognitive domain and encompasses a broad spectrum of mental processes, including context representation and maintenance, and attention allocation (Cohen, Dunbar, & McClelland, 1990). In so far as the aforementioned processes are central to episodic memory, working memory and attention, which are processes found to be particularly deficient in schizophrenia using standard neuropsychological measures, it is possible that problems with cognitive control underlie, or at least contribute to, the deficits. Furthermore, cognitive control is implicated with prefrontal cortex (PFC) function. This point is highly relevant to schizophrenia considering the current neurochemical and psychopharmacological data concerning the illness. The PFC is known to be a primary projection area for the mesocortical dopamine system, and dopamine level disturbances have been frequently documented in schizophrenia (e.g. Losonczy, Davidson, & Davis, 1987; Meltzer & Stahl, 1976). Specifically, mesocortical dopamine is often reduced in schizophrenia and this reduction has been demonstrated to correlate negatively with cognitive function as measured by standard neuropsychological assessments (e.g. Cohen & Servan-Schreiber, 1992). Considered together, these two points serve to strengthen the hypothesis that cognitive control processes may operate less efficiently in schizophrenia patients and emphasise the importance of understanding which particular operations within cognitive control are aberrant.

Successful engagement of cognitive control processes has been linked to contributions from multiple brain regions including dorsolateral prefrontal cortex (DLPFC), medial frontal cortex (including anterior cingulate cortex) and parietal regions (e.g. Botvinick, Braver, Barch, Carter, & Cohen, 2001; Yarkoni et al., 2005). These regions interact with each other, as well as other regions, in order to successfully control behaviour. For example, functional Magnetic Resonance Imaging (fMRI) and repetitive Transcranial Magnetic Stimulation (rTMS) studies suggest that the DLPFC has a principal role in maintaining rules for action, through integrating short-term memory representations with goal-directed motor behaviour (Asaad, Rainer, & Miller, 2000; Hadland, Rushworth,

Passingham, Jahanshahi, & Rothwell, 2001; Schumacher & D'Esposito, 2002). On the other hand, medial frontal cortex, specifically anterior cingulate cortex, has been hypothesised to play a critical role in response-conflict detection, and can interact with DLPFC to signal when control-related activity should be increased in service of performance (e.g. Egner & Hirsch, 2005; Kerns et al., 2005). Parietal regions, by contrast, have been proposed to provide DLPFC with information about stimulus-response pairings (e.g. Bunge, Hazeltine, Scanlon, Rosen, & Gabrieli, 2002; Bunge, Kahn, Wallis, Miller, & Wagner, 2003). Possible functions for these regions, and how they interact, have been identified on the basis of functional imaging data acquired from healthy participants whilst completing tasks requiring cognitive control (e.g. Liston, Matalon, Hare, Davidson, & Casey, 2006; Yeung, Nystrom, Aronson, & Cohen, 2006), and through the demonstration of predictable deficits in cognitive control following damage to the aforementioned brain regions (Miller, 2000). For example, patients and primates with prefrontal damage exhibit more perseveration errors following rule changes in the Wisconsin Card Sorting Task compared to healthy control participants (Dias, Robbins, & Roberts, 1996; Milner, 1963). Whilst a complete review of the literature surrounding the involvement of prefrontal cortex (PFC) regions in control mechanisms is beyond the scope of this thesis, it is important to summarize its contribution with regards to cognitive processes.

PFC integrity is fundamental to the integration of incoming information and the implementation of 'top down' processing in order to co-ordinate behaviour (Miller, 2000). Given that various pathways in the brain are involved in information processing, inherently there is competition in the selection of an appropriate behavioural response, as a result of multiple inputs (Lesh et al., 2011). Miller and Cohen (2001) proposed that the PFC manages this competition by acting as an 'online storage' that maintains rules to facilitate the evaluation of incoming information (as well as internal states) and guide response selection in service of current goals. By this view, when confronted with conflicting information, the PFC provides cognitive control by restricting neural processing across the brain according to the rules necessary for successful performance (Lesh et al., 2011). By performing in this way, PFC can bias neural processing in various ways, with one important example being a bias away from prepotent but incorrect responses and towards appropriate responses (Lesh et al., 2011). Considering the focus of this thesis is to understand whether cognitive control deficits contribute to the

memory deficits experienced by patients with schizophrenia, the following sections will describe the ways in which cognitive control can contribute to memory.

## COGNITIVE CONTROL IN MEMORY

Cognitive control in memory presumably acts both during memory encoding and memory retrieval. For example, at the time of encoding the ability to focus on task-relevant contents is a determinant of successful retrieval (Otten & Rugg, 2001). At retrieval an interaction between a retrieval cue and a memory trace (Schacter, Eich, & Tulving, 1978; Semon, 1921) is critical to retrieval success, but also important are processes that precede as well as follow this interaction. Moreover, it is important to acknowledge that encoding and retrieval processes should not be considered in isolation since the outcome of retrieval processes is dependent on the compatibility of the information encoded and the availability of retrieval cues (Tulving & Thomson, 1973). The model given below is one way in which control operations in memory have been articulated.

Ranganath et al. (2008) proposed that there are a number of points at which cognitive control could exert an effect at both encoding and retrieval. Encoding processes are critical for determining the subsequent content and accessibility of an event. When an event is encoded, several processes are engaged including perceptual, conceptual and action processes (Figure 1A). However, these processes do not act in isolation. Cognitive control mechanisms are recruited to direct attention to task-relevant processes and away from those which are task-irrelevant (Ranganath et al., 2008). Furthermore, cognitive control permits relational binding, which is the integration of multiple representations into a coherent concept, a process known to contribute to later successful memory retrieval ( Craik & Lockhart, 1972; Ranganath et al., 2008). The number of representations incorporated into the coherent concept is in turn a product of the degree of cognitive control exerted during the selection of task-relevant processes (Ranganath et al., 2008). The kinds of control mechanisms utilised, as well as the degree to which processes are engaged, influence the efficacy of encoding processes (e.g. Atkinson & Shiffrin, 1968; Craik & Lockhart, 1972). For example, it has been repeatedly demonstrated in word list learning that when items are encoded in terms of their surface features (e.g. size, colour or font of text), or in a process-specific way (e.g. relational

binding is not engaged), memory is consistently worse than when items are encoded using item-specific strategies, (e.g. forming a mental image about the word; Blumenfeld & Ranganath, 2007; Craik & Lockhart, 1972), or when relational binding is implemented. This evidence suggests that the degree and kinds of processes engaged in service of encoding can influence the likelihood of later retrieval, and cognitive control influences which processes are utilised and which are suppressed (Atkinson & Shiffrin, 1968; Craik & Lockhart, 1972; Ranganath et al., 2008).

*Image redacted in accordance with point 7.2 of the Senate Regulations for the Presentation and Submission of Research Degree Theses at Cardiff University*

***Figure 1 – A schematic representation of the processes that support memory encoding and retrieval reproduced from Ranganath, Minzenberg, and Ragland (2008). (A) Episodic memories require many different representations to be bound into a coherent concept, namely perceptual, conceptual and action representations. Cognitive control influences which processes will be utilised as well as which will be suppressed. (B) Context cues and more specific retrieval cues elicit recovery of episodic information during retrieval. Cognitive control processes play a critical role in the generation of retrieval cues, filtering of recovered information, and the selection of the criteria necessary to produce a response.***

Processes engaged around the time of retrieval also play a critical role in determining whether information surrounding a prior event is successfully and accurately recovered (Figure 1B; Raaijmakers & Shiffrin, 1981). As previously stated



(page 45), interactions between retrieval cues and memory traces are critical to successful retrieval of events (Schacter et al., 1978). Often, the likelihood of accurately retrieving information from memory depends on the availability of retrieval cues and the conditions under which the retrieval attempt occurs (Ranganath et al., 2008; Tulving, 1983). For example, it is possible that one retrieval cue activates multiple memory traces. Often, this occurs as a result of interference. One conceptualisation of interference is the interaction and competition between multiple retrieval cues for memory traces. Under this view, the likelihood of successfully retrieving an episodic event is contingent not only on how strongly the cue is related to the trace, but also how many other cues are related to the trace, and the strength of these relationships (Anderson & Neely, 1996; Levy & Anderson, 2002). Another, related conceptualisation of interference refers to any events occurring in between the current retrieval attempt and the past, to-be-remembered event (Tomlinson, Huber, Rieth, & Davelaar, 2009). The degree to which the interim events are similar to the to-be-remembered event influences the amount of interference (McGeoch & McDonald, 1931). In cases of high similarity, there is increased competition between the specific retrieval cues that differentiate the episodic event in question from other events occurring in a similar context, making it more difficult to retrieve the to-be-remembered event (Ranganath et al., 2008). In such cases, control mechanisms can facilitate the activation of task-relevant traces, and inhibit task-irrelevant traces. This can be done at several levels. At the level of specific context or retrieval cues, cognitive control can constrain processing of task-irrelevant cues and prioritise the processing of task-relevant cues (Anderson & Bjork, 1994; Bjork, 1989; Ranganath et al., 2008). Context cues can be defined as any intrinsic or extrinsic characteristic of a presentation or item (Smith, Glenberg, & Bjork, 1978). Cognitive control can also be implemented once information has been retrieved and/or during response selection (Ranganath et al., 2008). Processes engaged once information has been retrieved are often referred to as source monitoring processes (Johnson, Hashtroudi, & Lindsay, 1993), and permit individuals to evaluate recovered information in relation to the task at hand. Failure to successfully monitor information at this stage can result in memory distortions or inappropriate response selections (Johnson et al., 1993). However, as highlighted by Lindsay, Johnson, and Kwon (1991) the efficacy of cognitive control processes occurring after context and retrieval cues processing is dependent on the ability to distinguish such cues in the initial instance. Lindsay et al. (1991) demonstrated that increasing the

perceptual (e.g. female/female vs. male/female voices) or semantic (e.g. content) similarity between two sources of information resulted in poorer source-memory performance (e.g. attributing the information to the appropriate voice). These results were explained in terms of reduced ability to discriminate between memory traces due to increased competition between retrieval cues (e.g. the similarity of the sources). These conclusions emphasise the importance of effective cognitive control during memory retrieval.

The principal focus of this thesis is to understand the ways in which cognitive control can contribute to memory deficits in patients with schizophrenia. A retrieval or context cue refers to any stimulus that brings a memory to consciousness or into behaviour (Tulving, 1985). Thus, this thesis will not directly examine processes acting pre-retrieval cue presentation, though considerations of these processes may be made at times. More detailed considerations of how cognitive control during memory retrieval can be investigated will be discussed in Chapter Three: Memory Models and Frameworks (page 67). First, the following sections describe some of the key evidence from studies investigating cognitive control deficits in patients with schizophrenia and those using measures of schizotypy, in addition to reviewing some of the challenges associated with this line of work.

#### EVIDENCE FOR COGNITIVE CONTROL DEFICITS IN SCHIZOPHRENIA

Evidence for deficient control processes in schizophrenia comes from a variety of sources, including patient and animal model studies. For example, Kerns (2007) identified two symptom clusters that were differentially associated with the use of cognitive control mechanisms during working memory and both episodic and semantic retrieval tasks in schizophrenia patients. Assessments of working memory consisted of two tasks: the N-Back task (Cohen et al., 1997) and the Sternberg Probe Item Recognition Task (SPRIT; Jonides, Smith, Marshuetz, Koeppe, & Reuter-Lorenz, 1998). Measures of controlled retrieval similarly consisted of two tasks: the SPRIT (Jonides et al., 1998) and the Semantic Comparison Task (Wagner, Paré-Blagoev, Clark, & Poldrack, 2001). Formal thought disorder (FTD; disorganised symptom), but not poverty of speech (negative symptom; both measured using structured interview), was associated with poor working memory performance. In contrast, poverty of speech, but not FTD, was associated with

poor controlled retrieval. Moreover, FTD was predicted by an interaction between working memory and controlled retrieval performance. Kerns (2007) suggested that this interaction implied that patients with the highest levels of FTD experience both poor working memory and poor controlled retrieval.

The intention in the study conducted by Kerns (2007) was to relate symptom clusters to particular deficits in cognitive control, but there are several important confounds that limit the utility of the findings. First, the same task (SPRIT) was used as an assessment of both working memory capacity and controlled retrieval. Although different dependent measures were used to assess each process, both measures were derived from the same task. Consequently lower performance is difficult to interpret as it could be due to deficits in each individual process or the integration of these processes (Lesh et al., 2011). Nonetheless, the two dependent measures obtained from SPRIT did not correlate (Kerns, 2007). Whilst these findings are reassuring in that they suggest the different dependent measures are not contaminated by another process, this does not escape the fact that the task itself assesses multiple cognitive processes simultaneously, as do many other cognitive tasks. This highlights the importance of using measures that might be able to identify the contributions of specific processes to behavioural output, such as ERPs.

A further, related limitation of this design is that, as previously highlighted (page 45), control processes operating during memory retrieval can be implemented at multiple levels (e.g. context and retrieval cues, post-memory trace retrieval). The tasks utilised here to assess controlled retrieval do not provide a measure of the level at which such control processes are acting. Therefore, the findings obtained by Kerns (2007) indicate only partially how controlled retrieval processes are affected in schizophrenia patients. The findings primarily highlight that collectively a set of processes do not operate as effectively (Lesh et al., 2011).

A final comment regarding the conclusions drawn by Kerns (2007) concerns the validity of the proposition that the interaction between working memory performance and controlled retrieval accentuates the importance of retrieval processes to successful task performance. Considering working memory consists of several subcomponents (e.g. encoding, maintenance and higher executive functions required for the manipulation of information), this study is limited in its ability to separate retrieval control mechanisms from other processes in working memory tasks. Other researchers have attempted to

overcome this criticism by using event-related fMRI designs, which make it possible to differentiate the contributions of the subcomponents of working memory to task performance, in so far as this can be inferred from activity in discrete brain regions. Schlösser et al. (2008) demonstrated that during the executive manipulation part of a working memory task, schizophrenia patients exhibited a significantly stronger activation pattern in fronto-parietal networks compared to control participants. In contrast, during the stimulus encoding part of the task, schizophrenia patients exhibited significantly decreased activation in prefrontal cortex (PFC) and anterior cingulate gyrus compared to controls. These altered activations in schizophrenia patients were accompanied by lower performance compared to controls across all elements of the working memory task. The authors interpreted these findings as suggesting that altered activity during executive control is preceded by abnormal encoding of information, which could contribute to poorer performance.

The results obtained by Schlösser et al. (2008) have two important implications. First, that the encoding subcomponent of working memory performance is indeed disrupted in schizophrenia. However, as retrieval control processes were not examined by Schlösser et al. (2008), the full extent of the conclusion drawn by Kerns (2007) could not be tested. Nonetheless, this disruption to encoding processes has been found to have functional significance in that such deficits contribute to reduced performance on working memory tasks. Second, PFC activation is associated with the encoding subcomponent of working memory performance. This association provides further support for the previously discussed importance of PFC to a variety of cognitive operations (page 44).

Other researchers have employed behavioural measures to isolate retrieval processes. In pursuit of this, many researchers have used word fragmentation completion (WFC) paradigms. During the study phase of these tasks, participants are serially presented with words (e.g. SHADE) and during the subsequent test phase, participants are presented with the same items but in fragmented form (e.g. with missing letters; SH\_ \_E). WFC tasks are able to examine encoding separately from retrieval processes, considering during such paradigms individuals are encouraged to focus on the orthographic aspects of items, limiting the type and amount of information encoded, and thus, the type of information available during retrieval. This task simultaneously increases the need to use

retrieval cues to inhibit task-irrelevant completions, due to the competition between memory representations (e.g. SH\_ \_E could be completed as SHADE, SHAME, SHAPE; Rass, Leynes, Hetrick, & O'Donnell, 2011). Rass et al. (2011) conducted a variant of the WFC paradigm using different trial types to further inform the understanding of how cognitive control mechanisms are dysfunctional in schizophrenia. Participants were presented with control trials, where the word fragment (e.g. BAL\_ \_N\_) was preceded by a string of ampersands; blocking trials, in which the word fragment was preceded by an irrelevant, but orthographically related word (e.g. BALLOON); and priming trials where the completed word was presented before the word fragment (e.g. BALCONY). Rass et al. (2011) demonstrated that patients with schizophrenia completed fewer word fragments for all trial types than control participants, despite exhibiting comparable repetition priming effects (e.g. faster reaction times [RTs] to priming trials, compared to control trials; Healey, Campbell, Hasher, & Osher, 2010) and blocking magnitude (e.g. slower RTs to blocking trials compared to control trials; Smith & Tindell, 1997). Furthermore, schizophrenia patients exhibited more intrusion errors (e.g. incorrect word completions) on blocked trials, and fewer omission errors (e.g. withholding of a response) compared to controls. The authors suggested that the comparable magnitude of priming and blocking effects across the patient and control group indicated intact orthographic and lexical priming in schizophrenia patients (e.g. intact encoding processes, at least for this task). Moreover, Rass et al. (2011) proposed that schizophrenia patients are more sensitive to implicit memory interference, as indicated by the increased number of intrusion errors on blocking trials, as a result of deficient lexical selection processes (e.g. deficient retrieval control processes at the level of response selection). Overall, this provides evidence for deficits in control mechanisms at the level of selection and inhibition of competitors in patients with schizophrenia.

As with encoding, retrieval control mechanisms have similarly been associated with PFC function. Ragland et al. (2009) conducted a meta-analysis of 36 functional imaging studies (fMRI and positron emission tomography [PET]). Ten of these studies reported episodic retrieval results for schizophrenia patients and healthy control participants. Patient participants consistently demonstrated reduced dorsolateral and ventrolateral PFC activation compared to control participants during episodic retrieval. However, reduced ventrolateral PFC activation was not apparent in studies where patients were provided with encoding strategies (four studies). Nonetheless, dorsolateral PFC

activation was still reduced in these cases and was not secondary to group performance deficits. These findings suggest that PFC is important to both retrieval and encoding control mechanisms. Furthermore, they imply that specific areas of PFC are differentially involved with separable cognitive control mechanisms.

The importance of PFC to retrieval control processes has been further elucidated using animal models. Haddon and Killcross (2007) conducted a study in which rats were trained to complete a Stroop task (Stroop, 1935) adapted for rodents. The animals were presented with two study contexts (different cage environments), and completed a different task in each one (an auditory or a visual discrimination task). During the test phase, rats were presented with audiovisual compounds in each of the study contexts. Half of these trials required responses that were congruent with the training environments and half were created in such a way that the individual components dictated different responses in each of the study contexts (e.g. one element of the compound would be incongruent with the current study context). Previous research has indicated that rats use contextual information (e.g. the current cage environment) to disambiguate the response conflict (e.g. Haddon & Killcross, 2006). Generally, infusions of a dopamine-1 ( $D_1$ ) agonist into the prelimbic PFC improved performance on incongruent trials, but impaired performance on congruent trials. Moreover, the improvement observed on incongruent trials was modulated depending on baseline performance. Rodents that exhibited low baseline performance, determined via median split, demonstrated improved accuracy performance during incongruent study trials, whereas high performing rodents exhibited reduced performance following infusions. These findings indicate a role for prefrontal dopamine levels in the use of contextual information to appropriately limit interference from task-irrelevant cues. Furthermore, they provide support for the inverted-U hypothesis of dopamine function (Arnsten, 1998; Zahrt, Taylor, Mathew, & Arnsten, 1997) to cognitive performance, which suggests there are optimal levels of  $D_1$  receptor activity that facilitate the use of contextual cues. However, the most crucial finding here is that the infusions of  $D_1$  agonists modulated performance depending on baseline performance. This latter point may be particularly pertinent to consider in relation to the patient studies reported in this thesis, considering mechanisms of action for antipsychotic medications include the dopamine system.

To conclude, deficits in maintaining contextual information have been consistently associated with dopamine dysfunction, particularly in the PFC (Braver, Barch, & Cohen, 1999). Such views complement current opinions in psychiatry regarding the origin of schizophrenia symptoms. Positive symptoms have been reliably associated with hyperactivity of the mesolimbic dopaminergic system, and negative symptoms with hypoactivity of the mesocortical dopaminergic system (Malik & Balkoski, 2007). Despite the wealth of information suggesting cognitive control deficits in memory in patients with schizophrenia, several challenges remain. Most studies use tasks tapping multiple cognitive processes, which makes drawing conclusions relating to specific processes difficult. The strengths of these criticisms can be reduced by taking a focused cognitive process approach and deploying specific tasks, which have the capacity to isolate specific cognitive processes. Moreover, similar deficits have been identified in unaffected first-degree relatives of schizophrenia patients (e.g. Snitz, MacDonald, & Carter, 2006), emphasising the dimensionality of such deficits.

#### EVIDENCE FOR COGNITIVE CONTROL DEFICITS IN SCHIZOTYPY

Several researchers have investigated mechanisms of cognitive control in schizotypal individuals. For example, schizotypal individuals high in the negative symptom of social anhedonia performed significantly worse compared to controls on spatial and emotional delayed match-to-sample tasks, but there were no significant performance differences between controls and those high in social anhedonia on an identity delayed match-to-sample task (Gooding & Tallent, 2003). Moreover, group differences could not be explained in terms of reduced emotional experience in the high social anhedonia group because there were no significant associations between measures of emotional experience and working memory performance. Gooding and Tallent (2003) suggested these results arose because of greater difficulty or inefficiency in cognitively demanding tasks for those high in social anhedonia.

Martin, Cicero, and Kerns (2012) have similarly found evidence for the association between negative symptoms and cognitive control processes. Participants completed a primed evaluation task, in which affective prime words and target words were presented sequentially. Both prime and target words were either positive or negative in valence and were presented either in congruent or incongruent formations. Participants were

required to judge the affective valence of the target items. It is thought that participants utilise cognitive control mechanisms throughout such tasks to compensate for the prime during evaluation of the target (e.g. Klauer, Teige-Mocigemba, & Spruyt, 2009). Those high in social anhedonia, compared to those high in perceptual aberration or control participants, experienced greater interference of the prime, demonstrated by slower RTs for incongruent trials. Furthermore, there were no significant differences in incongruent RTs for those high in perceptual aberration or control participants, emphasising that the negative dimension, but not the positive dimension, is associated with poor affective control.

By contrast, other researchers have highlighted strong associations between both positive and negative symptom dimensions and cognitive control deficits. Chang et al. (2011) investigated the relationship between Wisconsin Card Sorting Task (WCST; Heaton et al., 1993) performance and positive and negative dimensions of schizotypy. Participants were selected based on the first and fourth quartiles of scores from the Schizotypal Personality Questionnaire (SPQ; Raine, 1991). Those in the first quartile were individuals who exhibited both high negative and high positive scores (high schizotypy), whereas those in the fourth were individuals with low scores on both of these dimensions (low schizotypy). Those high in schizotypy completed fewer categories on the WCST compared to those low in schizotypy.

To further add to these mixed findings, there are numerous studies where there has been no evidence for an association between either positive or negative dimensions of schizotypy and cognitive control. For example, Spitznagel and Suhr (2002) found that schizotypal individuals demonstrated no impairments compared to controls on a range of executive functioning tasks (e.g. WCST; Heaton et al., 1993; Trail Making Test [TMT]; Reitan, 1958). Kerns (2006) suggested that the discrepancies between these findings could be explained by the fact that the disorganised dimension of schizotypy, rather than positive or negative dimensions, is more predictive of cognitive control deficits. In one relevant study (Kerns, 2006), participants completed a range of schizotypy and other personality measures, in addition to completing three behavioural measures of cognitive control: Stroop Task (Kerns et al., 2004; Stroop, 1935), Simon Task (Fan, Flombaum, McCandliss, Thomas, & Posner, 2003) and Preparation for Overcoming a Prepotent response (POP; Barber & Carter, 2005). Only the disorganised dimension of



schizophrenia was associated with poor cognitive control, particularly performance in the POP task. Other researchers investigating the association of disorganised symptoms with cognitive control have identified similar associations (e.g. Gooding, Tallent, & Hegyi, 2001; Moritz, Andresen, Naber, Krausz, & Probsthein, 1999), emphasising that investigations into the importance of the disorganised dimension to more specific elements of cognitive control may be fruitful.

Whilst these investigations have been informative for understanding the ways in which cognitive control can broadly influence behavioural task performance, there is a dearth of studies investigating schizotypy specifically in relation to memory tasks. Those that have, typically focus on working memory tasks. For example, Park and McTigue (1997) found a weak positive trend between spatial working memory performance and total SPQ score (Raine, 1991). Further examination of the three factors of the SPQ revealed that the negative dimension appeared to drive this association, specifically the 'no close friends' subscale (Raine et al., 1994), which had a weak but significant positive association with errors on the spatial working memory task. The authors suggested further, higher powered studies would be required to determine the reliability of this association.

## CHAPTER TWO SUMMARY

Ranganath et al (2008) have proposed a model for how cognitive control may contribute to memory performance at different stages of encoding and retrieval. Taken together, the aforementioned studies provide evidence indicating cognitive control process may be aberrant in both patients with schizophrenia and those high in schizotypy. Nonetheless, there are methodological issues limiting the strength of the present conclusions. Many of the measures used to date have not been sufficiently specific to effectively dissociate which cognitive processes are dysfunctional. To overcome this, the experiments reported in this thesis utilised behavioural and neural measures that will permit a sensitive assay of these processes. The subsequent chapter in this thesis will contain a discussion of the memory processes that will be examined in this thesis in relation to cognitive control, as well as how the measures used to assess these processes can be used to investigate the cognitive control processes that contribute to successful memory performance.

## CHAPTER THREE: MEMORY, MODELS AND FRAMEWORKS

The primary focus in this thesis is on control over recollection, which is the recovery of contextual information about a prior encounter. Recollection is the kind of memory that is most prominently absent in amnesia, and deficits in recollection ensue from hippocampal and frontal cortical insults. It is a process that is generally considered to be subject to conscious control and is consequently a sensible target to consider in respect of control deficits associated with schizophrenia. Much of the debate about the properties of the process of recollection, and how it might be distinguishable from other memory processes, has been conducted via discussions of the validity of dual-or single-process models supporting recognition memory.

### DUAL-PROCESS MODELS OF RECOGNITION

There has been rigorous debate regarding the processes contributing to recognition memory performance. Broadly, proposed models of recognition can be divided into two classes: those that posit recognition memory performance can be explained by one process, and those that advocate two processes. Proponents of single-process models suggest that recognition performance can be explained by a graded signal strength process which some believe assesses the degree of similarity between a previously encountered event (e.g. studied item) and the present situation (e.g. test item; Glanzer, Kim, Hilford, & Adams, 1999; Wixted & Stretch, 2004). In contrast, dual-process models propose that recollection contributes to recognition performance in addition to a graded signal strength process: familiarity (Diana, Reder, Arndt, & Park, 2006; Yonelinas, 2002). One conceptualisation of this latter process is that the signal strength is proportional to the frequency with which the present combination of perceptual features has been encountered, or the amount of intra-item integration (Mandler, 1980). The term “recollection” is often used to refer to the retrieval of episodic memories; in other words, recovery of qualitative information about a prior event (Evans & Wilding, 2012; Yonelinas, 2002). Most dual-process models consider this process to act in an “all or none” fashion, whereby individuals either succeed or fail in recovering associative details (Yonelinas, 1994).

As already noted, the experiments in this thesis are designed primarily to investigate how control over recollection contributes to successful memory performance, and how these

retrieval control processes may operate less efficiently in patients with schizophrenia. However, the behavioural paradigms used in pursuit of these questions, as well as the behavioural and ERP data reported in this thesis, make considerations of the process of familiarity pertinent. To this effect, it is important to review the key evidence for considering recollection as separable from familiarity.

## APPROACHES TO SEPARATING THE CONTRIBUTIONS OF RECOLLECTION AND FAMILIARITY TO RECOGNITION MEMORY

### Behavioural Paradigms

The methods that have been used to separate contributions of these two processes can be broadly classified as either task-dissociation methods or process-estimation methods. Task-dissociation methods aim to identify test conditions or tasks that isolate particular processes of interest, whereas process-estimation methods are sets of model equations which can be used to derive parameter estimates representing the differential contributions of particular processes to task performance (Yonelinas, 2002). One example of a task-dissociation method is the response-deadline task (Reed, 1973, 1976). Participants are instructed to make speeded recognition judgments within a specified time following presentation of a stimulus. Performance from this condition is then contrasted to that obtained from a non-speeded recognition judgment condition (Yonelinas, 2002). Using this procedure, Hintzman, Caulton, and Levitin (1998) found participants were able to identify a studied item from a list comprising studied and unstudied items more quickly than they could recollect specific information regarding the studied items (e.g. when and where the item was encountered). When additional response time was permitted, however, the probability of accepting an item that was either new, but similar to a studied item, or from an inappropriate study list decreased, producing a biphasic accuracy/response-time function (Doshier, 1984; Hintzman & Curran, 1994; Rotello & Heit, 2000). Findings of this kind are consistent with the view that two processes support memory judgments. The interpretation supporting this view is that incorrect endorsements of similar lures are due to the contribution of a fast-acting process – familiarity – and the reduction in these incorrect endorsements when more time is available reflects the fact that a slower process – recollection – carries sufficient information to accurately separate similar lures from studied items. An important

limitation of this method, however, is that the task instructions are different in the two task conditions (Yonelinas, 2002). It could be the case that differences in task instructions influence how the processes of familiarity and recollection operate, complicating insights gained from contrasting performance in the two task conditions (Yonelinas, 2002). Moreover, this task, along with other task-dissociation procedures, provides imprecise estimates of the contributions of recollection and familiarity to task performance, making interpreting the results obtained from such paradigms ambiguous (Yonelinas, 2002).

To overcome this limitation, several process-estimation methods have been developed. One of the first methods of this kind was the process-dissociation procedure (Jacoby, 1991). The process-dissociation procedure operationalises recollection as the ability to report where or when an event occurred (Yonelinas, 2002). In the most common version of this task, participants are presented with study items, half of which are presented in one study context and half are presented in another study context. Under one test condition, the inclusion condition, participants are required to make positive recognition judgments to items presented in either study context on one response key, and reject new items on another response key. Under another test condition, the exclusion condition, participants are required to make positive recognition judgments for items previously presented in a specific context (targets) on one response key, and reject new items along with items from the other context (non-targets) on another response key. The procedure permits estimates of the contributions of recollection and familiarity to task performance if certain assumptions hold. For the inclusion condition, both familiarity and recollection can be used to make positive recognition judgments. Assuming the processes are independent, the probability of correctly accepting a previously studied item is equal to the probability an item was recollected plus the probability an item was not recollected but accepted on the basis of familiarity [ $P(\text{Inclusion})=R+(1-R)F$ ]. For the exclusion task, the likelihood of incorrectly accepting an item presented in the non-target condition is equal to the probability that the item is familiar in the absence of recollection [ $P(\text{Exclusion})=(1-R)F$ ]. Estimates of recollection and familiarity can then be calculated by comparing behavioural performance across inclusion and exclusion conditions [ $R=P(\text{Inclusion})-P(\text{Exclusion})$ ;  $F=P(\text{Exclusion})/(1-R)$ ].

It is also possible to obtain estimates of recollection and familiarity by asking participants to complete two exclusion tasks in which target/non-target designation is switched. In each of the two tasks the equivalent of the  $P(\text{Inclusion})$  estimate given above can be taken from the likelihood of making a correct judgment to a target. This approach has advantages over the inclusion/exclusion procedure. First, because estimates of recollection and familiarity for each of the studied contexts can be obtained from only two tasks and second, because the use of the same instructions in each task makes the approach less susceptible to the concern that there is different reliance on recollection and familiarity across the tasks. Despite these advantages, however, there remain potential limitations.

Jacoby (1991) noted that there are three principal assumptions that underlie the process dissociation procedure: i) the probability of correctly responding old to an item would be equal across both the inclusion and exclusion conditions, were it not for recollection, ii) the probability of recollecting information is equivalent across inclusion and exclusion conditions, and iii) recollection and familiarity are independent bases for judgments. Point ii) has already been addressed above. For point i), Graf and Komatsu (1994) suggested that estimates of familiarity would be inaccurate if participants adopted different response criteria across tasks. They were concerned primarily with the inclusion/exclusion procedure, but the concern might extend to the exclusion/exclusion procedure as well. In defence of the invariance of familiarity assumption, however, Toth, Reingold, and Jacoby (1995) emphasised that if participants were to utilise familiarity differentially across conditions (e.g. alter their response criterion) this would be reflected in different false alarm rates, and advised that estimates be treated with caution when false alarm rates differ.

Considering the assumption of independence Curran and Hintzman (1995) suggested there are several circumstances under which this assumption is violated and that when this occurs, estimates of recollection and familiarity can be artificially dissociated. For example, if the contributions of recollection and familiarity are positively correlated, high and low estimates of recollection will be associated with high and low estimates of familiarity respectively, resulting in estimates of familiarity being underestimated, especially for conditions associated with higher estimates of recollection (Curran & Hintzman, 1995). The subsequent debate surrounding this critique is two-fold: i) the

importance of careful experimental design and, ii) appropriate measures to examine this assumption (Hintzman & Curran, 1997; Jacoby, Begg, & Toth, 1997; Jacoby & ShROUT, 1997). To first address the evidence reported by Curran and Hintzman (1995) which suggested the independence assumption was often violated, Jacoby (1998) systematically varied the instructions given to participants during the process dissociation procedure. Results similar to those obtained by Curran and Hintzman (1995) were produced only when participants were encouraged to use a generate/recognise strategy, and when direct-retrieval instructions were utilised, no paradoxical dissociations were identified. Consequently, Jacoby (1998) took steps towards providing a user guide for the process dissociation procedure, and emphasised the importance of careful experimental design to ensure this assumption is met. Furthermore, examination of the methods used to demonstrate this assumption had been violated revealed that direct assessments, such as correlations, cannot be used to examine the validity of this assumption (Yonelinas & Jacoby, 2012). As demonstrated by Jacoby and ShROUT (1997), the assumption of process independence is based on an individual's response to an individual item. Thus, it is impossible to compute correlations at this level considering there is only a single observation. Similarly, correlations cannot be computed by collapsing across items or subjects because of the effects of aggregations. For example, there may be particular items that are more likely to engage recollection or familiarity compared to others, or likewise, some participants may have higher estimates of recollection or familiarity compared to others; distorting the mean estimates even when the processes operate independently (Yonelinas & Jacoby, 2012).

There is also another point relevant to the accuracy of recollection estimates. One potential limitation of the method is the stringent measure of recollection; whether participants are able to retrieve details about the study context items were presented in (Yonelinas, 2002). Study context in this task can be defined by multiple features, such as encoding manipulation or study modality, hence retrieving details of any one of these features provides a basis for excluding items (Yonelinas, 2002). However, recollecting other details of the study event, such as coughing when the item was presented, does not support the required discrimination and therefore is not measured as recollection (Yonelinas, 2002). The recollection of this latter type of information is often referred to as partial or incidental recollection (Yonelinas, 2002). Whilst there are some reports indicating partial recollection can influence parameter estimates (e.g. Gruppuso,

Lindsay, & Kelley, 1997; Wagner, Gabrieli, & Verfaellie, 1997), such evidence typically arises when using very similar study lists and participants can retrieve many details that do not support list discrimination. Under the conditions initially described by Jacoby (1991), partial recollection occurs infrequently (e.g. Yonelinas, 2001; Yonelinas & Jacoby, 1996), and even if it were to occur this would not influence estimates of recollection considering such details will not necessarily facilitate discrimination performance and this measure only indexes memory for details supporting discrimination (Toth et al., 1995). Nonetheless, it is important to acknowledge that concerns relating to this assumption in particular are a concern for many other methods of deriving estimates of familiarity and recollection, not just the procedure described above (e.g. Buchner, Erdfelder, & Vaterrodt-Plünnecke, 1995; Yonelinas & Jacoby, 1994; Yonelinas, Regehr, & Jacoby, 1995).

Another method that has been employed is the Remember/Know procedure (Yonelinas, 2002). In this procedure participants are asked to indicate whether positive recognition judgments are based on recovering contextual details or by simply a feeling of knowing that the item was encountered before. If it is assumed that Remember judgments are supported by recollection, and Know judgments by familiarity, then this approach permits estimates of the contributions of the two processes to task performance. Remember and Know judgments have been shown to dissociate in ways that suggest recollection and familiarity are distinct processes, and the results using this approach have been shown to converge with those of the process-dissociation procedure, providing appropriate corrections to calculations are made (Yonelinas & Jacoby, 1995). Yonelinas (2002) has emphasised the importance of the use of different methods that can strengthen theoretical claims when they converge on similar outcomes. The same logic applies to neural measures of cognitive operations, with which the following section is concerned.

### Cognitive Electrophysiology

Event-Related Potential (ERP) measures can be used in several ways to investigate cognitive processes. First, their millisecond resolution permits insights into the time courses of cognitive processes (Hillyard & Kutas, 1983; Luck, 2005). By understanding the timing and ordering of processes engaged during particular cognitive activities it is possible to make inferences about parallel, serial or hierarchical relationships (Hillyard &

Kutas, 1983). Second, given that particular cognitive processes, such as recollection and familiarity, have been found to be strongly associated with particular neural indices (for a review in the context of memory processes see Wilding & Sharpe, 2003), by using ERP measures it is possible to ascertain the degree to which these particular cognitive processes are engaged under specific experimental manipulations. Together, this suggests that ERP measures in conjunction with behavioural measures would be particularly useful for elucidating the mechanisms underlying memory problems. In this thesis the focus is on memory problems in people with schizophrenia. The following sections will review the evidence for key ERP effects that will be important to analyse in pursuit of this research focus.

### Midfrontal Old/New Effect

The midfrontal old/new effect is a negative deflection in the EEG recording that is evident from 300-500ms post-stimulus presentation (Mecklinger, 2006; Rugg et al., 1998). Old/new effects are differences between neural activities associated with correct judgments to studied and unstudied stimuli (Curran, 1999; Yonelinas, 2002). The midfrontal old/new effect comprises activity that is relatively more positive going for correct responses to old items than correct responses to new items (Curran, 1999, 2000). It is largest at midfrontal electrode locations, as its label implies. The midfrontal old/new effect is also known as the FN400 due to the similarity in latency and polarity with N400 (Kutas & Hillyard, 1980), though the FN400 has a more anterior maximum (Curran, 1999). It has been argued that this effect indexes familiarity (Curran, 2000).

Rugg et al. (1998) were the first to suggest this effect as an index of familiarity. Participants completed a depth of processing recognition paradigm while ERPs were acquired. When ERPs elicited by correct responses to new items were contrasted with those for old items that received correct responses, magnitudes for shallow-encoded items and deep-encoded items were equivalent over frontal sites from 300-500ms and both were more positive-going than those associated with correct rejections, as well as those associated with misses. The authors proposed the greater positivity over midfrontal sites found for correctly recognised items, irrespective of encoding condition, but not for misclassified old items could represent an index of a form of explicit memory, namely familiarity. In so far as depth of processing manipulations do not influence



familiarity markedly this is a reasonable claim (Yonelinas, 2002, although see also Rugg & Allan, 2000).

Further evidence that the midfrontal old/new effect indexes familiarity comes from experimental manipulations designed to influence the degree of similarity between test items. Curran (2000) presented participants with a list of singular and plural items (e.g. TABLE, CUPS) during a study phase. At test, participants were presented with studied items (e.g. TABLE), similar lures (e.g. items presented in the opposite plurality to that of studied words [CUP]) and new items (unstudied words [CHAIR]). Participants were instructed to accept only items presented in the original plurality. It was anticipated that studied items and similar lures would be more familiar than new words, and thus exhibit comparable levels of familiarity. The false alarm rate for similar lures was significantly greater compared to new items, consistent with the expectation that similar lures would be associated with greater familiarity than new items. The midfrontal old/new effect was the same size for studied items as well as for similar lures judged incorrectly to be old. Given the correspondence between behaviour and the ERP effects, these outcomes support the view that the midfrontal old/new effect indexes stimulus familiarity.

Other researchers have tested the functional significance of the midfrontal old/new effect by establishing the sensitivity to manipulations of response criterion. Azimian-Faridani and Wilding (2006) manipulated the test instructions across test phases by instructing participants to either respond 'old' only when they were confident the item was old, or respond 'new' only when they were confident the item was new. In doing so, it was assumed this manipulation would encourage participants to adopt conservative and liberal response criteria respectively, and hence influence the degree of familiarity required for an 'old' response, since changes in criterion influence familiarity to a greater extent than recollection (Yonelinas, 2002). The behavioural data showed a change in criterion, and while the midfrontal old/new effects were the same size under both criteria, the ERPs associated with old and new items were more positive-going in the conservative than in the liberal condition. These outcomes support a familiarity interpretation of the midfrontal old/new effect because under conservative criteria a higher level of familiarity should be required to facilitate a correct old as well as a correct new response than under liberal criteria (Azimian-Faridani & Wilding, 2006).

Despite the evidence in favour of interpreting this index as a measure of familiarity, some researchers have suggested this ERP signature may actually index conceptual priming. Priming is the differential processing of an item due to prior exposure. Conceptual priming is a change in processing due to prior exposure to a semantically related item (Schacter, Chiu, & Ochsner, 1993). Some researchers have argued that most data supporting the familiarity interpretation of the midfrontal old/new effect can be equally well explained by conceptual priming (Paller, Voss, & Boehm, 2007). This alternative account was proposed following observations that the midfrontal old/new effect is often observed in tasks that contain an element of conceptual overlap between study and test phases. For example, in the study conducted by Curran (2000) the similar lures were potentially conceptual primed to the same degree as preserved-plurality targets during the study phase, which could have produced the comparable midfrontal old/new effects observed for both item types. Further evidence in favour of the conceptual priming account comes from studies using items lower in semantic attributes, for example, unknown faces (MacKenzie & Donaldson, 2007; Yovel & Paller, 2004), kaleidoscope images (Voss & Paller, 2009), hard to define words (Voss, Lucas, & Paller, 2010) and squiggle shaped forms (Voss & Paller, 2007). Considering these stimuli have fewer semantic attributes, the items should therefore be less inclined to exhibit conceptual priming. Consistent with this proposition, studies using these kinds of stimuli from Paller and colleagues have generally not demonstrated a midfrontal old/new effect.

Whilst the conceptual priming account has received some support, it is important to acknowledge that this account cannot explain the results of some studies which show the midfrontal old/new effect is sensitive to degree of perceptual similarity between items presented at study and test, despite conceptual similarity remaining constant (e.g. Ecker & Zimmer, 2009; Ecker, Zimmer, & Groh-Bordin, 2007; Groh-Bordin, Zimmer, & Ecker, 2006). These findings suggest the midfrontal old/new effect cannot be reduced to a correlate of conceptual priming, but do not preclude the possibility that priming contributes to familiarity-based judgments (Bridger, Bader, Kriukova, Unger, & Mecklinger, 2012; Groh-Bordin et al., 2006; Rugg & Curran, 2007).

#### Left-Parietal Old/New Effect

The left-parietal old/new effect is a positive deflection in the EEG recording, largest over left parietal recording sites from 500-800ms post-stimulus presentation (Rugg & Wilding,

2000). This effect comprises a greater relative positivity for old compared to new items (e.g. Rugg & Wilding, 2000). Some of the first evidence suggesting this effect could be an index of recollection was provided by Smith (1993) who collected ERPs while participants completed a modified Remember/Know memory task (Tulving, 1985). Smith (1993) demonstrated the left-parietal old/new effect was larger for Remember than Know responses. This outcome has since been replicated by many researchers (Duarte, Ranganath, Winward, Hayward, & Knight, 2004; Düzel, Yonelinas, Mangun, Heinze, & Tulving, 1997; Leynes & Phillips, 2008; Smith, 1993; Vilberg, Moosavi, & Rugg, 2006), and suggests that the effect indexes the process of recollection.

Unlike the midfrontal old/new effect, the greater relative positivity for old items in the left-parietal old/new effect increases with the amount of contextual information retrieved from episodic memory (Vilberg et al., 2006; Vilberg & Rugg, 2009; Wilding, 2000). Some of the strongest evidence suggesting that this effect is sensitive to the recovery of contextual details comes from Wilding, Doyle, and Rugg (1995). Cues indicated whether study items would be presented aurally or visually. Participants were asked to press one response key if study items were words and another if study items were non-words. During a subsequent test phase, participants initially indicated whether test items were old or new items. For items identified as old, participants were required to make an additional response to indicate the study presentation modality (a source judgment). ERPs for items attracting correct old judgments and subsequent correct source judgments were more positive going than items attracting correct old judgments but incorrect source judgments. This pattern of results is consistent with the view that the left parietal old/new effect indexes recollection (Sanquist, Rohrbaugh, Syndulko, & Lindsley, 1980; Vilberg et al., 2006; Wilding, 2000; Wilding et al., 1995; Wilding & Rugg, 1996b)

This interpretation received further support from Wilding and Rugg (1996b). Here, participants heard items spoken in either a male or a female voice. In a subsequent test phase, these items were re-presented interspersed with new items. Participants were required to indicate if the item had been previously presented, and if so, in which voice. There was an increased positivity over left-parietal electrode locations for items attracting correct source judgments compared to either those attracting incorrect source judgments or correct rejections. Similar results were obtained in a more recent

replication where studied items could elicit two source memories ([i] mode of presentation: male/female voice [ii] encoding task: action/liking; Wilding, 2000). The left-parietal old/new effect was larger for items attracting two correct source judgments compared to those attracting one or none (Wilding, 2000). Together, these findings suggest the left-parietal old/new effect is sensitive to the amount or quality of information retrieved from episodic memory in a graded fashion (Vilberg et al., 2006).

Some of the strongest evidence in favour of this ERP effect indexing recollection comes from investigations using patients with selective hippocampal lesions. The hippocampus has been shown to be implicated in the process of recollection, whereas parahippocampal formations have been implicated in the process of familiarity (Aggleton & Brown, 1999; Diana, Yonelinas, & Ranganath, 2007; Düzel et al., 2003; Schacter, Alpert, Savage, Rauch, & Albert, 1996). Jon experienced early brain injury resulting in relatively isolated bilateral hippocampal damage, but intact parahippocampal formations (Vargha-Khadem et al., 1997). Vargha-Khadem et al. (1997) demonstrated that Jon had relatively spared recognition memory performance, and it was hypothesised this was because the intact parahippocampal formations maintained recognition performance through familiarity. This proposition would be supported if Jon exhibited comparable neural indices of familiarity but impaired indices of recollection to controls. Düzel, Vargha-Khadem, Heinze, and Mishkin (2001) found that compared to control participants, Jon demonstrated significantly poorer recognition memory performance (88.3% vs. 69.3%) and slower reaction times (approximately 200ms) on old/new recognition judgments. Furthermore, despite exhibiting a comparable ERP index of familiarity Jon, unlike control participants, did not show the aforementioned ERP index of recollection. Taken together, this suggests that recognition performance in individuals with selective hippocampal injury may be relatively spared since recognition judgments may be made via item familiarity rather than the process of recollection. The absence of the left-parietal old/new effect in conjunction with behavioural evidence for recollection deficits suggests that this ERP effect indexes recollection.

Taken together, this ERP evidence supports dual-process accounts since there is evidence for separate processes with different time courses and scalp distributions operating during memory tasks. The following section will review key evidence showing

how the left-parietal old/new effect can and has been used to investigate how cognitive control may influence when recollection occurs.

### INVESTIGATING HOW COGNITIVE CONTROL INFLUENCES RECOLLECTION

The critical first finding that suggested ERPs can provide a window to observe cognitive control over recollection is due to Herron and Rugg (2003). Level of encoding was manipulated across two exclusion task experiments and left-parietal old/new effects for target and non-target items attracting correct responses were compared. In Experiment 1 participants rated the pleasantness of target words at study, whereas in Experiment 2 participants read aloud the target words. The encoding context for non-target words was consistent across both experiments, requiring participants to generate a sentence incorporating each presented word. Target accuracy was higher for items rated for pleasantness compared to those read aloud. Reliable target and non-target left-parietal old/new effects were found except for non-targets in Experiment 1. This is a surprising finding because, if one assumes that non-targets (subject to the same encoding operations) should be equally likely to elicit recollection, then non-target left-parietal old/new effects of equivalent magnitudes should be observed in both cases. Because of this outcome, Herron and Rugg (2003) proposed that participants utilised strategic recall processes for the deep encoding task (Experiment 1), but not for the shallow encoding task (Experiment 2; Craik & Lockhart, 1972). The authors suggested participants varied their retrieval strategy depending on the likelihood of successfully retrieving target information, with retrieval control processes only being used when successful target recollection was likely. That is, participants focused on recovery of target information to a greater degree when succeeding or failing to recollect information about targets was a good means of performing well on the task. During debriefing, the majority of participants confirmed the authors' suggestion that when sufficient information regarding the source of a target item is available, items were rejected solely on the basis of not eliciting this information.

Whilst such conclusions are reasonable, there are some caveats. It may have been the case that non-target items in Experiment 1 (deep encoding condition) were simply forgotten, rather than participants exerting strategic control over recollection. Considering that non-target items that are forgotten attract the same response as those

that are remembered in exclusion tasks, this is a very real possibility. Herron and Rugg (2003) addressed this possibility by conducting an additional behavioural experiment which replicated Experiment 1, except that participants were required to exclude study block two items (previously target items) and treat study block one items (previously non-targets) as targets. Response accuracy levels suggested that non-targets were not often forgotten, thereby providing some support for the account preferred by Herron and Rugg (2003).

Other researchers have attempted to assess the account offered by Herron and Rugg (2003) by using two test phases and requiring participants to treat items from different study contexts as targets in each phase. In a study conducted by Dzulkipli and Wilding (2005) participants completed an exclusion task where they first saw words. In one study context participants were required to indicate how difficult an item would be to draw and in another context indicate how difficult it is to think of a function for the item. This design overcomes the difficulties previously described as, given the two-test phase design, it is possible to assess how memorable targets and non-targets are. For both target designations, target items elicited larger left-parietal old/new effects compared to both non-target and new items. Considering target designation changed during the test phase, and given the similarity of behaviour performance across both blocks, this attenuation of the left-parietal old/new effect for non-target items cannot be explained in terms of non-target items being forgotten. These findings, and those in several similar studies from different research groups, have been considered in terms of prioritisation of recollection of certain task contents when it is strategically beneficial to do so. A common assumption, stemming from the initial suggestion of Herron and Rugg (2003), is that the driver for when control over recollection will be exerted is the likelihood of recollecting target material (Evans, Wilding, Hibbs, & Herron, 2010; Leynes, 2012). When target information can be easily recollected, retrieval control processes can be utilised. Other researchers however have suggested that the ease with which non-target information can be recollected influences when retrieval control processes are utilised.

Rosburg, Mecklinger, and Johansson (2011b) conducted an exclusion task where participants were presented with a word followed by a white frame at study. For 50% of the study words, the white frame contained a black and white line drawing of the object denoted by the word (perceive condition). For the other words, participants were

required to imagine a drawing of the object denoted by the word (imagine condition). In separate conditions words from the imagine and the perceive conditions were designated as targets. When items from the perceive condition were designated as targets left-parietal old/new effects were present for target items only, and the likelihood of a correct target judgment was higher than when items from the imagine condition were designated as targets. Both target and non-target items elicited left-parietal old/new effects of the same size in the latter designation. The magnitude of the left-parietal old/new effect for non-targets in the imagine condition was also found to correlate with discrimination measures (Pr; Snodgrass & Corwin, 1988) of both conditions. The authors proposed this correlation indicated non-target retrieval occurred when this information was easier to retrieve than target information and that non-target retrieval may in fact be driven by bottom-up mechanisms. These data can, however, be equally well explained by the account offered by Herron and Rugg (2003), in so far as the correlation demonstrates a reliance on non-target information in the condition where target accuracy is lower.

Elward and Wilding (2010) investigated the relationship between working memory capacity (WMC) and retrieval control. A comparison of the ERPs for target and non-target items revealed a reliable attenuation of the left-parietal old/new effect for non-targets only for those high in WMC, independent of target accuracy. A follow-up study, where participants were given a surprise post-task free recall test following the retrieval stage of the exclusion task, revealed that those with lower WMC recalled significantly more non-targets than those higher in WMC (Elward, Evans, & Wilding, 2012). Moreover, a manipulation assumed to reduce WMC temporarily (e.g. Muraven & Baumeister, 2000; Muraven, Tice, & Baumeister, 1998) resulted in comparable left-parietal old/new effects for targets and for non-targets, even among those initially high in WMC. These findings suggest that individual difference variables at the very least mediate, and in principle explain entirely, the conditions under which ERP evidence of control over recollection is exerted.

Taken together, this suggests that using the exclusion paradigm, in conjunction with ERP measures provide a means of understanding the processes that contribute to the exertion of cognitive control during memory retrieval. Importantly the conclusions drawn from the aforementioned evidence are consistent with one way in which another

framework, the Source Monitoring Framework (SMF; Johnson et al., 1993), can be operationalised. Thus, the following section will describe the key aspects of the SMF and why it will be useful to consider this framework when interpreting the results presented in this thesis.

### Source Monitoring Framework

Source monitoring refers to the differentiation of memories based on their characteristic source information (Johnson et al., 1993). This framework is an extension of the reality-monitoring framework (Johnson & Raye, 1981), which focuses on differentiating memory for internally generated information from memory for externally generated information. In addition to these internal-external differentiations, the SMF also incorporates: i) distinguishing memories from two or more external sources of information (external source monitoring) and ii) distinguishing memories from multiple internal sources of information (internal source monitoring). According to this framework, the term source refers to characteristics that specify the conditions under which an episode was committed to memory. A source can therefore incorporate features relating to perceptual or semantic qualities as well as affective experiences and cognitive operations engaged at the time of the event (Johnson et al., 1993).

According to the SMF, source attribution (deciding from which source a memory was retrieved) utilises the average difference in characteristics of memories from various sources. For example, determining whether something was seen on the television or heard on the radio may depend on the extent to which source information contains visual information. Source attributions can also be based on the degree of matching between qualities of memories and activated schemas for particular sources of information. For example, deciding whether something was said aloud by oneself or another person may depend on the extent to which the source information matches the representation of your own voice. Several decision-making processes are assumed to be engaged when making source attributions, including weighting certain features depending on the situational requirements. Typically, these processes are classified as either heuristic or systematic (Chaiken & Eagly, 1989). Heuristic processes are relatively fast and non-deliberative. When these processes are engaged, source monitoring is typically based on the qualitative characteristics of the activated memory (e.g. amount or type of perceptual detail). In contrast, systematic processes tend to be more



considered and deliberate. Here, supporting memories can also be recovered to assess the validity of a source attribution. Importantly, both processes require setting criteria for judgments to be made and both processes can be influenced by biases, metamemory assumptions and current goals (Johnson et al., 1993). According to the SMF, this inherent need for flexible criteria means that both encoding and retrieval are constructive and reconstructive processes (Johnson et al., 1993; Mitchell & Johnson, 2009).

The ease and accuracy with which a source can be identified is, according to the SMF, dependent on three principal factors. First, the amount and type of memory characteristics reactivated in the information recovered from memory. Unlike in some models including the process of recollection, source is not considered to be an “all-or-none” concept (Johnson et al., 1993). Rather, source can be specified to varying degrees. For example, it may be possible to recollect who you were speaking with, and where, but not what was said. Importantly, recovering source details does not necessarily result in accurate source judgments, though, recovering more details is associated with increased source accuracy (Johnson et al., 1993). Second, the number of unique memory characteristics for particular sources. When memory characteristics are similar between two or more sources there is increased difficulty in correctly attributing source to information recovered from memory. Third, the judgment processes and criteria used to make source attributions, with the application of appropriate criteria and processes being associated with more accurate source attribution. For example, one can attribute a statement to a particular friend by drawing on general knowledge about that person and the present general context (e.g. Sam was the only person there who would say something like that so it had to be him; Johnson et al., 1993).

The SMF assumes that comparable processes underlie performance in all episodic memory tasks (Johnson, 1992), but what differs is the extent to which particular processes are engaged and the amount of other information utilised (e.g. knowledge and beliefs) under a specific set of task requirements (Mitchell & Johnson, 2009). Under this assumption, whilst behavioural performance associated with different episodic tasks would be expected to differ; there should also be some consistency with regards to estimates of some processes that contribute to memory performance. In light of this, given comparable behavioural process estimates between tasks, there should also be

some consistency in terms of neural activity and the brain regions recruited during the tasks (Steffens, Buchner, Martensen, & Erdfelder, 2000; Yu & Bellezza, 2000).

Whilst not formally described in the original manuscript, there are two possible ways in which the SMF can be operationalised. Source monitoring may confer a passive process whereby individuals simply weigh the amount of evidence in favour of one source and compare this to the amount of evidence in favour of another source when making source attributions. Alternatively, source monitoring may act as a strategic process in that based on the characteristic qualities of various sources individuals may target and search for particular information, and this is the immediate point of contact between the SMF and the differences between target and non-target old/new effects in the exclusion task. Many researchers have proposed this latter interpretation for their findings (Anderson & Bjork, 1994; Bjork, 1989; Dzulkipli & Wilding, 2005), though the locus at which these strategic processes operate is debated. One possibility is cue-bias (Anderson & Bjork, 1994; Bjork, 1989), whereby processes are engaged to ensure the internal representation of certain retrieval cues are more likely to be associated with memory traces, thus increasing the likelihood that recollection will be limited to a particular study context. Alternatively, it may be that the locus of control is with memory representations themselves rather than retrieval cues. According to this view, strategic processes act to influence the accessibility of particular memory traces through inhibiting certain representations, exciting other representations or a combination of both operations (Anderson & Bjork, 1994). A final possibility is attentional-bias, which assumes that only certain products of retrieval are attended to (Dywan, Segalowitz, & Arsenault, 2002; Dywan, Segalowitz, & Webster, 1998; Dywan, Segalowitz, Webster, Hendry, & Harding, 2001). The multiple levels at which these control processes have been proposed to operate is broadly consistent with the loci of control identified by Ranganath et al. (2008), discussed in more detail in Chapter Two: Cognitive Control (page 43). Taken together, this suggests that strategic retrieval processes at multiple levels may operate to facilitate accurate source attribution, and attenuation of old/new effects might be attributable to biases acting at different stages.

This framework emphasises the importance of the quality of the information encoded in addition to the quality and suitability of judgment processes engaged when making source attributions. Importantly, recognition and source monitoring are not seen as

fundamentally different processes. On the contrary, in typical recognition paradigms, such as the previously described process-dissociation procedure (Jacoby, 1991), participants are required to differentiate items previously presented in the experimental session to familiar items experienced outside of the experimental session. Hence, performance in these tasks requires some degree of source monitoring to differentiate the relative item familiarity. False alarms and misses can therefore be considered as failures in source monitoring.

Taken together, this highlights the importance of considering this framework when interpreting the behavioural and ERP findings of the experiments reported in this thesis. However, as described by (Johnson et al., 1993), source monitoring processes are typically engaged once information is retrieved from memory. Thus, examining ERP correlates of recollection alone may not fully characterise the ways in which cognitive control difficulties could contribute to the memory problems experienced by patients with schizophrenia. To this effect, it may be important to consider other ERP correlates that emerge after the left-parietal old/new effect. Thus, the final section of this chapter will review other ERP modulations that may also provide valuable insights into the ways in which cognitive control can influence recognition memory performance, and is linked to memory deficits in patients with schizophrenia.

## OTHER EVENT-RELATED POTENTIAL MODULATIONS OF INTEREST

### Late Posterior Negativity

The Late Posterior Negativity (LPN) comprises a relatively greater sustained negativity over midline posterior electrode sites for correctly identified old items compared to correct rejections (Curran, 1999; Cycowicz, Friedman, & Snodgrass, 2001; Donaldson & Rugg, 1998, 1999; Dywan et al., 2002; Herron, 2007; Senkfor & Van Petten, 1998). This effect starts 600-800ms post-stimulus presentation and endures for up to 1200ms (Herron, 2007). This effect is unlikely to be an index of recollection, considering LPN appears post-responding; typically after the emergence of the left-parietal old/new effect, believed to index recollection (Herron, 2007). Furthermore, the LPN has been documented to display equivalent magnitude irrespective of source accuracy judgments (Friedman, Cycowicz, & Bersick, 2005), in addition to being larger in magnitude for false alarms compared to veridical recognition judgments (Wilding & Rugg, 1997). It was

initially proposed that this modulation reflected response-related processing, as opposed to core mnemonic processes, because one study found the magnitude of the LPN to be positively correlated with RT (Wilding & Rugg, 1997). However, once the LPN was documented for old items not eliciting longer response times (Cycowicz et al., 2001), it was proposed that the LPN actually reflected processes related to the retrieval of perceptual information from the encoding context (e.g. stimulus colour), termed the perceptual-specificity hypothesis. Despite the re-conceptualisation of the functional significance of this effect, the perceptual-specificity hypothesis fails to account for all findings, considering LPNs have been identified in recognition tasks requiring simple old/new decisions (e.g. Curran, 1999; Nessler & Mecklinger, 2003) and in source monitoring tasks that do not require the explicit retrieval of perceptual information (e.g. Leynes & Bink, 2002). Therefore more recent attempts to elucidate the functional significance of LPN have focused on identifying distinct subcomponents of this effect.

Johansson and Mecklinger (2003) re-analysed data from two studies (Johansson, Stenberg, Lindgren, & Rosén, 2002; Nessler & Mecklinger, 2003). They assessed both stimulus and response locked ERPs and demonstrated that the LPN can be decomposed into at least two functionally dissociable components. Under conditions of high-conflict (e.g. those observed in the study conducted by Nessler & Mecklinger, 2003), response-locked ERP analyses revealed two important findings. First, both true and false recognition judgments were more negative going compared to correct rejections, at anterior midline recording sites, peaking approximately 70ms post response production. This modulation resembles the error-related negativity (ERN) observed in choice reaction-time tasks (Johansson & Mecklinger, 2003), believed to result from fast guessing or impulsive responding (Coles, Scheffers, & Holroyd, 2001). Second, false recognition judgments elicited significantly larger ERNs at midline posterior sites compared to true recognition judgments, and this posterior ERN was delayed compared to the aforementioned anterior ERN (Nessler & Mecklinger, 2003). The authors proposed that the anterior ERN reflects error detection, and the posterior ERN is related to action monitoring in situations of high response conflict (Nessler & Mecklinger, 2003). The critical finding is that the LPN effects observed in the stimulus-locked analysis are functionally and temporally similar to those elicited by false recognition judgments at posterior locations during response-locked analyses (Johansson & Mecklinger, 2003). Because of this, Johansson and Mecklinger (2003) proposed that the posterior response-

related ERN shaped the overall LPN, and furthermore that cross-trial variability in RT contributed to the sustained time course of the LPN observed in the stimulus-locked analyses.

Under low-conflict conditions however (e.g. those seen in Johansson et al., 2002), LPNs cannot be explained in terms of response-related activity. Rather, under these circumstances, additional processing contributes to the LPN, highlighting that at least two dissociable processes contribute to the characterisation of LPN components observed in stimulus-locked analyses. It was proposed that these additional processes reflect the requirement to retrieve contextual information, and attempts to reconstruct the study episode by retrieving and evaluating attribute conjunctions (Johansson & Mecklinger, 2003). However, further evaluation of the additional processes implicated is required to elucidate the particular factors that contribute to the LPN (Johansson & Mecklinger, 2003).

In another study, Herron (2007) had participants complete four study-test blocks. After two study-test blocks, the response requirements were altered. The stimulus-locked ERP analysis showed that the LPN consisted of functionally dissociable elements. One element, occurring 600-1200ms post-stimulus onset, was found to show graded attenuation with each successive block. This quantitative difference between blocks suggests that the same neural generators were involved across blocks but to varying degrees (Herron, 2007). Herron (2007) proposed that this aspect of the LPN may reflect the search and/or retrieval of source-diagnostic information, which becomes less effortful with increasing practice. However, it is important to acknowledge that this element of the LPN was absent in block four. Due to the difficulty associated with interpreting null results, it is unclear whether this result is due to the termination of this process in block four, or due to the activity being attenuated to such a degree that it is no longer detectable at recording sites on the scalp (Herron, 2007).

Stimulus-locked ERP analyses also identified a further element 1200-1900ms post stimulus presentation, which was found to be invariant to the effect of block. Herron (2007) interpreted this invariance as indicating that this component related to the requirement to retrieve episodic information, and is unaffected by other factors such as task fluency. This characterisation is consistent with the proposition put forward by

Johansson and Mecklinger (2003) that at least one subcomponent of the LPN reflects retrieving and/or evaluating attribute conjunctions.

Finally, response-locked ERP analyses revealed LPN activity 50-300ms post-responding. This component was most negative going for all old items, least negative going for new items in blocks two and four (e.g. response-fluent blocks), and intermediately negative going for new items in blocks one and three (e.g. less response-fluent blocks). This behaviour is broadly consistent with the view that this effect reflects action-monitoring processes (Johansson & Mecklinger, 2003). These interpretations are further supported by the behavioural data which indicated slower RTs for hits compared to correct rejections; suggestive of greater need for response monitoring for old items compared to new items (Herron, 2007). Nonetheless, the fact that response-fluent blocks compared to those associated with less motoric fluency were associated with significantly larger response-locked LPNs seems to contradict this interpretation. However, individual analyses of hits and correct rejections highlighted that effects of block were driven by ERPs to correct rejections. During stimulus-locked analyses, ERPs to correct rejections are more positive going post-response reversal (e.g. during block three), in contrast to response-locked analyses where ERPs were more negative going. Herron (2007) proposed that this effect was not identified through stimulus-locked analyses due to its relatively small effect size and the variability in response RT. This interpretation is supported by the behavioural data in which RTs for correct rejections were slower in blocks one and three, potentially indicating participants adopted a task set whereby all responses were monitored to a greater degree (Herron, 2007).

Whilst the aforementioned studies do not provide an extensive review of the LPN literature, they highlight two important issues for the work in this thesis. First, that LPN activity is heterogeneous depending on the conditions of the experiment. Second, that the LPN can be better thought of in terms of several distinct subcomponents that contribute to the overall characterisation of the effect. Consequently, given the consistent interpretation that at least one subcomponent of this effect reflects retrieving and/or evaluating attribute conjunctions, examining this effect in relation to schizotypy and patients with schizophrenia provides a means of investigating whether processes operating at this level contribute to the reported memory problems in these patients.

### Right Frontal Old/New Effect

The right frontal old/new has, as the name suggests, a right frontal distribution starting from perhaps as early as 400ms post-stimulus presentation and lasting for up to 1500ms. The effect comprises a greater relative positivity for studied compared to unstudied items (Cruse & Wilding, 2011; Senkfor & Van Petten, 1998; Wilding & Rugg, 1996b). Furthermore, this effect is more pronounced for tasks requiring the retrieval of contextual information compared to those in which only an old/new response is required (Johansson et al., 2002; Senkfor & Van Petten, 1998; Wilding & Rugg, 1996b).

The authors of one of the earliest studies reporting this effect proposed that the right-frontal old/new effect indexes processes necessary for creating a successful representation of a prior event (Wilding & Rugg, 1996b). However, findings from more recent studies suggest that this interpretation may be inaccurate considering this ERP does not predict the accuracy of source judgments in all circumstances (e.g. Senkfor & Van Petten, 1998). Consequently, other authors have suggested a more generic retrieval processing account of this effect since equivalent right-frontal old/new effects have been observed in both source monitoring and semantic retrieval tasks (Hayama, Johnson, & Rugg, 2008).

Hayama et al. (2008) offered two accounts. First, that the right-frontal old/new effect is sensitive to the number of internal decisions required for task completion. Second, that the effect indexes processes involved in the monitoring of retrieved information in service of task goals. A study conducted by Cruse and Wilding (2009) provided a strong test of the former account, in addition to providing a means of assessing the latter account. At study, participants were presented with words in one of two colours. In the following retrieval phase, participants were presented with studied and unstudied items in a neutral colour. Participants were required to make initial old/new judgments. For items attracting old responses, participants had to make a subsequent source judgment (e.g. the colour of presentation at study), in addition to indicating confidence in the source judgment. The right-frontal old/new effect was greater in magnitude for high compared to low confidence correct source judgments. Furthermore, the magnitude of the effect correlated with the proportion of low confidence judgments. Since both high and low confidence judgments were associated with an equivalent number of decisions, these findings provide evidence against the decision-number account of the right-frontal

old/new effect. However, if the monitoring account is correct, one would expect greater monitoring with decreasing quality of retrieved information. Hence, the correlation between the magnitude of the effect and judgment confidence reported by Cruse and Wilding (2009) provides evidence in favour of the retrieval monitoring account.

Similar right-frontal old/new effects have been documented using variants of the exclusion paradigm (e.g. Evans et al., 2010). Participants were initially presented with objects denoted by concrete nouns and were required to indicate whether i) it had pleasant or unpleasant connotations, ii) it was typically smaller or larger than a shoe box, or iii) it was easy or difficult to draw. During the test phase, participants were required to make one response for items previously presented in the drawing task and another response for all other previously encountered words (e.g. pleasantness and shoe box items), as well as new (unstudied) items. There was a greater relative positivity for target items (drawing task items) at right anterior scalp locations from 800ms onwards (Evans et al., 2010). These findings were interpreted in terms of monitoring processes involved in the evaluation of recovered information, in service of task-relevant goals (see also Rugg, Allan, & Birch, 2000).

Such interpretations are also consistent with findings from depth of processing manipulations. Rugg et al. (2000) presented participants with two encoding tasks: either an orthographic or a semantic task. At test participants were required to make a simple old/new judgment. Items encoded in the orthographic condition exhibited a significantly larger right frontal old/new effect than items encoded in the semantic condition. Considering items processed in terms of orthographic features are often associated with relatively few contextual details (Craik & Lockhart, 1972), these findings suggest post-retrieval monitoring processes are engaged to a greater degree when trying to recovering shallowly encoded information.

Collectively, this evidence suggests that observing how the right-frontal old/new effect varies with group, experimental manipulations and personality characteristics may be a fruitful approach to pursue in the experiments reported in this thesis. Considering this effect is considered to index post-retrieval control mechanisms, there is the opportunity to explore whether retrieval control mechanisms at this level are aberrant in patients with schizophrenia.



## CHAPTER THREE SUMMARY

The evidence covered in detail in this chapter indicates strongly that there are multiple processes that contribute to successful memory retrieval and thus multiple loci for potential deficits for patients with schizophrenia. This is consistent with the model of cognitive control proposed by Ranganath et al (2008; page 45) which suggests there are multiple points at which cognitive control can contribute to successful memory performance. Taken together, this highlights the need for investigations such as the ones reported in this thesis to better understand the ways in which these processes may contribute to the memory problems experienced by those with schizophrenia.

Importantly, one behavioural paradigm that has been successfully employed in conjunction with ERPs to examine cognitive control during recollection in healthy volunteers is the exclusion paradigm (Jacoby, 1991). Thus, the experiments reported in this thesis employed these methods to better understand these processes in relation to people with schizophrenia.

The next chapter will bring together the key topics that have been presented so far and introduce studies that have used methods similar to those adopted in the present investigation to research memory processes in patients with schizophrenia. Specifically, the studies discussed in the next chapter investigate the contributions of recollection and familiarity to memory deficits observed in patients with schizophrenia. Through presenting this work we establish the current knowledge of memory processes in people with schizophrenia and highlight the need for further investigations.

## CHAPTER FOUR: MEMORY AND SCHIZOPHRENIA

It has been suggested that the processes contributing to episodic memory performance (see Chapter Three: Memory, Models and Frameworks [page 56] for more detail) are not equally affected in schizophrenia. For example, memory performance is disproportionately compromised when patients are required to organise information during encoding, recall associations between items rather than individual items or complete recall rather than recognition tests (Achim & Lepage, 2003; Iddon, McKenna, Sahakian, & Robbins, 1998; Ranganath et al., 2008). This latter evidence particularly suggests schizophrenia patients may have selective deficits in recollection considering successful recall performance requires the retrieval of contextual details from the encoding phase. This is in contrast to recognition performance which can also be supported by item familiarity (Yonelinas, 2002).

Danion, Kazes, Huron, and Karchouni (2003) used the Remember/Know Procedure (Tulving, 1985) and provided some of the first evidence suggesting selective deficits in recollection for patients with schizophrenia. Participants were presented with positive, negative and neutral words. They were required to read them aloud and indicate their subjective feelings of pleasantness towards them. In the subsequent recognition test, patients gave significantly fewer Remember responses compared to control participants. By contrast, patients gave more Know responses compared to control participants. Assuming proportions of Remember and Know responses reflect recollection and familiarity respectively (Gardiner, 1988; Yonelinas & Jacoby, 1995), the pattern of behavioural responses here could indicate patients with schizophrenia experience selective difficulties with recollection and hence rely more heavily on familiarity when making recognition judgments.

Other researchers have investigated memory deficits in patients with schizophrenia using the process-dissociation procedure (Jacoby, 1991), and have reported familiarity deficits. Guillaume et al. (2007) used a face recognition task where intrinsic (facial expression) or extrinsic (background scene) perceptual information was manipulated. During the exclusion phase, participants were encouraged to only accept faces that appeared with the same facial expression and background scene and reject recombined items along with new items. A recombined item, depending on the version of task used, was either a new facial expression on an old background scene (intrinsic manipulation)

or an old facial expression on a new background scene (extrinsic manipulation). During the inclusion phase, participants were encouraged to accept both faces that appeared with the same facial expression and background scene and recombined items, but reject new items. Patient response accuracy was significantly lower than that for controls in the inclusion condition only. No group differences were found for estimates of decision criterion ( $B''$ ; Macmillan & Kaplan, 1985; Pollack & Norman, 1964). Furthermore, only estimates of familiarity significantly differed between participants, with patients having significantly lower estimates compared to controls. There were, however, different false alarm rates for patients and controls, and as noted earlier the accuracy of estimates under these circumstances is questionable (Toth et al., 1995).

Other researchers have used neuroimaging techniques to investigate memory processes in people with schizophrenia. Ragland, Ranganath, et al. (2012) collected fMRI data using the Relational and Item-Specific Encoding Task (RISE; Murray & Ranganath, 2007), to assess the contributions of different encoding and retrieval processes. Participants were presented with vertical arrays of three coloured pictures, followed by a probe item from the initial vertical array along with a number. On rehearse trials participants were required to indicate whether the number matched the serial presentation of the item. These trials were considered to assess item memory. On reorder trials participants were instructed to mentally reorder the items from lightest to heaviest and indicate whether the number matched the serial position in the reordered memory set. These trials were considered an assessment of relational memory. Estimates of recollection were higher for relational compared to item encoding trials. Furthermore, estimates of recollection and familiarity were higher for control participants compared to patient participants. Whereas estimates of recollection were equally impaired across tasks, estimates of familiarity demonstrated larger deficits following relational versus item-encoding. Consistent with previous literature (e.g. Murray & Ranganath, 2007), reorder trials were associated with increased DLPFC activity compared to rehearse trials. Whilst DLPFC activity was numerically reduced in patients compared to controls, there were no significant between group differences. In patients however, patterns of activation were less focal compared to control participants. Taken together, this study provides evidence to suggest patients with schizophrenia do exhibit familiarity as well as recollection deficits.

In other studies, assessments of the contributions of recollection and familiarity have been made based upon ERP data. The findings are inconsistent (e.g. Guillaume, Guillem, Tiberghien, & Stip, 2012; Tendolkar, Ruhrmann, Brockhaus, Pukrop, & Klosterkotter, 2002). For example, Guillaume et al. (2012) asked participants to complete the intrinsic manipulation inclusion task described above. Compared to control participants, patients with schizophrenia exhibited decreased discrimination performance ( $A'$ ; Macmillan & Kaplan, 1985; Pollack & Norman, 1964). No group differences were found for estimates of decision criterion, however ( $B''$ ; Macmillan & Kaplan, 1985; Pollack & Norman, 1964). This pattern of performance was accompanied by the absence of midfrontal and left-parietal old/new effects for items with facial-expression changes in patient participants. This is in contrast to unchanged-expression items where both groups exhibited the aforementioned ERP indices of familiarity and recollection respectively. The authors proposed that when patient participants were not required to consider changes in facial expressions, the observed recognition deficit arose from impairments in the mechanisms underlying the emergence, assessment or utilisation of familiarity. This divergence, however, was not accompanied by differences in behavioural performance between conditions, thus limiting the strength of conclusions that can be drawn based on these data.

Tendolkar et al. (2002) collected ERP data whilst participants completed a Remember/Know task. During study, participants were instructed to generate 3-4 word sentences incorporating study words. At test, control participants gave significantly more Remember responses compared to patients and patient participants gave significantly more Know responses compared to controls. When estimates of familiarity were calculated, however, there were no significant group differences (Yonelinas & Jacoby, 1995). When ERP difference measures from 500-800ms post-stimulus were compared, no group differences were found for the old/new effects associated with Remember responses. By contrast, old/new effects associated with Know responses were more positive going for control participants at temporo-parietal sites, but more positive going for patient participants over frontal sites. By 800-1100ms, only control participants exhibited old/new effects for Remember responses at temporo-parietal sites, though patients continued to exhibit more positivity over frontal sites compared to controls for old/new effects associated with Know responses. In the 1100-1400ms epoch, patients did not exhibit old/new effects for either Remember or Know responses. Control

participants however, did exhibit old/new effects for Remember responses, and these were more frontally distributed compared to the effects in previous epochs. Analyses of the topographies for Remember and Know responses revealed only the old/new effects associated with. Know responses differed by group. For controls, this effect was present over left temporo-parietal locations in the 500-800ms epoch. For patients though, this effect exhibited a widespread frontal distribution from 500-1100ms. The authors proposed this frontally distributed activity for Know responses may represent the engagement of monitoring processes in service of task performance to compensate for recollection deficits. These latter findings further highlight the importance of considering indices of post-retrieval monitoring in the experiments reported in this thesis. Nonetheless, it is important to acknowledge that, comparably to Guillaume et al. (2012), the lack of correspondence between group differences in behavioural estimates and the ERP data moderates the claims that can be made.

Libby, Yonelinas, Ranganath, and Ragland (2013) conducted a quantitative reanalysis of 19 published articles investigating recollection and familiarity in patients. In contrast to some previous conclusions that recollection is selectively impaired in schizophrenia, Libby et al. (2013) also found evidence of familiarity deficits. This latter finding, however, was found to be more variable with frequent small-to-medium effect sizes in contrast to the medium-to-large effect sizes that were more consistently associated with recollection. One of the most important implications of this outcome is that recollection can be viewed as an important therapeutic target for improving episodic memory performance in patients with schizophrenia (Libby et al., 2013).

The importance of investigating cognitive mechanisms that contribute to successful recollection in patients is further emphasised by evidence suggesting individuals with schizophrenia have difficulty discriminating between particular encoding contexts, namely reality monitoring. Reality monitoring requires people to differentiate between self-generated and externally presented information (Johnson, Foley, Suengas, & Raye, 1988; Johnson, Kounios, & Reeder, 1994; Rosburg et al., 2011b). Discrimination between such contexts may be more difficult for people with schizophrenia as one hypothesis for the occurrence of some positive symptoms (e.g. hallucinations) is that patients have a particular difficulty discriminating between internally and externally generated events (for a review see Ditman & Kuperberg, 2005; Frith, 1992; Johns et al., 2001).

Frith (1992) proposed that auditory verbal hallucinations arise due to patients failing to successfully monitor their intentions to perform a task (e.g. inner speech) as it is being performed, resulting in patients misattributing the event to an external source. This monitoring of inner speech is often termed verbal self-monitoring. Johns et al. (2001) examined the source attributions made by hallucinating and non-hallucinating schizophrenia patients, in addition to healthy controls. Participants were shown a series of words and asked to read them aloud. Participants either heard their own voice, or that of the experimenter through headphones. The presented voice in two thirds of trials was distorted. Furthermore, the emotional valence of the words was manipulated: one third of trials were positive, neutral and negative respectively. Both hallucinating and non-hallucinating schizophrenia patients made more attribution errors than control participants when presented with their own distorted speech. Most of the errors committed by hallucinating patients were a result of misattributing their own distorted voice to an external source (91% compared to 65% and 59% for hallucinating, non-hallucinating and control participants respectively). Furthermore, the valence significantly influenced the number of errors, with hallucinating patients making more errors on negative words, regardless of condition (e.g. own speech or other speech). Similar findings have been found by using variations of this paradigm to investigate other modalities (e.g. Blakemore, Smith, Steel, Johnstone, & Frith, 2000; Johns & McGuire, 1999), further emphasising that source monitoring retrieval processes may be deficient in schizophrenia.

More recent studies using self-monitoring recognition tasks have similarly identified relationships between hallucinations and source misattribution. Brébion et al. (2000) presented participants with a category name (e.g. fruit) from which the experimenter verbally produced an example (e.g. plum), followed by a picture of a second example (e.g. grapes). The participant was then invited to provide a third example from the category. Following a distractor task, the experimenter read a list of all examples produced intermixed with new examples. Participants had to indicate if the item had been produced or not, and if so, whether the item was produced by the experimenter, themselves or was a picture. Hallucinating patients were found to misattribute self-produced items to another source (e.g. experimenter or picture) compared to healthy control participants. Similar associations between false recognition and positive symptomology, specifically hallucinations, have been identified using variations on this

paradigm (e.g. Brébion, Smith, Amador, Malaspina, & Gorman, 1998; Brébion, Smith, Gorman, & Amador, 1997).

#### CHAPTER FOUR SUMMARY

A variety of behavioural tasks have been employed in pursuit of understanding how processes contributing to successful memory performance are affected in patients with schizophrenia. The stimuli employed across these tasks often vary greatly, including but not limited to emotional valence of words, faces and object pictures (e.g. Danion et al., 2003; Guillaume et al., 2007; Ragland, Ranganath, et al., 2012). This heterogeneity limits the strengths of claims that can be made, but perhaps the strongest claim is that recollection is compromised to a greater degree than is familiarity.

Recollection is a process that is generally assumed to be under conscious control. Control mechanisms allow us to modify our behaviour flexibly in accordance with task demands (Lesh et al., 2011) and previously it has been hypothesised that many of the deficits observed in schizophrenia patients arise at least in part due to failures in cognitive control operations (Cohen & Servan-Schreiber, 1992). This possibility motivated the work in this thesis, employing changes in the left-parietal old/new effect in exclusion task conditions as the marker for control over recollection. Moreover, the tasks included encoding contexts in which individuals with schizophrenia are known to have problems: namely reality monitoring.

As a first pass at addressing whether failures of cognitive control contribute to memory problems in people with schizophrenia, control mechanisms contributing to memory retrieval were investigated in relation to schizotypy. This was the approach adopted in the first two large scale experiments reported in this thesis: ERPs were acquired during completion of exclusion tasks, and ERP evidence for control over retrieval was assessed in relation to a range of individual difference measures. These studies are followed by a report of findings in similar paradigms in which neural and behavioural measures from patients with schizophrenia and controls were the variables of interest.

## CHAPTER FIVE: EXPERIMENT ONE

The principal aim of this experiment was to investigate whether retrieval control is modulated by schizotypy scores. A reality monitoring version of the exclusion paradigm was used, similar to that used by Rosburg et al. (2011a; 2011b), in conjunction with ERP recordings. This was followed by a free recall task as applied by Elward et al. (2012). In addition, participants completed a variety of questionnaires assessing general and specific aspects of schizotypal and working memory capacity. The reason for using both general and specific measures of schizotypy, was to allow investigations of which symptom clusters are associated with retrieval control.

Strong predictions about outcomes are difficult to make in this first experiment, as is evident from the very mixed outcomes reported previously and reviewed in Chapters One and Four [pages 37 and 80]. However, given that one hypothesis underlying hallucinations in patients with schizophrenia is the difficulty distinguishing between internally and externally generated information, positive schizotypy has been hypothesised as being of principle importance. Specifically, it is anticipated that positive schizotypy will be negatively correlated with the magnitude difference between target and non-target old/new effects.

The new measure used here is the ERP index of control over retrieval, and of central interest is how this varies with schizotypy ratings: a link between lower estimates of control and some schizotypy dimensions would indicate the utility of this combination of ERP and individual difference measures, as well as supporting the view that deficits in cognitive control are part of the cognitive challenges associated with schizophrenia. Further comment on possible links between measures of behaviour (accuracy and RTs) and schizotypy is deferred until the Discussion.

## METHODS

### Participants

Fifty four participants were recruited from Cardiff University using an online participant management system, and paid at a rate of £10/hour. Ethical approval for this study was obtained from the Cardiff University School of Psychology Ethics Committee. Participants spoke English as a first language, had normal or corrected-to-normal vision, were right-



handed, had no prior diagnosis of dyslexia and reported that they were not currently taking psychotropic medication. Participants provided written informed consent in advance, and were aware they could withdraw from the study at any point without reason or penalty. Data from six participants were excluded from analysis due to: experimenter error (1), poor behavioural performance (1) and excessive EEG artefact (4). For behavioural and EEG rejection criteria see the EEG Acquisition and Analysis Procedures sections of this chapter respectively. Of the remaining 48 participants, (mean age = 21.92 years, range = 19-28 years) 27 were female.

## OVERVIEW OF PROCEDURE

All participants completed tasks in a fixed order. Initially, participants completed the exclusion paradigm while ERPs were acquired during study and test blocks. They subsequently completed a free recall task, where they were required to recall as many words as they could from the exclusion task. Following this, participants completed an automated version of the O-SPAN task (Unsworth, Heitz, Schrock, & Engle, 2005), widely accepted as a measure of working memory capacity (Turner & Engle, 1989). Participants then completed a battery of psychometric measures including; an adapted version of the Vividness of Visual Imagery Questionnaire (VVIQ; Cui, Jeter, Yang, Montague, & Eagleman, 2007; Marks, 1973), the Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE; Mason et al., 1995), the 21-item Peters et al. Delusion Inventory (PDI; Peters, Joseph, Day, & Garety, 2004) and the Launay-Slade Hallucination Scale-Revised (LSHS-R; Launay & Slade, 1981; Morrison, Wells, & Nothard, 2000).

### Exclusion Task

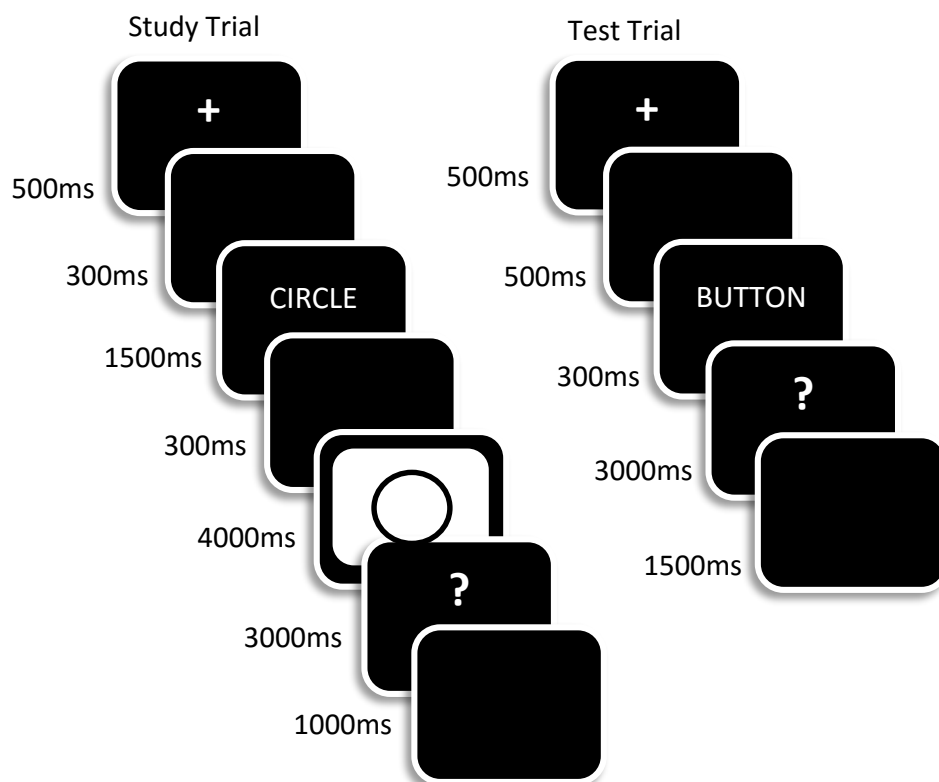
Three hundred and sixty pictures and the corresponding word labels were selected from the International Picture Naming Project database (<http://crl.ucsd.edu/experiments/ipnp/>). All picture-word lists used in this task had a mean percentage naming frequency of 93% (Bates et al., 2003). The words had a frequency range of one to nine/million, and ranged from three to ten letters in length. Frequency counts reported in this database were taken from the CELEX lexical database (Baayen, Piepenbrock, & Gulikers, 1995) and transformed according to Snodgrass and Yuditsky (1996). Stimuli were programmed using E-Prime 2.0 (Psychology Software Tools, Pittsburgh, PA). Words were presented in white on a black background in Time

New Roman, subtending maximum visual angles of 0.5° (vertical) and 2.4° (horizontal). Pictures were presented centrally and subtended maximum visual angles of 7.6° (vertical) and 5.7° (horizontal). Stimuli were presented on a screen positioned 1.2m in front of the participant. Critical words were divided into three lists (120 picture-word pairs/list). The study phase comprised two picture-word lists (240 picture-word pairs); one picture-word list was used for the imagined study context and other for the perceived study context. All 240 words presented during study were repeated during the test phase along with words from another list (360 picture-word pairs in total). Twelve versions of each paradigm were programmed. Factors that were counterbalanced were: word list associated with imagined, perceived or new items, response hand at test and which class of items (imagined or perceived) were presented as targets during the first test phase. Participants did not complete a practice session prior to completing the exclusion task as on the basis of pilot behavioural performance (6 participants, data not presented), this was not required.

All study trials started with a fixation cross. Participants were then presented with a word followed by a white frame (see **Figure 2** below for details of timings). In the study phase there were two encoding contexts: imagine and perceive. Participants were unaware of the encoding context on every trial until the white frame was presented. For perceive trials, a black and white line drawing of the object denoted by the word was presented within the white frame, for the duration of the presentation of the white frame, which participants were instructed to study while it remained visible. For imagine trials, the white frame only was presented. During these trials, participants were instructed to imagine a line drawing of the object denoted by the word for the duration of the presentation of the white frame. Participants had to indicate the quality of the perceived or imagined representation (good, fair, poor) when the question mark was presented. Participants made their responses using their index, middle and ring fingers. The hand used at study was counterbalanced between participants and was the opposite to that used for target items during the test phase. Following this response, the trial was terminated and the next trial commenced after the inter-trial interval (ITI) during which the screen was blanked. If participants did not respond, the next trial still commenced after the ITI.

All test trials started with a fixation cross (see **Figure 2** for details of timings). Participants were then presented with a word, which was either one that was previously presented in the study phase, or an unstudied (new) item. When the question mark was presented, participants were required to make a binary decision using their index fingers to indicate whether the item was either a target or a non-target/new item. After responding, the trial was terminated and the next trial commenced following the ITI. If participants did not respond in time, the next trial still commenced after the ITI. For half of the test items (180 words) perceived items were designated as targets and for the other half (180 words) imagined items were designated as targets. The order of target designation was counterbalanced between participants.

Presentation of study and test items was randomised and participants received a brief break after every 60 trials during both phases of the experiment. When participants failed to respond within the time limit, these responses were excluded from the analysis. This criterion applied to less than 1% of trials.



**Figure 2 – A schematic representation of the study trials (left) and test trials (right) for Experiment One.**

To determine whether participants could discriminate between targets, non-targets and new items, two discrimination values (Target – Non-Target and Target – New) were calculated for each condition using the formula  $Pr = p(\text{hit}) - p(\text{false alarm})$  (Snodgrass & Corwin, 1988). For both measures,  $p(\text{hit})$  was the likelihood of a correct response to a target item. For the Target – Non-Target discrimination,  $p(\text{false alarm})$  was the likelihood of making an incorrect (target) response to a non-target item, whereas for the Target – New discrimination  $p(\text{false alarm})$  was the likelihood of making an incorrect (target) response to a new item. Participants were excluded from analysis if  $Pr$  values were below 0.1 (with scores below this presumably indicating participants could not discriminate well between the different stimulus types).

### Free Recall Task

This task was completed immediately after completion of the exclusion task, and before the EEG cap was removed. Participants were provided with a lined piece of paper and were asked to write down as many words as they could remember from any phase of the exclusion task. Participants were given five minutes to complete this task. When participants produced items that were not presented at any point during the study and test phase, these items were excluded from the analysis. This criterion applied to less than 5% of items. This measure was included to investigate whether changes in the left-parietal old/new effect for non-target items were associated with differential memorability for these items. If the ERP index for retrieval control is associated with differential prioritisation of target and non-target items, this can be reflected by the proportion of target and non-target items recalled on a later test (Elward et al., 2012).

### Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE; Mason et al., 1995)

The O-LIFE is a four-scale questionnaire assessing the four personality dimensions that characterise schizotypy. The four scales measure unusual experiences (UnEx), cognitive disorganisation (CogDis), introvertive anhedonia (IntAn) and impulsive non-conformity (ImpNon). The UnEx scale contains 30 items which are consistent with the positive symptoms of psychosis, including perceptual aberrations and magical thinking. As such, this scale is considered to measure positive schizotypy. The CogDis subscale consists of 24 items assessing deficits in cognitive abilities including attention and concentration. In addition, some items measure social anxiety. This aspect of schizotypy has been likened

to the disorganised element of psychosis. Twenty seven items measure the lack of enjoyment from various activities, including emotional and physical contact, and make up the IntAn subscale. This trait is analogous with negative symptoms of psychosis. The ImpNon subscale (23 items) is concerned with disinhibited and reckless characteristics, including self-abusive and violent behaviours. This subscale is not considered to be consistent with the three-factor model of schizotypy, thus was not considered further in this thesis. In this study, an automated version of the O-LIFE was used. Participants respond yes or no to each item. The score for each subscale is the sum of affirmative responses, with reverse scoring where appropriate, to relevant items. This measure has both high internal consistency ( $\alpha > 0.77$ ; Mason et al., 1995) and test-retest reliability (Burch et al., 1998).

#### 21-Item Peters et al Delusion Inventory (PDI; Peters et al., 2004)

The 21-item PDI (Peters et al., 2004) is based on the original 40-item measure produced by Peters et al. (1999). The selection of the 21 items was based on the highest loading items according to principal components analysis (Peters et al., 1999). Participants respond yes or no to these items, which assess various delusional beliefs. Yes responses are followed up with three 5-point Likert scales which assess the amount of distress caused, the preoccupation with and the strength of conviction for each belief. For each Likert scale, a score of one represents no distress, preoccupation with or conviction in the beliefs and a score of five represents a great deal of distress, preoccupation or conviction. The PDI produces five total scores: Yes, Distress, Preoccupation, Conviction and Total. The Yes score is calculated by summing the number of yes responses to all items. The Distress, Preoccupation and Conviction scores are calculated by summing the responses on the Likert scales for each item to which participants respond yes. The Total score is calculated by summing all totals from Yes, Distress, Preoccupation and Conviction scores.

#### Launay-Slade Hallucination Scale-Revised (LSHS-R; Launay & Slade, 1981; Morrison et al., 2000)

The LSHS-R was based upon the original 12-item measure produced by Launay and Slade (1981). The questionnaire was modified by Morrison et al. (2000) to incorporate measures of predisposition to visual hallucinations, and to allow items to measure

frequency, rather than a forced true or false response. The LSHS-R consists of 15 items assessing various hallucinatory experiences. All items are assessed on a four-point scale of never, sometimes, often, always. Never answers correspond to a score of one and always answers correspond to a score of four. The LSHS-R produces five scores: Proneness to vivid or intrusive thoughts (three items), auditory hallucinations (four items), vivid daydreams (three items) and visual hallucinations (five items), along with a total score (15 items). Each score is calculated by summing the responses to the relevant items.

#### Vividness of Visual Imagery Questionnaire (VVIQ; Cui et al., 2007; Marks, 1973)

The adapted VVIQ consists of the original 16 items produced by Marks (1973). Participants are presented with four scenarios (a person they know well, a rising sun, the front of a shop they know well and a country scene). Participants are asked four questions about each scene, each requiring the participant to focus on a particular aspect of the scene in question. In the adapted version, participants are required to initially complete the questionnaire rating each item between one and five (one representing an image that is perfectly clear, five representing no image at all) with their eyes open, and subsequently complete the same items with their eyes closed. In the original version, participants were just required to rate each item and whether eyes should be open or closed was not specified. The adapted VVIQ is scored by summing all responses together (producing a maximum score of 160, rather than 80 in the original version). This measure was initially included as a potential covariate to performance in the exclusion task. For all experiments, however, no significant correlations between measures of behavioural performance and VVIQ were identified, thus this measure is not considered further in this thesis.

#### O-SPAN (Unsworth et al., 2005)

Participants completed an automated O-SPAN task (Unsworth et al., 2005); for task see <http://psychology.gatech.edu/renglelab>). Participants initially completed three practice sessions. The first practice session consisted of a letter span task, where participants were presented with individual letters sequentially and were required to recall the letters in the same order as the items were presented via mouse click using a matrix of letters. During the second practice session, participants performed simple mathematic

operations to which they were provided with a solution and asked to respond true or false. The percentage of correct maths solutions was displayed in the upper right hand corner of the screen and participants were instructed to try and keep this value at 85% or above. The final practice session consisted of participants performing both the letter span task and solving the mathematical operations together. After participants had completed all practice sessions, the programme progressed to the experimental trials. The experimental trials consisted of three sets of each set size, with set sizes ranging from three to seven trials, the order of which was randomised for each participant. A total of three sequences of each set size were presented. In total, participants were presented with 75 letters and mathematical operations. The O-SPAN score was calculated as the sum of all items from perfectly recalled sets. For example, recalling all items from the three-letter sequences and only two sets from the four-letter sequences would result in a score of 17 (3+3+3+4+4).

## EEG ACQUISITION

The electroencephalogram (EEG) was recorded from 25 silver/silver chloride embedded in an elasticated cap and from two further electrodes placed on left and right mastoid processes. Recording sites were based on the International 10-20 system (Jasper, 1958) and included midline (Fz, Cz, Pz), fronto-polar (Fp1/Fp2), frontal (F7/8, F5/6, F3/4), central (T7/8, C5/6, C3/4), parietal (P7/8, P5/6, P3/4) and occipital sites (O1/2). Vertical and horizontal eye movements were recorded from additional bipolar electrodes placed above and below the right eye (vertical electro-oculargram [VEOG]) and on the outer canthi (horizontal electro-oculargram [HEOG]). EEG was recorded at 250Hz with an averaged reference. Data were re-referenced offline to the average signal at the mastoids. EEG and EOG were recorded with a bandwidth of 0.03-40Hz. Trials containing large EOG, muscular or alpha artefacts were rejected, as were trials containing A/D saturation or baseline drift exceeding  $\pm 75\mu\text{V}$ . EOG blink artefacts were corrected using the Gratton, Coles, and Donchin (1983) algorithm. Total epoch length for all segments was 1800ms, with a 200ms pre-stimulus baseline, relative to which all mean amplitude measures were taken.

## ANALYSIS PROCEDURES

The principal motivations for the work described in this chapter are: i) to understand the relationship between measures of behaviour and schizotypy, ii) to investigate whether schizotypy measures are associated with an index of retrieval control, and iii) to investigate whether schizotypy measures are associated with post-retrieval ERP processes.

In keeping with this, discrimination measures, reaction times and process estimates were correlated with five schizotypy measures; UnEx, CogDis and IntAn subscales of the O-LIFE and total scores from the PDI and LSHS-R. Initial examinations of the ERP data were restricted to parietal electrodes between 500-800ms post-stimulus presentation, which is where and when left-parietal old/new effects are commonly observed (e.g. Wilding, 2000; Wilding & Rugg, 1996a; Wilding & Rugg, 1997; Wilding & Sharpe, 2003).

ERP analyses of late posterior negativity and right frontal old/new effects were restricted to parietal electrodes and frontal electrodes from 900-1800ms post-stimulus respectively, as this is where these effects are commonly observed (e.g. Cruse & Wilding, 2011; Herron, 2007). Analyses for this time period will be conducted for three segments of 300ms, in keeping with the analysis strategy adopted by Rosburg et al. (2011b).

Once old/new ERP effects had been identified at the group level, correlational analyses were conducted to identify whether the five schizotypy measures were associated with the magnitudes of these effects. For the late posterior negativity and right-frontal effects the correlations were assessed against the difference scores obtained by subtracting mean amplitudes associated with correct responses to new items from those associated with target and non-target items as appropriate. For the analyses of left-parietal ERP old/new effects, the correlations were assessed against the difference scores obtained by subtracting the mean amplitude associated with non-targets from those associated with targets. Analyses of left-parietal old/new effects were conducted on the average amplitudes across P7, P5 and P3 electrode sites. The specific sites included in analyses of late posterior negativity and right frontal old/new effects were dependent on the outcome of higher level analyses for each epoch.



Finally, to investigate the correlation identified by Elward and Wilding (2010), for details see page 68 correlational analyses were conducted to identify whether the magnitude of the difference between target and non-target left-parietal old/new effects was correlated with WMC score. As for the assessments involving schizotypy ratings, these analyses were conducted on the average amplitudes across P7, P5 and P3 electrode sites within the 500-800ms epoch.

## RESULTS

Where necessary, all ANOVAs reported in this thesis were corrected for nonsphericity using the Greenhouse-Geisser correction (Greenhouse & Geisser, 1959). Statistically significant effects ( $p < 0.05$ ) are only reported if they involved the factors of target designation and/or response category.

### PRINCIPAL BEHAVIOURAL RESULTS

#### Exclusion Task

Response accuracies and reaction times for each category of stimulus and split by target designation are presented in **Table 1**. Pr values were reliably above zero in each case (smallest  $t(47) = 33.33, p < 0.001$ ). A 2x2 repeated measures ANOVA of these discrimination scores split by target designation revealed a main effect of discrimination only, where Target – New discrimination was superior to Target – Non-Target discrimination ( $F(1, 47) = 37.02, p < 0.001$ ).

**Table 1 – Probabilities of correct responses (accuracy) and reaction times (RT) for targets, non-targets and new items split by target designation (imagine/perceive) for Experiment One. Standard deviations (SD) are in parentheses. Hit = correct response, FA = incorrect response.**

Proportion	Imagine (SD)		Perceive (SD)	
	Accuracy	RT	Accuracy	RT
Target (T)	0.84 (0.12)	1114 (177)	0.82 (0.13)	999 (200)
Non-Target (NT)	0.89 (0.08)	1116 (186)	0.93 (0.05)	1066 (212)
New	0.96 (0.05)	1010 (203)	0.98 (0.04)	950 (194)
<b>P(T Hit – NT FA)</b>	0.73 (0.16)		0.74 (0.15)	
<b>P(T Hit – New FA)</b>	0.80 (0.14)		0.79 (0.14)	

When process estimation formulae were applied to the present data,  $pR = 0.77$  and  $0.70$ ;  $pF = 0.34$  and  $0.38$  for imagine and perceive target designations respectively. A 2x2 repeated measures ANOVA of these estimates by target designation revealed a main effect of estimate ( $F(1, 47)=175.65, p<0.0001$ ), and an interaction ( $F(1, 47)=6.90, p=0.012$ ). Pairwise Bonferroni-corrected  $t$ -tests (adjusted alpha = 0.025) between target designations revealed only that estimates of recollection for imagine items were significantly higher than those for perceive items ( $t(47)=2.83, p=0.007$ ).

A 3x2 repeated measures ANOVA of reaction times (RTs) for response category (correct responses to target, non-target and new items) and target designation (imagine and perceive) revealed significant main effects of target designation ( $F(1, 47)=18.46, p<0.001$ ) and response category ( $F(1.9, 87.0)=31.39, p<0.001$ ) as well as an interaction ( $F(1.7, 81.0)=5.62, p=0.007$ ). Pairwise Bonferroni-corrected  $t$ -tests (adjusted alpha = 0.006) for each item type revealed significantly faster RTs for perceive targets and new items compared to imagine target and new items (smallest  $t(47)=2.87, p=0.006$ ), and no significant difference between conditions for non-targets.

**Table 2 – Mean psychometric scores for Experiment One. Standard Deviations (SD) are in parentheses. Values in bold represent the measures entered into initial analyses. Normative values are included where possible (Mason et al., 1995; Peters et al., 2004; Unsworth et al., 2005; for O-LIFE, PDI and O-SPAN respectively).**

Measure	Mean (SD)	Min	Max	Normative Value (SD)
<b>O-SPAN</b>				
<b>Absolute Score</b>	<b>43.13 (15.80)</b>	15	75	39.16 (17.41)
<b>O-LIFE</b>				
<b>UnEx</b>	<b>6.85 (5.94)</b>	0	24	9.70 (6.70)
<b>CogDis</b>	<b>11.35 (5.66)</b>	0	22	11.60 (5.80)
<b>IntAn</b>	<b>4.21 (3.41)</b>	0	16	6.20 (4.60)
<b>PDI Total</b>	<b>35.42 (28.13)</b>	0	126	58.90 (48.00)
<b>Yes</b>	3.81 (2.86)	0	13	6.70 (4.40)
<b>Dis</b>	9.83 (8.73)	0	40	15.50 (14.10)
<b>Con</b>	9.23 (7.93)	0	29	15.40 (14.10)
<b>Pre</b>	12.35 (9.81)	0	45	20.40 (16.00)
<b>LSHS-R Total</b>	<b>24.02 (5.23)</b>	16	36	
<b>VivTh</b>	5.84 (1.75)	3	10	-
<b>AudHal</b>	5.34 (1.40)	4	9	-
<b>VivDay</b>	5.47 (2.06)	3	11	-
<b>VisHal</b>	7.03 (1.79)	5	11	-

## Psychometric Measures

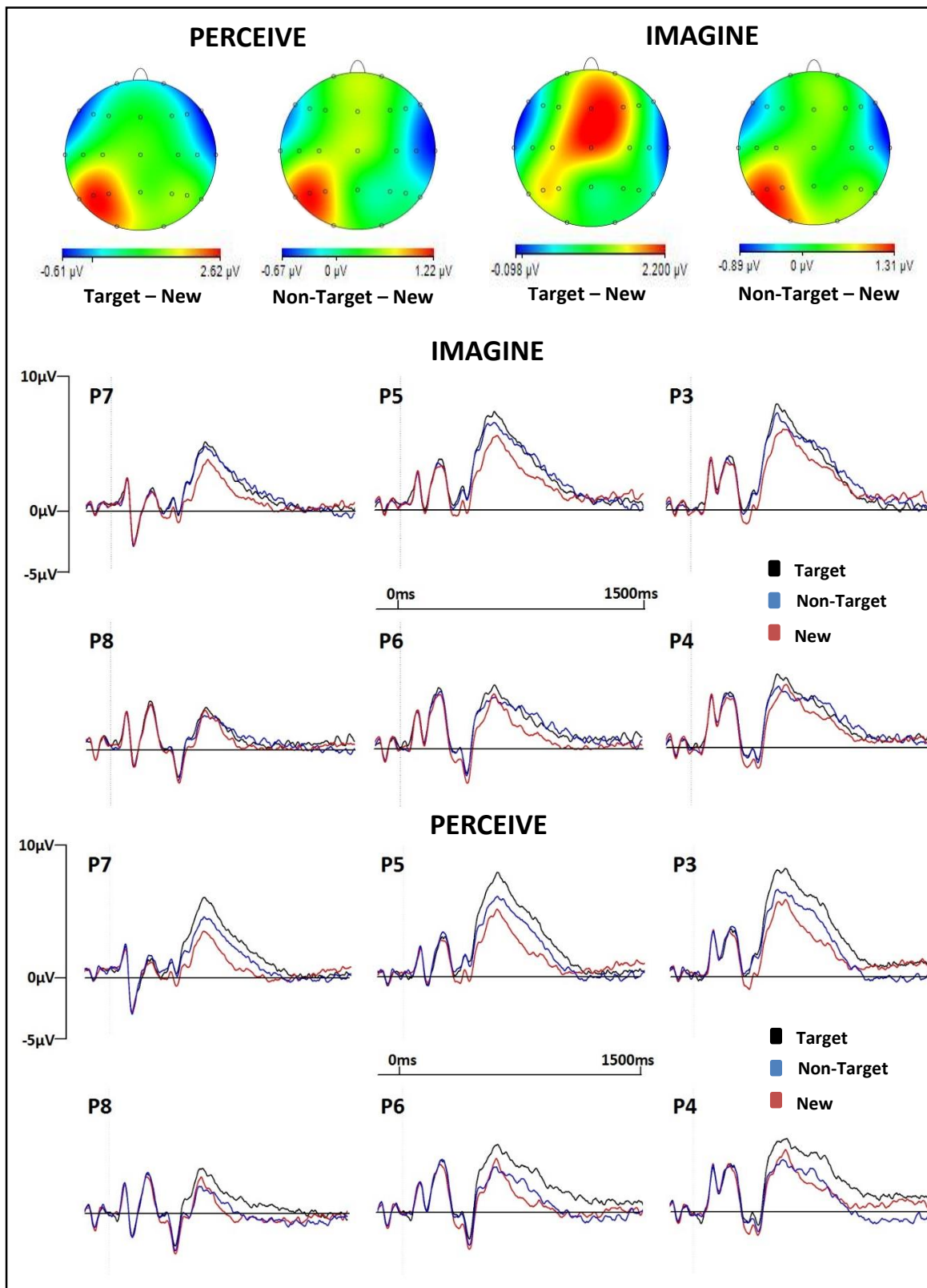
Mean scores for the O-SPAN, O-LIFE, PDI and LSHS-R for this sample as well as normative values (where available) can be seen in **Table 2**. Generally, the measures obtained from this sample are in accordance with the normative values for each measure (Mason et al., 1995; Peters et al., 2004; Unsworth et al., 2005; for O-LIFE, PDI and O-SPAN respectively). Where the measures obtained here diverge from those obtained for the normative sample, the values are still in accordance with other studies using these measures (e.g. Bradbury, Stirling, Cavill, & Parker, 2009; Elward et al., 2012; Evans et al., 2007; Jones & Fernyhough, 2009; PDI, O-SPAN, O-LIFE and LSHS-R respectively).

### PRINCIPAL CORRELATIONS BETWEEN BEHAVIOURAL MEASURES AND SCHIZOTYPY

Reaction times, discrimination values and estimates of familiarity and recollection were correlated with schizotypy measures. When discrimination values were assessed, no reliable relationships were identified. However, analysis of reaction times revealed several positive correlations with the UnEx dimension of the O-LIFE, as well as a correlation with LSHS-R Total and one which approached significance (**Table 3**). Focusing on reaction times to imagine targets only, further analysis of the LSHS-R subscales revealed no significant correlations. Finally, analysis of estimates of familiarity and recollection revealed a significant negative correlation between estimates of familiarity for perceive items and PDI Total ( $r(46)=-0.29, p=0.043$ ).

**Table 3 – Correlations between schizotypy measures and reaction times to correct responses to targets, non-targets and new items split by target designation (imagine/perceive) from Experiment One. \* $p<0.05$ , \*\* $p<0.01$ , †  $p<0.1$ . Correlations have not been corrected for multiple comparisons refer to Sensitivity Issues (page 192) for discussion.**

	O-LIFE			PDI	LSHS-R
Reaction Times	UnEx	CogDis	IntAn	Total	Total
<b>Imagine</b>					
Target	<b>0.44**</b>	0.07	-0.05	0.22	<b>0.33*</b>
Non-Target	0.26	0.13	-0.07	-0.04	0.17
New	<b>0.29*</b>	-0.02	-0.19	0.17	0.18
<b>Perceive</b>					
Target	<b>0.29*</b>	0.00	-0.04	0.17	0.28 <sup>†</sup>
Non-Target	0.26	-0.13	-0.15	0.13	0.26 <sup>†</sup>
New	0.15	-0.13	-0.26	0.14	0.19



**Figure 3 – Topographic maps showing old/new effects for targets and non-targets split by target designation (imagine/perceive) from Experiment One for the 500-800ms epoch. The maps were computed from difference scores obtained by subtracting mean amplitudes for correct responses to new items from those associated with targets and non-targets respectively. ERP waveforms are from electrodes included in the left-parietal old/new effect analysis.**

## PRINCIPAL ERP RESULTS

Mean amplitudes were calculated for epochs of interest and separated according to trial type and target designation. The mean numbers of trials (range in parentheses) contributing to each condition of interest were as follows: imagine target = 40 (25-60), perceive target = 39 (18-56), imagine non-target = 43 (22-58), perceive non-target = 40 (16-57), imagine new = 43 (18-59) and perceive new = 47 (17-60).

### Left-Parietal Old/New Effects

As can be seen in **Figure 3** there is a positive deflection in the EEG recording reaching maximal amplitude from 500-800ms post-stimulus presentation. This effect is largest at left-parietal electrode sites and is more positive going for old items (targets and non-targets) compared to new items. An initial ANOVA with factors of target designation (two levels; imagine and perceive), response category (three levels; correct responses to target, non-target and new items), hemisphere (two levels; left and right) and site (three levels; inferior [P7/8], medial [P5/6] and superior [P3/4]) was conducted. This analysis revealed significant main effects of response category ( $F(2.0, 92.4)=23.49, p<0.0001, E=0.98$ ) as well as significant interactions between response category and hemisphere ( $F(1.6, 73.3)=18.16, p<0.0001, E=0.78$ ) and response category and site ( $F(2.2, 103.9)=4.95, p=0.007, E=0.55$ ). The interaction with site reflects the fact that the ERP old/new effects are largest at superior locations. Planned follow-ups on the interaction between response category and hemisphere revealed that over the left hemisphere ERP amplitudes to target items were more positive going than those to non-target and new items; and non-target items were more positive going than new items (smallest  $t(47)=3.70, p<0.001$ ). Over the right hemisphere planned comparisons revealed that ERP amplitudes to target items were more positive going than non-target and new items (smallest  $t(47)=3.99, p<0.0001$ ), but there were no reliable differences between non-target and new items.

**Table 4 – Mean numbers of target, non-target and new items split by target designation (imagine/perceive) free recalled in Experiment One. Standard deviation (SD) are in parentheses.**

Free Recall	Imagine (SD)	Perceive (SD)
Target	11.52 (4.29)	11.58 (5.00)
Non-Target	10.27 (4.07)	11.50 (4.23)
New	5.69 (3.19)	4.75 (3.49)

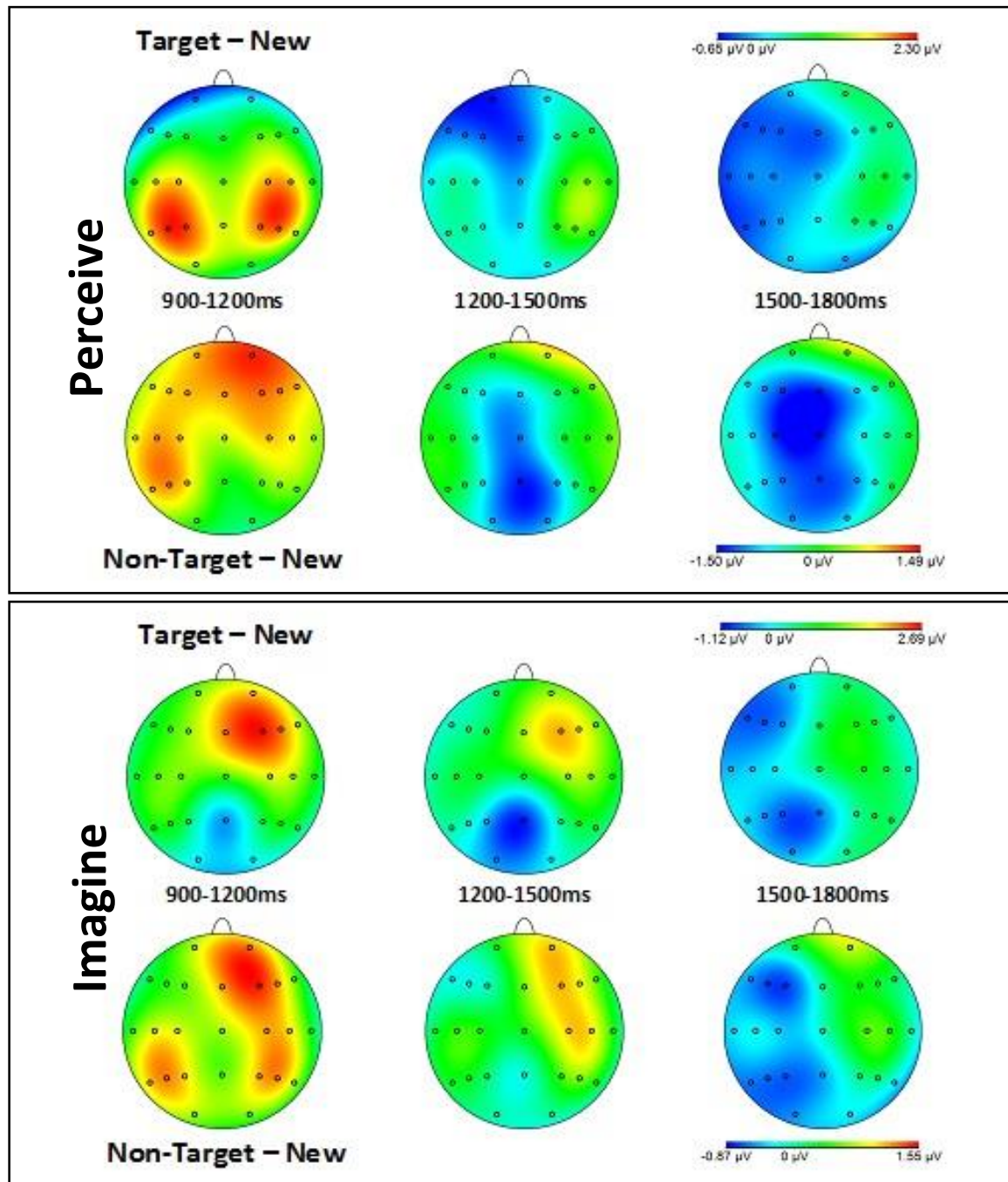
#### PRINCIPAL CORRELATIONS BETWEEN ERP MEASURES AND SCHIZOTYPY

The magnitude differences between the ERPs associated with correct responses to targets and non-targets for both the perceive and imagine target designations were calculated. These measures were averaged across the P7, P5 and P3 electrode sites within the 500-800ms epoch. Magnitude differences were calculated by subtracting the mean ERP amplitude for non-target items from the mean ERP amplitude for target items. The differences measures were then entered into correlation analyses with the schizotypy measures. No reliable relationships were identified between any of the aforementioned variables.

#### SUBSIDIARY BEHAVIOURAL RESULTS

Having established reliable attenuations of non-target compared to target left-parietal old/new effects, free recall performance was analysed to investigate if changes in the left-parietal old/new effects influenced the subsequent memorability of the test items.

The mean numbers of items recalled from each response category, split by target designation are presented in **Table 4**. A 3x2 repeated measures ANOVA with factors of target designation and response category revealed a significant main effect of response category only ( $F(1.9, 90.4)=74.30, p<0.001$ ). Free recall of target and non-target items was significantly greater than new items, but there was no significant difference between the number of target and non-target items recalled (smallest  $t(47)=7.80, p<0.001$ ).

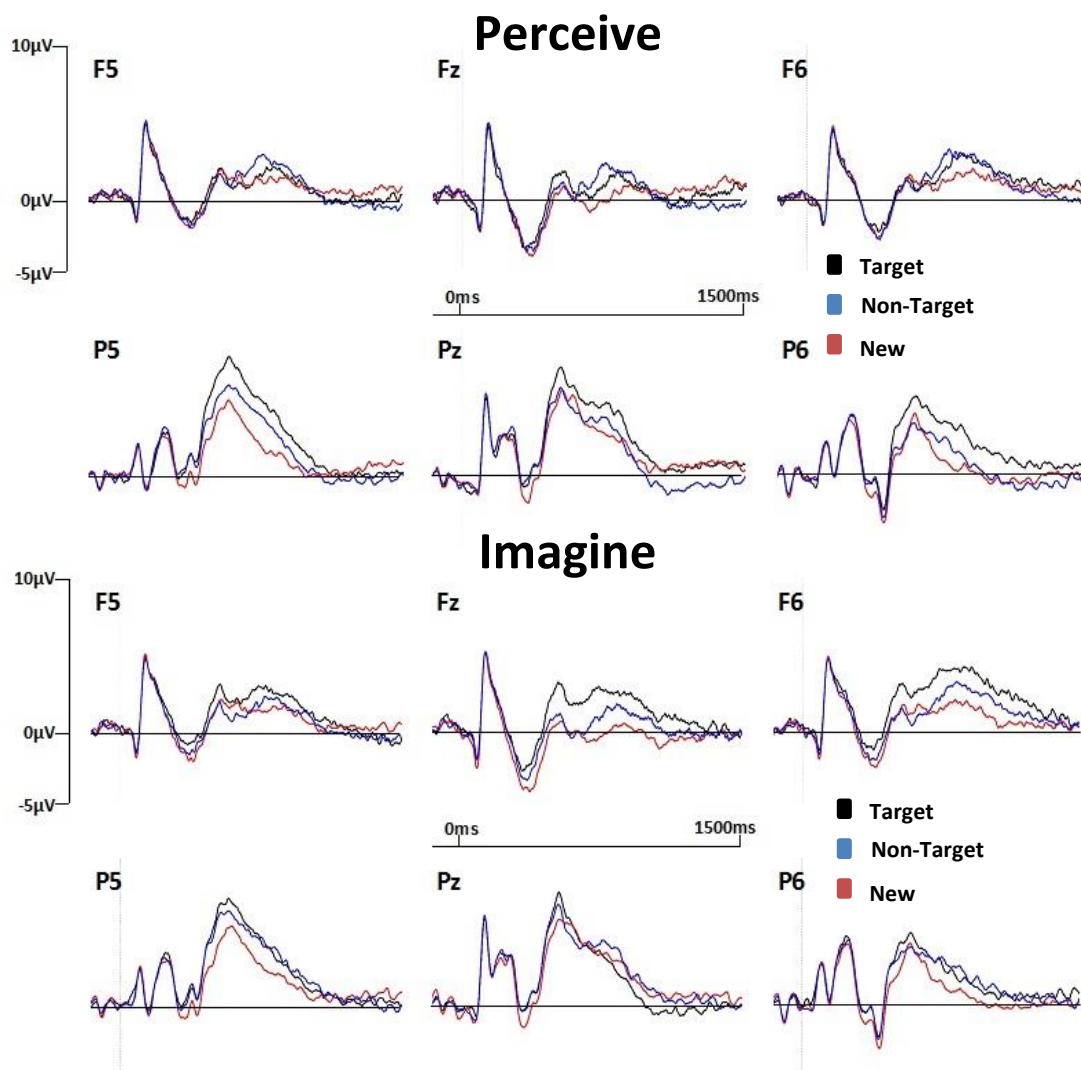


**Figure 4 – Topographic maps showing old/new effects for targets and non-targets split by target designation (imagine/perceive) for Experiment One for three epochs between 900 and 1800ms. The maps were computed from difference scores obtained by subtracting mean amplitudes for correct responses to new items from those associated with targets and non-targets respectively.**

## SUBSIDIARY ERP RESULTS

### Late Posterior Negativity

As can be seen in the waveforms and scalp maps in **Figure 4 and Figure 5**, a late posterior negativity emerges from approximately 900ms post-stimulus presentation and appears more negative going for imagine items. Initial ANOVAs with the factors of target designation (two levels; imagine and perceive) and response category (three levels; correct responses to target, non-target and new items) and site (three levels; P3, Pz and P4) were conducted across three epochs (900-1200ms, 1200-1500ms, 1500-1800ms). In the first two epochs there were interactions between target designation and response



**Figure 5 – Grand average ERP waveforms elicited by targets, non-targets and new items attracting correct judgments from left and right hemisphere and midline sites at frontal (F5, Fz, F6) and posterior (P5, Pz, P6) electrode sites split by target designation (imagine/perceive) for Experiment One**



category as well as response category and site (see for Table 5 for statistical outcomes of main analyses and follow-up analyses). In addition, in the 1200-1500ms epoch there was a significant interaction between target designation and site. For the final epoch (1500-1800ms) there was a significant interaction between target designation and site only.

In the 900-1200ms and 1200-1500ms epochs, following up the interaction between target designation and response category revealed no significant differences in the imagine target designation. By contrast in the 900-1200ms epoch, perceive target items were significantly more positive going than non-target and new items, but there was no significant difference between these latter items. In the second epoch, perceive non-target items were more negative going than target and new items. There was no significant difference between target and new items.

**Table 5 – Statistical outcomes from main and follow-up analyses of late posterior negativity for Experiment One. For follow up analyses, smallest t values are reported. TD = target designation, RC = response category, ST = site, I = imagine, P = perceive, T = target, NT = non-target and N = new.**

Epoch	TD x RC	RC x ST	TD x ST
<b>900-1200ms</b>	$F_{(1.8, 85.2)}=8.89$ $p<0.0001, E=0.91$  <i>IT&amp;NT&lt;PT&amp;NT</i> <i>IT=NT=N</i> <i>PT&gt;NT=N</i> $t_{(47)}=2.47, p=0.017$	$F_{(3.4, 158.1)}=8.26$ $p<0.0001, E=0.84$  <i>P3&amp;P4: N&lt;T</i> <i>T&amp;NT: P3&gt;Pz=P4</i> <i>N: P3=Pz&gt;P4</i> $t_{(47)}=2.41, p=0.02$	n.s.
<b>1200-1500ms</b>	$F_{(2.0, 92.3)}=4.36$ $p=0.016, E=0.98$  <i>INT&lt;PNT</i> <i>IT=NT=N</i> <i>PNT&lt;T=N</i> $t_{(47)}=2.10, p=0.041$	$F_{(3.2, 151.1)}=6.20$ $p<0.0001, E=0.80$  <i>P4: T&gt;NT</i> <i>T, NT&amp;N: Pz&lt;P4</i> $t_{(47)}=2.53, p=0.015$	$F_{(1.9, 87.5)}=4.95$ $p=0.011, E=0.93$  <i>I=P</i> <i>I: Pz&lt;P3</i> $t_{(47)}=2.59, p=0.013$
<b>1500-1800ms</b>	n.s.	n.s.	$F_{(1.9, 89.5)}=5.02$ $p=0.01, E=0.95$  <i>I=P</i> <i>P3=Pz=P4</i>

### Right-Frontal Old/New Effects

As can be seen in the scalp maps in **Figure 4**, in addition to the LPN, there is a positive right frontal modulation present. An initial ANOVA with the factors of target designation (two levels; imagine and perceive), response category (three levels; correct responses to target, non-target and new), hemisphere (two levels; left and right) and site (three levels; inferior [F7/8], medial [F5/6] and superior [F3/4]) was conducted separately for three epochs: 900-1200ms, 1200-1500ms and 1500-1800ms. In the 900-1200ms and 1200-1500ms epochs, there were significant three-way interactions between target designation, response category and hemisphere (see **Table 6** for statistical outcomes of main analyses and follow-up analyses). In the 1500-1800ms epoch, there was a significant interaction between response category and hemisphere, reflecting the fact that positive-going ERP old/new effects for targets and non-targets are similar in magnitude. In addition, there were significant interactions between response category and site in the 900-1200ms and 1500-1800ms epochs. (for statistical outcomes of main analyses and follow-up analyses). In addition, in the 1200-1500ms epoch there was a significant interaction between target designation and site. For the final epoch (1500-1800ms) there was a significant interaction between target designation and site only.

In the 900-1200ms and 1200-1500ms epochs, following up the interaction between target designation and response category revealed no significant differences in the imagine target designation. By contrast in the 900-1200ms epoch, perceive target items were significantly more positive going than non-target and new items, but there was no significant difference between these latter items. In the second epoch, perceive non-target items were more negative going than target and new items. There was no significant difference between target and new items.

Following up the three-way interaction for imagine items within the 1200-1500ms epoch revealed a significant interaction between response category and hemisphere ( $F(1.8, 83.4)=16.13, p<0.0001, E=0.89$ ). Over the left hemisphere, there were no significant differences between response categories. Only ERPs elicited by targets were significantly more positive going than those elicited by correct rejections over right hemisphere locations ( $t(47)=3.47, p=0.001$ ). An ANOVA for perceive items similarly revealed a significant interaction between response category and hemisphere ( $F(1.8, 86.2)=5.90, p=0.005, E=0.92$ ). While the follow up analyses did not reveal reliable effects

involving response category for either hemisphere, the likely reason for the reliable interaction is that right hemisphere amplitudes were more positive going than left hemisphere amplitudes.

**Table 6 – Statistical outcomes from main and follow-up analyses of right frontal old/new effects. For follow up analyses, smallest *t* values are reported for Experiment One. TD = target designation, RC = response category, ST = site, HM = hemisphere, I = imagine, P=perceive, T = target, NT = non-target, N = new, L = left and R = right.**

Epoch	TD x RC	RC x ST	RC x HM	TD x RC x HM
<b>900-1200ms</b>	$F_{(1.9, 90.9)}=3.39$ $p=0.04, E=0.97$  <i>IT&gt;PT</i> <i>I: T&gt;NT&gt;N</i> <i>P: NT&gt;N</i> $t_{(47)}=2.25, p=0.029$	$F_{(2.8, 131.3)}=8.03$ $p<0.0001, E=0.70$  <i>F7/8, F5/6, F3/4:</i> <i>T=NT&gt;N</i> <i>NT&amp;N:</i> <i>F7/8&gt;F5/6, 3/4</i> $t_{(47)}=2.04, p=0.046$	$F_{(1.6, 77.4)}=7.52$ $p=0.002, E=0.82$  <i>T&amp;NT: R&gt;L</i> <i>R: T=NT&gt;N</i> <i>L: NT&gt;N</i> $t_{(47)}=2.06, p=0.045$	$F_{(1.9, 90.0)}=4.04$ $p=0.022, E=0.96$
<b>1200-1500ms</b>	n.s.	n.s.	$F_{(1.6, 76.8)}=15.17$ $p<0.0001, E=0.82$  <i>T&amp;NT: R&gt;L</i> <i>R: T&gt;NT=N</i> <i>L: T=NT=N</i> $t_{(47)}=2.16, p=0.036$	$F_{(1.9, 87.1)}=3.57$ $p=0.036, E=0.93$
<b>1500-1800ms</b>	n.s.	$F_{(3.1, 144.0)}=3.25$ $p=0.023, E=0.77$  <i>F3/4: T&gt;NT</i> <i>T, NT&amp;N:</i> <i>F7/8&gt;F5/6, 3/4</i> $t_{(47)}=2.06, p=0.045$	$F_{(1.7, 80.0)}=12.58$ $p<0.0001, E=0.85$  <i>T&amp;NT: R&gt;L</i> <i>R: T=NT=N</i> <i>L: NT&lt;N</i> $t_{(47)}=2.69, p=0.01$	n.s.

#### SUBSIDIARY CORRELATIONS BETWEEN ERP MEASURES WITH SCHIZOTYPY

##### Late Posterior Negativity

The ERP analyses of this effect revealed no significant effects of response category in the 1500-1800ms epoch. Thus, only the 900-1200ms and 1200-1500ms epochs were analysed in terms of correlations with schizotypy measures. Furthermore, as no significant effects of target designation were reported for the imagine target designation, target and non-target old/new ERP differences were calculated for the

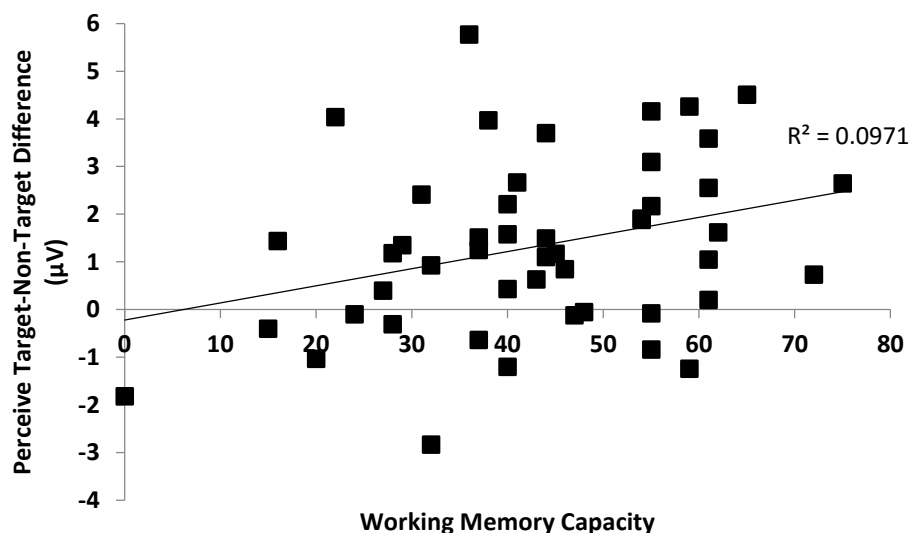
perceive target designation only. Magnitudes were calculated for Pz as ERP analyses revealed effects to be greatest at this site. No correlations were identified for either epoch of interest.

#### Right Frontal Old/New Effects

Target and non-target old/new ERP differences were calculated for the imagine target designation in the 900-1200ms and 1200-1500ms epochs only, considering no significant differences between response categories were identified over right hemisphere locations for the 1500-1800ms epoch or between response categories in the perceive target designation. Magnitudes were calculated from F8 because this is where the effect is largest. No significant correlations were identified for either epoch of interest.

#### CORRELATIONS WITH WORKING MEMORY CAPACITY

Following Elward et al. (2012) the magnitude difference between target and non-target old/new effects was calculated by subtracting mean amplitudes for old/new effects for non-targets from those for targets for each target designation. These measures were averaged across P7, P5 and P3 electrode sites within the 500-800ms epoch. The differences measures were then entered into regression analyses with O-SPAN score as a predictor. Working memory capacity predicted the magnitude difference between target and non-target amplitudes for the perceive target designation only ( $\beta=0.31$ ,



**Figure 6 – The relationship between O-SPAN score and the difference in magnitude between target and non-target old/new effects averaged across left parietal electrode sites (P7, P5, P3) in the perceive target designation for Experiment One.**

$t(46)=2.22, p=0.031$ ), explaining 9.71% of the variance ( $R^2=0.097$ ,  $F(1, 46)=4.95, p=0.031$ ). A plot of this difference against O-SPAN Absolute score can be seen in **Figure 6**.

## DISCUSSION

### PRINCIPAL ANALYSES

#### Left-Parietal Old/New Effects

The principal purpose of this experiment was to investigate whether retrieval control, as indexed by magnitude differences between target and non-target left-parietal old/new effects, is modulated by schizotypy scores. In pursuit of this, it was first imperative to determine whether, at the group level, left-parietal old/new effects for targets were reliably larger than those for non-targets items. This was the case. Furthermore, there were no significant differences between the old/new effects across target designations.

The principal ERP findings in this experiment are in contrast, at first pass, with those obtained by Rosburg et al. (2011b). They reported prioritisation of the recovery of target over non-target information in the perceive target designation only. The authors interpreted their data in terms of participants relying on retrieval of target information only in the less difficult condition. They assumed that successful discrimination of target and non-target items in the more difficult condition was reliant upon the retrieval of information regarding both stimulus types. Interpretations of difficulty were based on behavioural analyses which indicated that participants were worse at discriminating between target and non-target items in the imagine target designation compared to the perceive (Rosburg et al., 2011a). Given this set of assumptions the data reported here are consistent with those of Rosburg et al. (2011b), because in this experiment the accuracy of task judgments differed minimally with target designation.

Herron and Rugg (2003) and Rosburg et al. (2011b) have argued that the likelihood of recovering contextual information (either target, Herron & Rugg, 2003; or non-target, Rosburg et al., 2011b) has driven the extent to which retrieval control processes have been employed. Attenuation of non-target left-parietal old/new effects is typically observed when behavioural discrimination is higher for one target designation compared to another (e.g. Herron & Rugg, 2003; Rosburg et al., 2011b). The present pattern of data however suggests attenuated non-target left-parietal old/new effects can be observed

when behaviour is matched; suggesting task difficulty is not necessarily a driving factor for observing these effects, consistent with previous findings (e.g. Dzulkipli & Wilding, 2005; Wilding, Fraser, & Herron, 2005). In order to confirm this however, it would be necessary to increase task difficulty and replicate this pattern of results.

Interestingly, these non-target left-parietal old/new effect attenuations were not reflected in the correlation with subsequent recall of non-target items. Elward et al. (2012) found that participants with high WMC recalled more target compared to non-target items than those low in WMC. In the present study the likelihoods of recalling targets and non-targets do not differ when analysed separately for those high and low in WMC. Thus, these data do not support the claim that differential processing of target and non-target items during exclusion tasks influences the subsequent likelihood of recall (Elward et al., 2012). Elward et al. (2012) found target left-parietal old/new effects to be markedly different between groups, though non-target magnitudes were comparable and thus proposed the ERP results, in conjunction with the pattern of recall, could indicate differences in target processing between groups. In the present ERP data however, no significant differences between target designations were identified for any response category either. Though perceive targets were found to be marginally more positive going compared to imagine targets ( $p=0.064$ ), the power of this sample ( $n=48$ ) suggests even if there were differences in target processing, these are likely to be trivial to explaining the effects observed (Ioannidis, 2005). The reason for the failure to replicate the effect here remains unclear.

#### Correlations with Schizotypy

No significant correlations between schizotypy measures and the degree to which retrieval control was exerted, as indexed by magnitude differences between target and non-target left-parietal old/new effects, were identified.

There are two key reasons the correlations with ERP measures may not have been obtained in the present experiment. First, given university students were recruited for this study it may be the case that this sample is not representative of how retrieval control processes are utilised. University students have a tendency to be high-functioning individuals, well versed in learning and retrieving information. Therefore, even if these participants had difficulty in utilising particular retrieval control processes,

it may be the case that they have compensated for this difficulty by using other strategies. Second, it could be the case that when task demands are low, retrieval cues are easily accessible and likelihood of retrieval is high under all conditions. Therefore, it may be that by applying cognitive control, this strategy is actually more effortful than simply accessing information relating to all retrieval cues, given the relative ease with which this information can be accessed. This possibility was explored in the following experiment reported in this thesis, where task difficulty was increased.

Despite the lack of correlation with the ERP measures, several behaviours measures were correlated with schizotypy measures. Importantly, the correlations between reaction time and schizotypy measures were in the expected direction (e.g. slower reaction times given higher positive schizotypy scores). These findings compliment some of the aforementioned interpretations whereby participants may have applied strategies to compensate for some of the experienced difficulties. By contrast, the negative correlation between estimates of familiarity in the perceive condition and measures of positive schizotypy were not expected. As several studies have reported larger effect sizes for recollection compared to familiarity deficits in patients with schizophrenia (reviewed by Libby et al., 2013), negative correlations with estimates of recollection would have been anticipated. Though as previously suggested, if down-stream post-retrieval monitoring processes are contributing to memory performance more in those higher in schizotypy, it would make sense for earlier, more automatic processes to influence response selection to a lesser extent in these individuals.

## SUBSIDIARY ANALYSES

### Late Posterior Negativity

The analyses in which this effect was correlated with schizotypy measures were conducted to gain a better understanding of how post-retrieval control processes may vary with schizotypy. Target items were more positive going than non-target and new items in the perceive target designation in the 900-1200ms epoch. In the 1200-1500ms epoch, non-target items when perceive items were designated as targets were significantly more negative going than both target and new items. No significant correlations however were identified for the ERP magnitude difference between

perceive target and non-target items in either epoch of interest and measures of schizotypy.

#### Right-Frontal Old/New Effect

These analyses, comparably to the late posterior negativity analyses, were conducted to gain a better understanding of how variation in post-retrieval monitoring processes might be linked with schizotypy. In the 900-1200ms epoch, items in the imagine target designation were found to exhibit a target>non-target>new pattern of ERP amplitudes over right hemisphere locations. Similarly, in the second epoch (1200-1500ms) imagine targets were found to be significantly more positive going than new items over right frontal electrode sites. No correlations however were identified for the ERP difference between target and non-target items and measures of schizotypy.

#### CORRELATIONS WITH WORKING MEMORY CAPACITY

These analyses were conducted to examine the generality of the association between the difference between the magnitudes of target and non-target old/new effects and working memory capacity, as identified by Elward and Wilding (2010). Here, working memory capacity as indexed by O-SPAN score was identified as being a small but significant predictor of this magnitude difference in the perceive target designation. These results therefore provide a direct replication of the effects reported by Elward and Wilding (2010).

Some researchers have suggested that this magnitude differences is determined by the relative ease with which target or non-target information can be recollected (e.g. Herron & Rugg, 2003; Rosburg et al., 2011b). By contrast, Elward and Wilding (2010) found that working memory capacity but not response accuracy predicted the magnitude of the target – non-target ERP difference. Given that working memory capacity has been interpreted as an index of resources available to exert cognitive control, this finding suggests that strategic retrieval is implemented when sufficient cognitive resources are available to do so. The present behavioural and ERP data provide further support for this latter interpretation.



## CONCLUSIONS

Taken together, the present analyses suggest that those higher in schizotypy, whilst performing to the same accuracy level as those lower in schizotypy, may respond slower and this might facilitate memory performance. One possibility is that given a more difficult recognition task, those high in schizotypy will be less able to utilise compensation strategies and thus deficits in processes will become more evident. The second experiment in this thesis was designed to address this possibility.

## CHAPTER SIX: EXPERIMENT TWO

The previous study was designed to investigate the relationship between the use of retrieval control processes and schizotypy measures. Participants could prioritise recovery of target information over non-target information, however there was no correlation between schizotypy scores and ERP indices of retrieval control (Chapter Five: Experiment One, page 108). One potential explanation is that the likelihood of retrieving target information was high, enabling participants to easily apply retrieval control strategies.

Elward, Evans and Wilding (2012) using the exclusion paradigm demonstrated only those high in working memory capacity, compared to those low in working memory capacity, demonstrated differences between target and non-target left-parietal old/new effects. Importantly, the level of task performance was lower than reported in Experiment One ( $P(T \text{ Hit} - NT \text{ FA}) = 0.62$  collapsed across encoding conditions compared to 0.73 and 0.74 for the imagine and perceive target designations respectively in Experiment One). Assuming similar patterns would be evident with other individual difference variables, it was hypothesised that by increasing task difficulty this would increase the likelihood of detecting a correlation between differences between target and non-target left-parietal old/new effects and measures of schizotypy.

The present experiment was designed to assess this, by increasing task difficulty and consequently reducing the likelihood of successfully retrieving target information. It was assumed this manipulation would exacerbate any deficits in control people high in schizotypy may experience. In other words, it was hypothesised there would be a negative correlation between positive schizotypy and the magnitude difference between target and non-target old/new effects.

## METHODS

### Participants

Fifty four participants were recruited from Cardiff University using an online participant management system, and paid at a rate of £10/hour. Ethical approval for this study was obtained from the Cardiff University School of Psychology Ethics Committee. Participant inclusion criteria are listed in the Participants section for Experiment One. Six

participants were excluded from analyses for: poor behavioural performance (5) and excessive EEG artefact (1). For behavioural and EEG rejection criteria see the Exclusion Paradigm and EEG Acquisition sections for Chapter Five: Experiment One (pages 87 and 93 respectively). Of the remaining 48 participants, (mean age = 20.45 years; range 18-27 years) 40 were female.

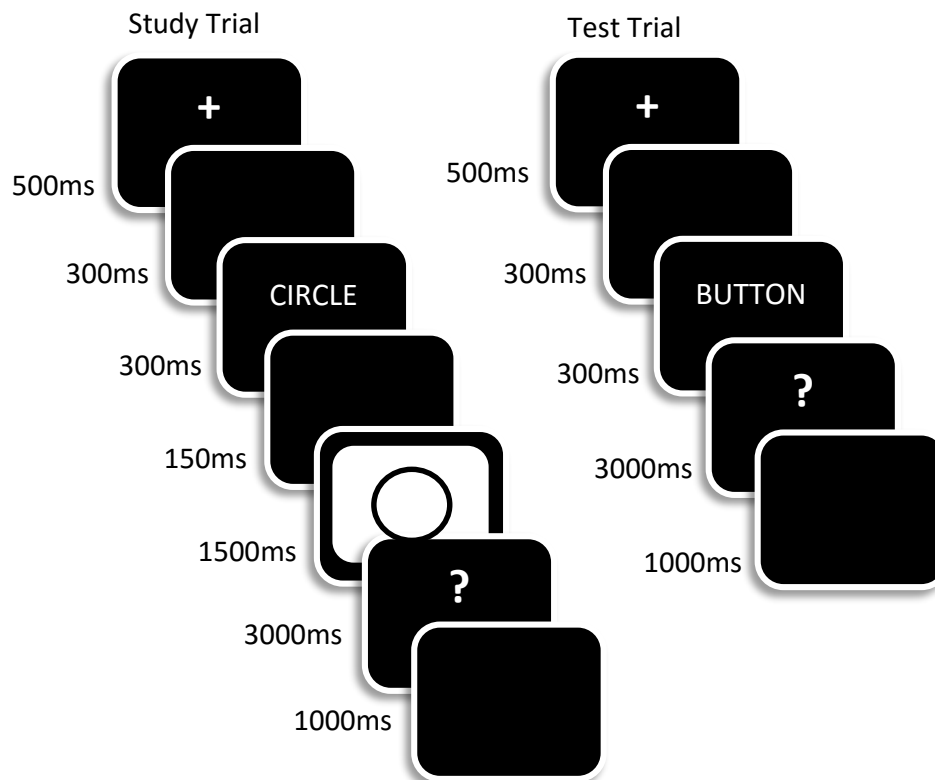
## OVERVIEW OF PROCEDURE

Initially, participants completed the study portion of the exclusion task. Subsequently, participants completed the schizotypy measures; the Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE; Mason et al., 1995), the 21-item Peters et al. Delusion Inventory (PDI; Peters et al., 2004) and the Launay-Slade Hallucination Scale-Revised (LSHS-R; Launay & Slade, 1981; Morrison et al., 2000). Participants then completed the test portion of the exclusion task whilst ERPs were acquired, and then subsequently completed a free recall task, where participants were required to recall as many words as they could from the exclusion task. To finish, participants completed an automated version of the O-SPAN task (Unsworth et al., 2005), widely accepted as a measure of working memory capacity (Turner & Engle, 1989) and an adapted version of the Vividness of Visual Imagery Questionnaire (VVIQ; Cui et al., 2007; Marks, 1973). For further details of measures besides the exclusion task, refer to the relevant sections in the Method section of Chapter Five: Experiment One (page 86). The EEG Acquisition and Analysis procedures were the same as that used for Experiment One (page 93).

### Exclusion Task

Four hundred and eighty six pictures and the corresponding word labels were selected from the International Picture Naming Project database (<http://crl.ucsd.edu/experiments/ipnp/>). All picture-word lists used in this task had a mean percentage naming frequency of 86%. This represented a significant difference in naming frequency between Experiment One (93%) and Two ( $t(844)=7.81, p<0.0001$ ). Critical words were divided into three lists (120 picture-word pairs/list). The study phase comprised two picture-word lists (240 picture-word pairs), one word list for imagined items and the other for perceived items. These were repeated during the test phase along with words from another list (360 picture-word pairs in total). The remaining 126 picture-word pairs were used as foils, which were presented during the study phase only

(63 picture-word pairs per condition; 26 at the beginning and 100 at the end of this phase). For more detailed information about the paradigm refer to the Exclusion Task section for Chapter Five: Experiment One (page 87). However, for a summary of the presentation durations for both the study and test phase refer to **Figure 7**. The principal difference between study phases for Experiment One and Two was that the presentation times for both words and pictures was shorter in Experiment Two.



**Figure 7 – A schematic representation of the study trials (left) and test trials (right) in Experiment Two.**

## RESULTS

### PRINCIPAL BEHAVIOURAL RESULTS

#### Exclusion Task

Response accuracies and reaction times for each category of stimulus, split by target designation are presented in **Table 7**. Both Pr discrimination values were reliably above zero in each target designation (smallest  $t(47)=23.77, p<0.0001$ ). A 2x2 repeated measures ANOVA on these discriminations by target designation revealed only that

Target – New discrimination was superior to Target – Non-Target discrimination ( $F(1, 47)=49.26, p<0.0001$ ).

In order to estimate the contributions of the processes of recollection and familiarity to performance in this task, the process dissociation procedure was used. When these formulae were applied to the present data,  $pR = 0.63$  and  $0.60$ ;  $pF = 0.37$  and  $0.35$  for imagine and perceive target designations respectively. A 2x2 repeated measures ANOVA of these estimates by target designation revealed a main effect of estimate only, where estimates of recollection were significantly higher than estimates of familiarity ( $F(1, 47)=106.65, p<0.0001$ ); though the main effect of target designation approached significance ( $F(1, 47)=3.74, p=0.059$ ).

A 3x2 repeated measures ANOVA of reaction times (RTs) for response category (correct responses to target, non-target and new items) and target designation (imagine and perceive) revealed a significant main effect of response category ( $F(1.9, 89.9)=27.81, p<0.001$ ) and an interaction ( $F(1.8, 84.4)=8.51, p=0.001$ ). Pairwise Bonferroni-corrected  $t$ -tests (adjusted alpha = 0.006) between target designations revealed significantly faster RTs for perceive targets compared to imagine targets ( $t(47)=3.83, p<0.001$ ), but no significant differences between target designations for non-target or new items.

**Table 7 – Probabilities of correct responses (accuracy) and reaction times (RT) targets, non-targets and new items split by target designation (imagine/perceive) in Experiment Two. Standard deviations (SD) are in parentheses. Hit = correct response, FA = incorrect response.**

Proportion	Imagine (SD)		Perceive (SD)	
	Accuracy	RT	Accuracy	RT
Target (T) Hit	0.76 (0.12)	1111	0.73 (0.15)	1044
Non-Target (NT) CR	0.86 (0.07)	1090	0.87 (0.08)	1101
New CR	0.92 (0.08)	1024	0.94 (0.07)	1009
Pr(T Hit – NT FA)	0.63 (0.15)		0.60 (0.17)	
Pr(T Hit – New FA)	0.68 (0.15)		0.67 (0.16)	

#### Psychometric Measures

Mean scores for the O-SPAN, O-LIFE, PDI and LSHS-R for this sample as well as normative values (where available) can be seen in **Table 8**. Generally, the measures obtained from

this sample are in accordance with the normative values for each measure (Mason et al., 1995; Peters et al., 2004; Unsworth et al., 2005; for O-LIFE, PDI and O-SPAN respectively). Where the measures obtained here appear to diverge from those obtained for the normative sample, the values are still in accordance with other studies using these measures (e.g. Bradbury et al., 2009; Elward et al., 2012; Evans et al., 2007; Jones & Fernyhough, 2009; PDI, O-SPAN, O-LIFE and LSHS-R respectively).

**Table 8 – Mean psychometric scores for Experiment Two. Standard Deviations (SD) are in parentheses. Values in bold represent the measures entered into initial analyses. Normative values are included where possible (Mason et al., 1995; Peters et al., 2004; Unsworth et al., 2005; for O-LIFE, PDI and O-SPAN respectively)**

Measure	Mean (SD)	Min	Max	Normative Value (SD)
<b>O-SPAN</b>				
<b>Absolute Score</b>	<b>36.42 (18.47)</b>	5	71	39.16 (17.41)
<b>O-LIFE</b>				
<b>UnEx</b>	<b>5.35 (4.80)</b>	0	17	9.70 (6.70)
<b>CogDis</b>	<b>10.67 (5.00)</b>	1	22	11.60 (5.80)
<b>IntAn</b>	<b>3.88 (3.24)</b>	0	12	6.20 (4.60)
<b>PDI Total</b>	<b>37.33 (27.29)</b>	0	113	58.90 (48.00)
<b>Yes</b>	4.15 (2.75)	0	11	6.70 (4.40)
<b>Dis</b>	10.33 (8.40)	0	36	15.50 (14.10)
<b>Con</b>	10.23 (8.24)	0	28	15.40 (14.10)
<b>Pre</b>	12.65 (8.81)	0	38	20.40 (16.00)
<b>LSHS-R Total</b>	<b>23.17 (5.46)</b>	15	38	
<b>VivTh</b>	5.98 (1.62)	3	9	-
<b>AudHal</b>	5.23 (1.42)	4	8	-
<b>VivDay</b>	5.25 (2.27)	3	12	-
<b>VisHal</b>	6.67 (1.54)	3	11	-

#### PRINCIPAL CORRELATIONS BETWEEN BEHAVIOURAL MEASURES AND SCHIZOTYPY

In order to investigate whether behavioural performance in the exclusion task was associated with schizotypy measures, reaction times, discrimination values and estimates of familiarity and recollection were correlated with these aforementioned measures. No significant relationships were identified for analyses of reaction times and discrimination measures. However, analysis of estimates of familiarity and recollection revealed a significant positive correlation between the estimate of familiarity for imagine items and UnEx ( $r(46)=0.35, p=0.014$ ), though the relationship between the estimate of recollection for imagine items and UnEx also approached significance ( $r(46)=-$

0.27,  $p=0.059$ ). Importantly however, these correlations have not been corrected for multiple comparisons. For a discussion of these issues refer to Sensitivity Issues in Chapter Nine: General Discussion (page 192).

## PRINCIPAL ERP RESULTS

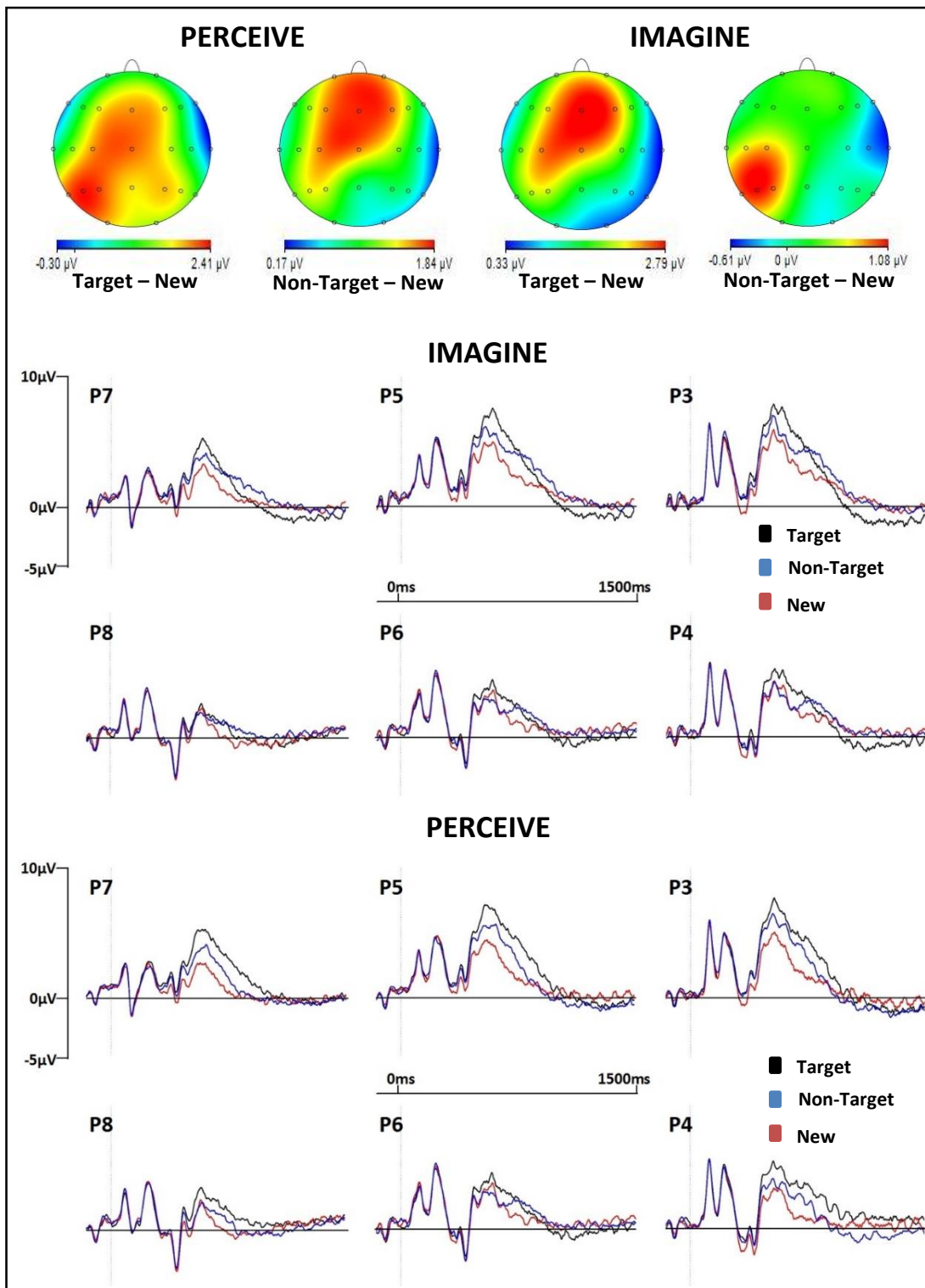
The mean numbers of trials (range in parentheses) contributing to each condition of interest were as follows: imagine target = 43 (20-58), perceive target = 41 (19-57), imagine non-target = 48 (28-57), perceive non-target = 48 (28-58), imagine new = 52 (33-60) and perceive new = 52 (24-60).

### Left-Parietal Old/New Effects

As can be seen in **Figure 7** there is a positive deflection in the EEG recording reaching maximal amplitude between 500-800ms post-stimulus presentation. This effect appears maximal over left-parietal electrode sites and is more positive going for old items (targets and non-targets) compared to new items. In order to confirm left-lateralisation, an initial ANOVA with factors of target designation (two levels; imagine and perceive), response category (three levels; correct responses to target, non-target and new), hemisphere (two levels; left and right) and site (three levels; inferior [P7/8], medial [P5/6] and superior [P3/4]) was conducted. This analysis revealed significant interactions between response category and hemisphere ( $F(1.6, 77.0)=16.77, p<0.0001$ ), response category and site ( $F(2.4, 110.7)=4.26, p=0.012$ ), target designation and site ( $F(1.1, 52.3)=4.09, p=0.044$ ), in addition to a three-way interaction between target designation, response category and site ( $F(2.7, 124.7)=3.57, p=0.02$ ).

Planned pairwise comparisons to investigate the interaction between response category and site revealed that ERP amplitudes were greatest at superior electrode sites; target items were more positive going than non-target and new items, and non-target items were more positive going than new items at all site locations (smallest  $t(47)=3.04, p=0.004$ ).

Following up on the interaction between response category and hemisphere revealed that all ERP amplitudes were greater over left compared to right hemisphere sites



**Figure 8 - Topographic maps showing old/new effects for targets and non-targets split by target designation (imagine/perceive) from Experiment Two for the 500-800ms epoch. The maps were computed from difference scores obtained by subtracting mean amplitudes for correct responses to new items from those associated with targets and non-targets respectively. ERP waveforms are from electrodes included in the left-parietal old/new effect analysis.**



(smallest  $t(47)=4.00, p<0.0001$ ). Over left hemisphere ERP amplitudes to target items were more positive going than those to non-target and new items; and non-target items were more positive going than new items (smallest  $t(47)=5.01, p<0.0001$ ). Over right hemisphere planned comparisons revealed that ERP amplitudes to target items were more positive going than non-target and new items (smallest  $t(47)=4.63, p<0.0001$ ), but there were no reliable differences between non-target and new items.

Exploring the three-way interaction between target designation, response category and site within the imagine target designation revealed significant main effects of response category ( $F(1.9, 89.5)=11.41, p<0.001$ ) as well as an interaction ( $F(2.2, 102.2)=5.54, p=0.004$ ). Planned pairwise comparisons to investigate the two-way interaction revealed that at medial and superior sites targets were significantly more positive going than non-target and new items, with no significant difference between non-target and new items (smallest  $t(47)=3.09, p=0.003$ ). However, at inferior sites contrasts revealed a target=non-target>new item pattern (smallest  $t(47)=2.63, p=0.011$ ). Within the perceive target designation only a significant main effect of response category was found ( $F(1.9, 89.7)=28.66, p<0.001$ ), indicating that mean amplitudes across all sites demonstrated a target>non-target>new items (smallest  $t(47)=3.79, p<0.001$ ). In summary, ERP old/new effects were larger for targets than for non-targets, particularly at left-hemisphere superior sites, and differed minimally with target designation.

#### PRINCIPAL CORRELATIONS BETWEEN ERP MEASURES AND SCHIZOTYPY

In order to examine whether ability to exert cognitive control during retrieval was associated with schizotypy measures the magnitude differences for target – non-target items for both perceive and imagine conditions were calculated. These measures were averaged across P7, P5 and P3 electrode sites within the 500-800ms epoch. Magnitude differences were calculated by subtracting the mean ERP amplitude for non-target items from the mean ERP amplitude for target items. The differences measures were then entered into correlation analyses with the schizotypy measures. However, no reliable relationships were identified between any of the aforementioned variables.

## SUBSIDIARY BEHAVIOURAL RESULTS

Having established reliable attenuations of non-target compared to target left-parietal old/new effects, the free recall performance was analysed to investigate if changes in the left-parietal old/new effects influenced the subsequent memorability of the test items.

The mean numbers of items recalled from each response category, split by target designation are presented in **Table 9**. A 3x2 repeated measures ANOVA of these target designations by response category revealed a significant main effect of response category only where free recall of target and non-target items was significantly greater than new items, but there was no significant difference between the number of target and non-target items recalled (smallest  $t(47)=7.72, p<0.0001$ ).

**Table 9 – Mean number of target, non-target and new items split by target designation (imagine/perceive) free recalled from Experiment Two. Standard deviation (SD) are in parentheses.**

Free recall	Imagine (SD)	Perceive (SD)
Target	9.88 (3.77)	11.04 (4.73)
Non-Target	9.48 (4.61)	9.96 (3.46)
New	4.40 (3.01)	4.54 (2.90)

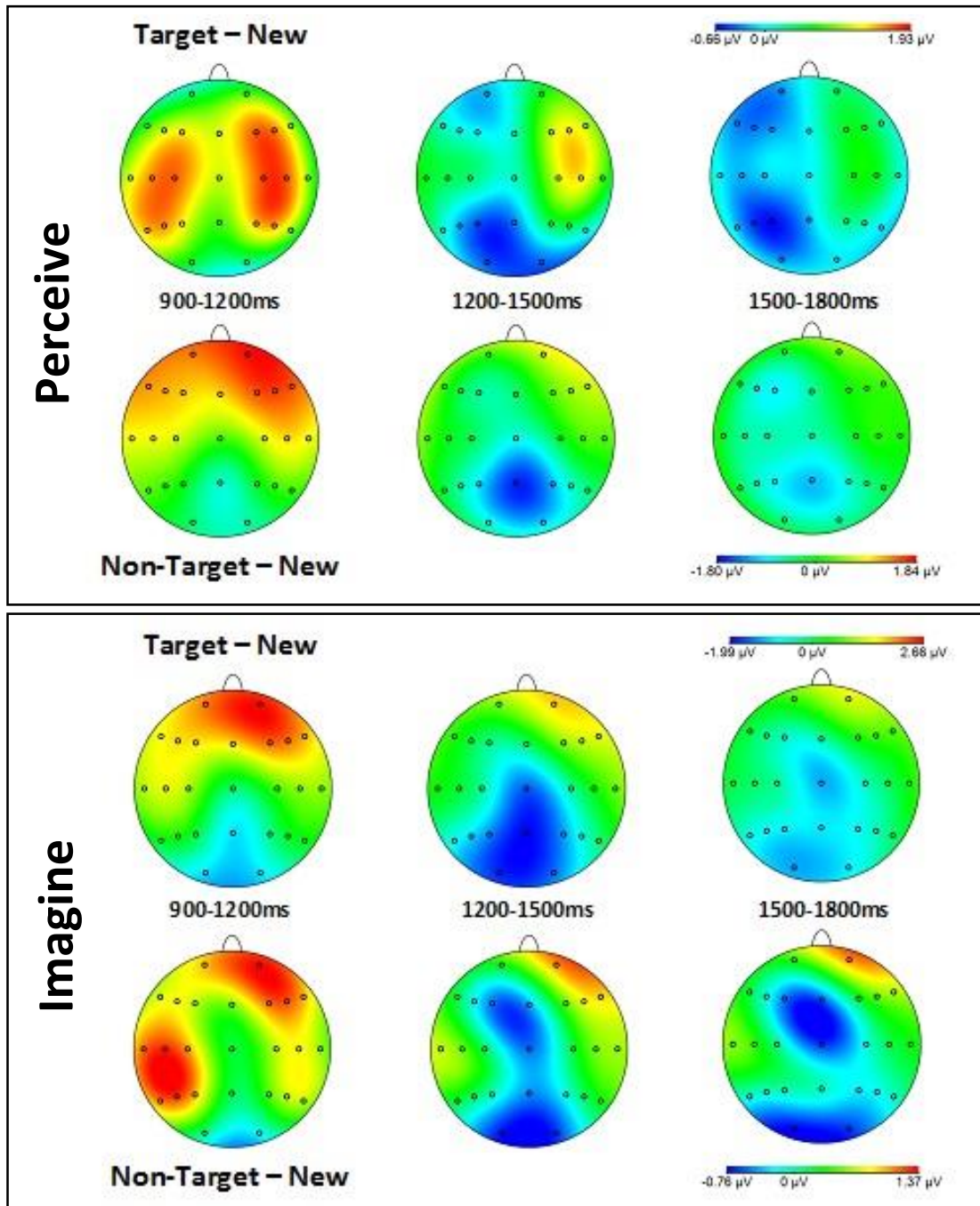
## SUBSIDIARY ERP RESULTS

### Late Posterior Negativity

As can be seen in the waveforms in *Figure 10*, there appears to be a late posterior negativity emerging from approximately 900ms post-stimulus presentation. This posterior negativity is further confirmed in the scalp maps (**Figure 9**) Initial ANOVAs with the factors of target designation (two levels; imagine and perceive), response category (three levels; correct responses to target, non-target and new items) and site (three levels; P3, Pz and P4) were conducted across three epochs (900-1200ms, 1200-1500ms, 1500-1800ms). Results from the first and second epoch indicated interactions between target designation and response category, target designation and site and response category and site (see Table 9 for statistical outcomes of main analyses and follow-up analyses). A main effect of response category was also found in the second epoch ( $F(1.8,$

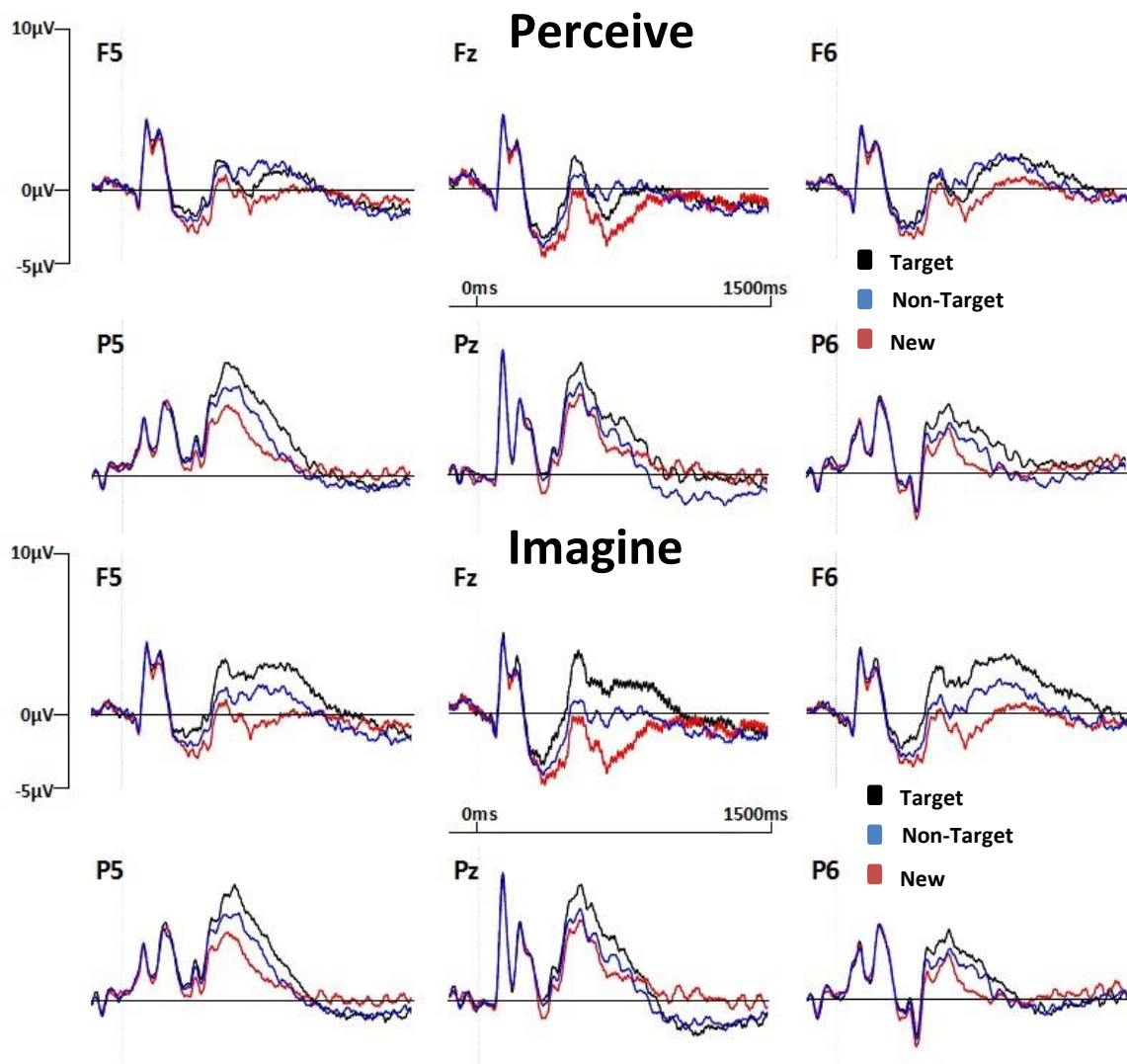
85.2)=3.64,p=0.035,E=0.91). For the final epoch (1500-1800ms) there was a significant interaction between target designation and site only.

Following up the target designation by response category interaction in the first and second epoch revealed that targets were more negative going than non-targets in the



**Figure 9– Topographic maps showing old/new effects for targets and non-targets split by target designation (imagine/perceive) for Experiment Two for three epochs between 900 and 1800ms. The maps were computed from difference scores obtained by subtracting mean amplitudes for correct responses to new items from those associated with targets and non-targets respectively.**

imagine target designation. In the second epoch only, imagine targets were also found to be more negative going than new items. Conversely, perceive target items were more positive going compared to non-target and new items in the perceive target designation in the first epoch. In the second epoch, non-target items in the perceive target designation were found to be more negative going than target and new items.



**Figure 10– Grand average ERP waveforms elicited by targets, non-targets and new items attracting correct judgments from left and right hemisphere and midline sites at frontal (F5, Fz, F6) and posterior (P5, Pz, P6) electrode sites split by target designation (imagine/perceive) for Experiment Two.**

**Table 10 – Statistical outcomes from main and follow-up analyses of late posterior negativity for Experiment Two. For follow up analyses, smallest *t* values are reported. TD = target designation, RC = response category, ST = site, I = imagine, P=perceive, T = target, NT = non-target and N = new.**

Epoch	TD x RC	RC x ST	TD x ST
<b>900-1200ms</b>	$F_{(1.9, 88.5)}=12.13$ $p<0.0001, E=0.94$  <i>INT&amp;N&gt;P</i> <i>IT&lt;NT</i> <i>PT&gt;NT=N</i> $t_{(47)}=2.29, p=0.027$	$F_{(3.1, 147.7)}=8.20$ $p<0.0001, E=0.79$  <i>T:P3&gt;Pz</i> <i>NT:P3&gt;Pz=P4</i> <i>N:P3=Pz&gt;P4</i> $t_{(47)}=3.08, p=0.003$	$F_{(1.9, 90.8)}=6.02$ $P=0.004, E=0.97$  <i>P3:P&lt;I</i> <i>I:P3&gt;Pz=P4</i> <i>P:P3=Pz=P4</i> $t_{(47)}=3.17, p=0.003$
<b>1200-1500ms</b>	$F_{(1.9, 90.0)}=8.17$ $p=0.001, E=0.93$  <i>IT&lt;PT</i> <i>IT&lt;NT=N</i> <i>PNT&lt;T=N</i> $t_{(47)}=2.26, p=0.021$	$F_{(3.1, 146.7)}=5.99$ $P=0.001, E=0.78$  <i>T:P3&amp;Pz&lt;P4</i> <i>NT:Pz&lt;P3&amp;P4</i> <i>P3:T&lt;N</i> <i>Pz:T&amp;NT&lt;N</i> $t_{(47)}=2.40, p=0.02$	$F_{(1.9, 87.6)}=8.41$ $p=0.001, E=0.93$  <i>P3:P&lt;I</i> <i>P4:I&lt;P</i> <i>I:P3=Pz=P4</i> <i>P:P3=Pz&lt;P4</i> $t_{(47)}=2.04, p=0.047$
<b>1500-1800ms</b>	n.s.	n.s.	$F_{(2.0, 92.6)}=6.69$ $p=0.002, E=0.99$  <i>Pz:P&lt;I</i> <i>P4:I&lt;P</i> <i>I:P3&lt;Pz</i> <i>P:P3=Pz&gt;P4</i> $t_{(47)}=2.84, p=0.007$

**Right-Frontal Old/New Effect**

As can be seen in the scalp maps in Figure 9, in addition to the LPN, there also appears to be a positive right frontal modulation present. To confirm the presence of this effect an initial ANOVA with the factors of target designation (two levels; imagine and perceive), response category (three levels; correct responses to target, non-target and new items), hemisphere (two levels; left and right) and site (three levels; inferior [F7/8], medial [F5/6] and superior [F3/4]) was conducted across three epochs: 900-1200ms, 1200-1500ms and 1500-1800ms. Results from the 900-1200ms epoch revealed main effects of target designation ( $F(1, 47)=23.49, p<0.0001$ ) and response category ( $F(1.9, 89.9)=20.45, p<0.0001, E=0.96$ ), and significant interactions between target designation and site and response category and site. Both the second and third epoch revealed a

main effect of target designation ( $F(1, 47)=10.64, p=0.002$ ;  $F(1, 47)=4.75, p=0.035$  for 1200-1500ms and 1500-1800ms respectively), and a significant interaction between response category and hemisphere ( $F(1.7, 78.6)=14.83, p<0.001, E=0.84$ ;  $F(1.7, 80.0)=12.58, p<0.001, E=0.85$  for 1200-1500ms and 1500-1800ms respectively; **Table 11**).

In the first epoch, target and non-target items were found to be more positive going than new items. In the second epoch, both target and non-target items were found to be more positive going over right hemisphere locations. In the final epoch, the only significant differences were that target and non-target items were more positive going over right hemisphere compared to left hemisphere locations.

**Table 11 – Statistical outcomes from main and follow-up analyses of right frontal old/new effects for Experiment Two. For follow up analyses, smallest t values are reported. TD = target designation, RC = response category, ST = site, HM = hemisphere, I = imagine, P = perceive, T = target, NT = non-target, N = new, L = left and R = right.**

Epoch	RC x HM	RC x ST	TD x ST
900-1200ms	n.s.	$F_{(2.6, 123.6)}=3.55$ $p=0.021, E=0.66$	$F_{(1.2, 58.3)}=4.50$ $p=0.031, E=0.62$
		$T\&NT>N$ $F7/8<F5/6<F3/4$ $t_{(47)}=2.03, p=0.048$	$P<I$ $I\&P: F7/8>F5/6>F3/4$ $t_{(47)}=2.81, p=0.007$
1200-1500ms	$F_{(1.7, 78.6)}=14.83$ $p<0.001, E=0.84$	n.s.	n.s.
	$T\&NT:R>L$ $L:T=NT=N$ $R:T\&NT>N$ $t_{(47)}=2.62, p=0.012$		
1500-1800ms	$F_{(1.7, 81.8)}=8.30$ $P=0.001, E=0.87$	n.s.	n.s.
	$T\&NT:R>L$ $L\&R:T=NT=N$ $t_{(47)}=4.75, p<0.001$		

## SUBSIDIARY CORRELATIONS WITH SCHIZOTYPY

### Late Posterior Negativity

As the ERP analyses of this effect revealed no significant effects of target designation in the last epoch (1500-1800ms), only the first two epochs (900-1200ms and 1200-1500ms) were analysed in terms of correlations with schizotypy measures. Target and non-target differences were calculated for both conditions from Pz considering this it typically were late posterior negativity is reported (e.g. Herron, 2007). No correlations however were identified in either epoch.

### Right Frontal Old/New Effects

The ERP analysis of this effect revealed significant interactions with response category in all the epochs of interest, though in follow-up analyses no significant differences between response categories were identified over right hemisphere locations for the 1500-1800ms epoch. Thus, only the 900-1200ms and 1200-1500ms epochs of interest were examined in relation to correlations with schizotypy measures. Furthermore, as no significant differences between target and non-target items were identified, target and non-target old/new effects were calculated. These measures were averaged across F8, F6 and F4 electrode sites. In both epochs, several positive correlations were identified (**Table 12**). Generally, positive and/or disorganised dimensions of schizotypy were positively correlated with magnitude differences involving imagined items.

**Table 12 – Correlations between target and non-target old/new differences split by target designation (imagine/perceive) averaged from F4, F6 and F8 and measures of schizotypy from Experiment Two. \* $p < 0.05$ , \*\* $p < 0.01$ , †  $p < 0.1$  T = target, NT = non-target and N = new.**

	PDI	LSHS-R	O-LIFE		
900-1200ms	Total	Total	UnEx	CogDis	IntAn
ImagineT-N	0.14	<b>0.31 *</b>	0.25	<b>0.38 **</b>	0.19
ImagineNT-N	0.09	0.19	0.17	0.22	0.21
PerceiveT-N	-0.13	0.05	-0.05	-0.05	0.01
PerceiveNT-N	0.03	0.22	0.26 †	-0.04	0.03
1200-1500ms					
ImagineT-N	0.10	<b>0.39 **</b>	0.28 †	<b>0.31 *</b>	0.06
ImagineNT-N	0.12	0.15	0.15	0.20	0.20
PerceiveT-N	-0.17	0.02	-0.08	-0.02	0.04
PerceiveNT-N	0.11	<b>0.30 *</b>	<b>0.35 *</b>	0.05	0.06

## CORRELATIONS WITH WORKING MEMORY CAPACITY

### Left-Parietal Old/New Effect

In an attempt to replicate the association of WMC and magnitude of left-parietal old/new effects found by Elward et al. (2012) the magnitude difference between target and non-target old/new effects was calculated by subtracting mean amplitudes of old/new effects for non-targets from those for targets for each target designation. These measures were averaged across P7, P5 and P3 electrode sites within the 500-800ms epoch. The differences measures were then entered into regression analyses with O-SPAN score as a predictor. The analyses revealed no significant effects.

## DISCUSSION

### PRINCIPAL ANALYSES

#### Left-Parietal Old/New Effects

The principal purpose of this investigation was to investigate whether retrieval control, as indexed by magnitude differences between target and non-target left-parietal old/new effects are modulated by schizotypy scores in a task that was more difficult than the one employed in the first experiment reported in this thesis. Despite again demonstrating reliable left-parietal old/new effects for both target and non-target items in both conditions, there were still no significant correlations between the schizotypy measures collected and the degree to which retrieval control was exerted, as measured by the difference between target and non-target left-parietal old/new effects. There were, however, relationships between the schizotypy measures and behavioural performances indices.

It has been suggested that attenuation of non-target left-parietal old/new effects is dependent on whether an assessment of target information alone is sufficiently diagnostic for target – non-target discrimination (e.g. Herron & Rugg, 2003; Rosburg et al., 2011b). When task difficulty is high, successful discrimination of target and non-target has been assumed to be dependent on retrieving information regarding both stimulus types. The present pattern of data however suggests that task difficulty does not necessarily determine the extent to which non-target left-parietal old/new effects



are attenuated, consistent with other studies where accuracy has been matched across target designations (e.g. Dzulkipli & Wilding, 2005; Wilding et al., 2005). Rosburg et al. (2011b) proposed bottom-up mechanisms may actually drive the retrieval of non-target information, in that the presentation of non-target cues reactivates this information. The authors suggested that these mechanisms may be complemented by top down mechanisms such as strategic retrieval under certain circumstances (e.g. low task difficulty). Whilst the present pattern of data does not preclude bottom-up mechanisms, the attenuated non-target old/new effects in light of the behavioural accuracy strongly suggest top-down mechanisms contributed. Further manipulation of task parameters that is beyond the focus of this thesis would be required to establish the boundary conditions for observing attenuated left-parietal old/new effects, and differentiate top-down and bottom-up mechanisms.

Once again, the attenuation of the non-target old/new effects was not reflected in the correlation with the subsequent free recall of non-target items. Thus, the present results provide further evidence against the generality of the claims made by Elward et al. (2012) and suggest that retrieval control mechanisms do not always influence the subsequent memorability of items.

#### Correlations with Schizotypy

There are at least two reasons why correlations between schizotypy and ERP markers of control over retrieval were not obtained in the present experiment. First, given university students were recruited for this study it may be the case that this sample is not representative of how retrieval control processes are utilised. This possibility was assessed in the subsequent experiment reported in this thesis, where participants were recruited from the community. Second, and related to the aforementioned point, it may be that schizotypy is more strongly related to control processes other than those examined in the principal ERP analysis. This point will be addressed more conclusively later in this section during discussion of the subsidiary analyses.

The correlation between estimates of familiarity for imagine items and schizotypy measures was in the expected direction (e.g. higher estimates of familiarity given higher positive schizotypy scores). These findings compliment previous findings suggesting patients with schizophrenia may compensate for difficulties in recollection by relying to

a greater extent on familiarity (e.g. Moritz, Woodward, Cuttler, Whitman, & Watson, 2004), though given, several studies have reported larger effect sizes for recollection compared to familiarity deficits, negative correlations with estimates of recollection would have been anticipated. This pattern of findings, in conjunction with the subsidiary ERP analyses, suggests those higher in schizotypy may have recruited more retrieval processes in service of task performance. Thus, together, these correlations with behavioural measures are all consistent with post-retrieval monitoring accounts.

## SUBSIDIARY ANALYSES

### Late Posterior Negativity

A late-posterior negativity emerged for imagine items irrespective of target designation, though this emerged later in the perceive target designation. No correlations however were identified between ERP measures of late posterior negativity and schizotypy.

### Right-Frontal Old/New Effect

In both the 900-1200ms and 1200-1500ms epochs, targets and non-targets were significantly more positive going than new items. This occurred over right frontal electrode sites in the 1200-1500ms epoch. There was no significant difference between target and non-target items. Positive correlations were identified between measures of positive and disorganised schizotypy and imagine target – new ERP differences in both epochs of interest. Perceive non-target – new differences were also found to positively correlate with measures of positive schizotypy in the second epoch. Taken together, this suggests that those higher in schizotypy engaged in more post-retrieval monitoring of imagine items irrespective of target designation, though these processes were engaged later in the perceive target designation.

## CORRELATIONS WITH WORKING MEMORY CAPACITY

These analyses were conducted to examine the generality of the association between the left-parietal target – non-target magnitude difference and working memory capacity identified by Elward and Wilding (2010). Here, working memory capacity as indexed by O-SPAN score was not identified as being a significant predictor of this magnitude difference. These findings lead one to question how robust the previous finding was, and

hence encourage caution in the generality of the claims that were made (Elward & Wilding, 2010). Nonetheless, given the current difficulty of this task in relation to those of Experiment One, the present findings may still suggest that strategic retrieval is only implemented when sufficient cognitive resources are available to do so.

## CONCLUSIONS

The outcomes in this experiment suggest that those higher in schizotypy rely on familiarity to a greater extent than those lower in schizotypy and recruit additional post-retrieval monitoring processes, which may facilitate memory performance. As indicated above, it is also possible that using a sample of university students for tasks of this kind limits the extent to which the findings can be generalised. Hence, in the third experiment in this thesis participants from a community based sample to were recruited to investigate this possibility.

## CHAPTER SEVEN: EXPERIMENT THREE

In the previous experiment the ERP data indicated that participants prioritised recovery of target information over non-target information, however there was no correlation between schizotypy scores and ERP indices of retrieval control (Chapter Six: Experiment Two, page 127). This was the case despite the fact that response accuracy was lower than in Experiment One, as intended. It is possible that the sample used in both experiments reported in this thesis is not representative of how retrieval control strategies are commonly utilised, as university students are highly versed in learning and retrieving information, and in participating in verbal memory experiments. The present experiment was designed to assess this possibility by recruiting participants from the general community. Moreover, the group recruited here were matched on key measures to permit them to serve as controls for data acquired from patients with schizophrenia, described in Chapter Eight: Experiment Four (page 151). In relation to Experiments One and Two, the hypotheses for this experiment are the same as those outlined previously (see the introduction of Chapter Five: Experiment One, page 86).

### METHODS

#### Participants

30 participants were recruited from the School of Psychology Community Panel (Cardiff University), and paid £40 for their participation. Ethical approval was obtained from the Cardiff University School of Psychology Ethics Committee. All participants spoke English as a first language, had normal or corrected-to-normal vision and hearing, were right-handed, had no prior diagnosis of a psychiatric disorder or neurological condition and were not currently taking psychotropic medication. Participants provided written informed consent and were aware they could withdraw from the study at any point without reason or penalty. Data from eight participants were excluded due to excessive EEG artefact (six female). For EEG rejection criteria see the EEG Acquisition sections for Chapter Five: Experiment One (page 93). Of the remaining 22 participants (mean age = 38.55, range = 19-59) 10 were female.

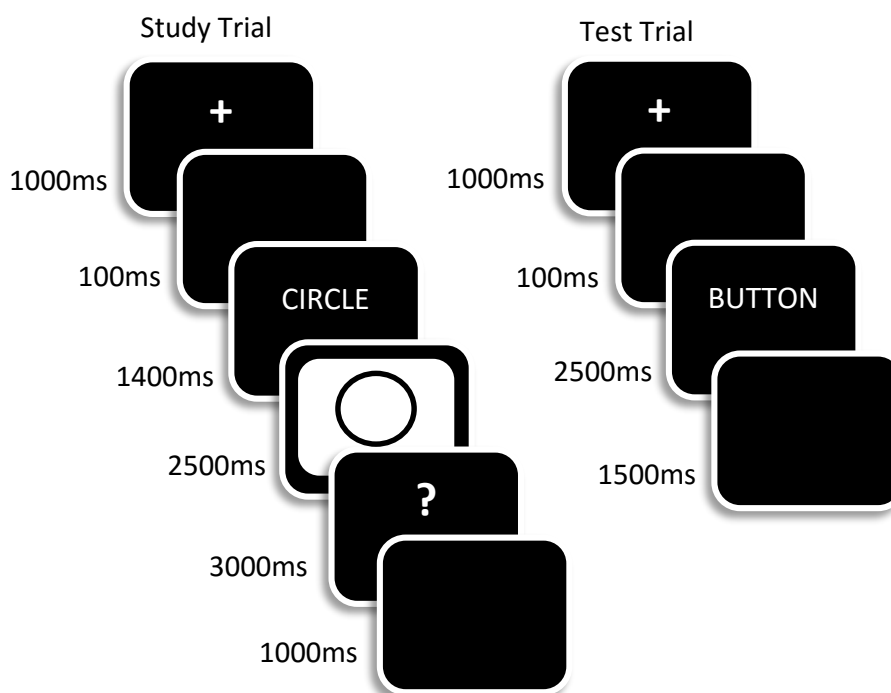
## OVERVIEW OF PROCEDURE

All participants completed tasks in a fixed order. Some of these tasks were not the same as those used in Experiments One and Two. The differences, and reasons for their inclusion here, are detailed in the relevant sections below. Initially, participants completed the exclusion task whilst ERPs were acquired. Following this, they completed the schizotypy measures; the Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE; Mason et al., 1995), the 21-item Peters et al. Delusion Inventory (PDI; Peters et al., 2004) and the Launay-Slade Hallucination Scale-Revised (LSHS-R; Launay & Slade, 1981; Morrison et al., 2000). Participants then completed a computerised working memory capacity task and the Vividness of Visual Imagery Questionnaire (VVIQ; Cui et al., 2007; Marks, 1973). Following this, participants completed a computerised classic Stroop task (Stroop, 1935), the Beck Anxiety Inventory (BAI; Beck, Epstein, Brown, & Steer, 1988) and the Beck Depression Inventory (BDI-II; Beck, Steer, & Brown, 1996). To finish, participants completed a learning task (Haselgrove & Evans, 2010) and the National Adult Reading Test (NART; Nelson, 1982). Details of the schizotypy and VVIQ measures can be found in the relevant Method sections of Chapter Five: Experiment One (page 86).

### Exclusion Task

Two hundred and forty pictures and the corresponding word labels were selected from the International Picture Naming Project database (<http://crl.ucsd.edu/experiments/ipnp/>). Twelve lists of 20 words and corresponding pictures were created. All picture-word lists used in this task had a mean percentage naming frequency of 98% (Bates et al., 2003). This percentage was significantly greater than the percentage naming frequencies of the lists used for Experiment One (93%;  $t(598)=8.30, p<0.0001$ ) and Experiment Two (86%;  $t(724)=11.85, p<0.0001$ ). A study phase consisted of two word-picture lists (40 words and pictures/phase; 20 in the imagine condition and 20 in the perceive condition). These words were represented in a subsequent test phase along with words from another list (60 words/phase; 20 imagined, 20 perceived and 20 new items). In total, participants completed four study-test blocks. Test instructions were reversed after two study-test blocks. Test instructions were blocked in this fashion, rather than interleaved, to reduce task demands arising from repeated instructions switches. To reduce the likelihood of participants prioritising a

particular study context based on previous test instructions (e.g. Anderson & Bjork, 1994), participants were informed before each study phase that the test instructions were randomly determined by the computer and therefore may change between blocks. Participants completed practice study phases to familiarise themselves with the response requirements. Similarly, participants completed two practice test phases; one for each set of testing instructions. For more detailed information about the paradigm refer to the Exclusion Task section of Chapter Five: Experiment One (page 87). However, for a summary of the presentation durations for both the study and test phase refer to **Figure 11**.



**Figure 11 – A schematic representation of the study trials (left) and test trials (right) from Experiment Three.**

#### Computerised Working Memory Capacity Task

This task was taken from <http://mindbrain.ucdavis.edu/labs/luck-lab/change-localization> and was adapted from Experiment 5 in Gold et al. (2006). Stimuli were presented on a screen positioned 50cm in front of the participant. Participants saw a sample array consisting of four coloured squares for 100ms followed by a 100ms retention interval. Square locations were randomly selected from 25 possible locations, defined by dividing the viewing area into a 5x5 grid. The test array was identical to the sample array except one square always changed colour. Participants were required to

indicate which square had changed using mouse click. Responses were self-paced. After responding the next trial commenced after a 1000ms inter-trial interval, during which a fixation point was presented. Participants initially completed ten practice trials. After completing this phase, participants received feedback on their performance (percentage correct) and were given the opportunity to repeat the practice if needed. Following this practice phase, participants proceeded to complete two blocks of 30 trials. This test produces one score: percentage of correct responses. This working memory task was selected over the one used in Experiments One and Two in this thesis as this task has been used in individuals with schizophrenia and has been found to be a reliable and valid measure (Gold et al., 2006).

#### Computerised Classic Stroop Task (Stroop, 1935)

A colour word or neutral string (XXXX) was presented in the centre of the screen, and participants were required to indicate the colour of the ink. There were four response options (green, blue, red or yellow) and participants responded via key press. Responses were self-paced. Response options were presented across the bottom of the screen throughout all trials to minimise participant demands. After responding the next trial commenced after a 1000ms inter-trial interval during which a fixation point was presented. Participants completed four blocks of 36 trials, resulting in a total of 144 trials. In each block, there were 12 congruent, 12 incongruent and 12 neutral trials. Congruent trials consisted of the colour word being presented in the same colour ink (e.g. Red). Incongruent trials consisted of the colour word being presented in a different colour ink (e.g. Red). Neutral trials consisted of a neutral string being presented in coloured ink (e.g. XXXX). Proportions of correct and incorrect responses and reaction times (RT) were calculated for each of the trial types (congruent, incongruent and neutral). Facilitation and interference scores were also calculated by subtracting RTs for neutral items from RTs for congruent items and incongruent items respectively (Carter, Mintun, & Cohen, 1995). This task is considered a classic measure of cognitive control (e.g. Homack & Riccio, 2004), and thus was included to investigate the relationship between the ERP and behavioural assessments of cognitive control.

Beck Anxiety Inventory (BAI; Beck et al., 1988) and Beck Depression Inventory (BDI-II; Beck et al., 1996)

The BAI consists of 21 items assessing various symptoms of anxiety. Participants were required to indicate on a four-point scale how much each item applied to them (not at all=0, mildly=1, moderately=2, severely=3). This measure produces one score which is calculated by summing responses to all items. The BDI-II consists of 21 items assessing various behavioural, physical and cognitive symptoms of depression. Participants similarly indicate on a four point scale how much each item applies to them, with 0 responses indicating the statement does not apply and 3 responses indicating the item applies severely to the participant. This measure produces one score which is calculated by summing responses to all items. The maximum score for both questionnaires is 63. These measures were included due to the high prevalence of depressive and anxiety symptoms in patients with schizophrenia (e.g. Buckley, Miller, Lehrer, & Castle, 2009), and are considered only after identifying significant effects in either behavioural or ERP analyses.

#### Learning Task (Haselgrove & Evans, 2010)

This task was taken from Haselgrove and Evans (2010). Participants were asked to play the role of a health and safety inspector who is visiting a hospital after several cases of food poisoning were reported. Participants are presented with the details of foods eaten by a number of fictitious patients and whether the food caused poisoning or not. In the final test trials, participants are presented with foods in the absence of feedback and asked to indicate how dangerous the food is. Further details of this paradigm can be found in the article by Haselgrove and Evans (2010). This measure was collected for a separate investigation and will not be considered further in the experiments reported in this thesis.

#### National Adult Reading Test (Nelson, 1982).

This test is considered to be an assessment of premorbid intelligence (Nelson, 1982). Participants were presented with 50 printed words in order of increasing difficulty and asked to read each one out loud. All words are irregular in that they violate common rules of pronunciation. An error is recorded if participants do not pronounce the word correctly. In this and the following experiment, only the estimated full scale IQ (FSIQ)



score was used. This estimate is calculated using the formula:  $FSIQ = 128 - (0.83 \times \text{NART Error Score})$ . The NART Error score is calculated by subtracting the number of correct responses from the total number of words (50). This measure was included to help differentiate general functioning deficits from those specific to memory in patients with schizophrenia.

#### EEG ACQUISITION AND ANALYSIS PROCEDURE

The electroencephalogram (EEG) was recorded from 32 active electrodes attached to an elasticated cap and from two further electrodes placed on left and right mastoid processes. Recording sites were based on the International 10-20 system (Jasper, 1958) and included midline (Fz, Cz, Pz, Oz), fronto-polar (Fp1/Fp2), frontal (F7/8, F5/6, F3/4, F1/2), central (T7/8, C5/6, C3/4, C1/2), parietal (P7/8, P5/6, P3/4, P1/2) and occipital sites (O1/2). Vertical and horizontal eye movements were recorded from additional monopolar electrodes placed above and below the right eye (vertical electro-oculogram [VEOG]) and on the outer canthi (horizontal electro-oculogram [HEOG]). EEG was recorded at 2048Hz referenced to linked electrodes situated midway between POz and PO3/PO4 respectively. Data were re-referenced offline to the average signal at the mastoids. EEG and EOG were down-sampled (256Hz) and filtered offline (0.03-40Hz). Trials containing large EOG, muscular or alpha artefacts were rejected, as were trials containing A/D saturation or baseline drift exceeding  $\pm 75\mu\text{V}$ . EOG blink artefacts were corrected using the Gratton, Coles, and Donchin (1983) algorithm. Total epoch length for all segments was 1800ms, with a 200ms pre-stimulus baseline, relative to which all mean amplitude measures were taken. Analysis procedures as described in the relevant section for Chapter Five: Experiment One (page 94) were employed.

One additional focus for this experiment was the relationship between an ERP index of retrieval control and a classic behavioural assessment of cognitive control, namely performance in the Stroop Task (Stroop, 1935). In pursuit of this, the magnitude difference between target and non-target left-parietal old/new effects was calculated (as described in the Analysis Procedures section of Chapter Five: Experiment One, page 94) and correlated with facilitation and interference RT scores from the Stroop task.

## RESULTS

### PRINCIPAL BEHAVIOURAL RESULTS

#### Exclusion Task

Response accuracies and reaction times for each category of stimulus, split by target designation are presented in **Table 13**. Pr values were reliably above zero in each case (smallest  $t(21)=21.97, p<0.001$ ). A 2x2 repeated measures ANOVA of these discriminations by target designation revealed a main effect of discrimination only where Target – New discrimination was superior to Target – Non-Target discrimination ( $F(1, 21)=6.01, p=0.023$ ). There were no significant differences in Pr measures between imagine and perceive target designations.

When process estimation formulae were applied, the estimates for recollection (pR) were 0.83 and 0.80, and familiarity (pF) were 0.29 and 0.71 for the imagine and perceive target designations respectively. A 2x2 repeated measures ANOVA of these estimates by target designation revealed a main effect of estimate ( $F(1, 21)=48.32, p<0.001$ ), a main effect of target designation ( $F(1, 21)=15.34, p=0.001$ ) and an interaction ( $F(1, 21)=23.62, p<0.001$ ). Pairwise Bonferroni-corrected  $t$ -tests (adjusted alpha = 0.0125) between target designations revealed estimates of familiarity for perceive items were significantly higher than those for imagine items ( $t(21)=4.51, p<0.001$ ), but there was no significant difference between the target designations in terms of estimates of recollection. Estimates of recollection were significantly greater than estimates of familiarity for imagine items ( $t(21)=6.77, p<0.001$ ), though there was no significant difference between estimates for perceive items.

A 3x2 repeated measures ANOVA of reaction times (RTs) for response category (correct responses to target, non-target and new items) and target designation (imagine and perceive) revealed significant main effects of target designation ( $F(1, 21)=20.79, p<0.001$ ) and response category ( $F(1.4, 28.5)=19.12, p<0.001$ ) as well as an interaction ( $F(1.3, 28.3)=9.73, p=0.002$ ). Pairwise Bonferroni-corrected  $t$ -tests (adjusted alpha = 0.006) between target designations revealed significantly faster RTs for perceive new compared to imagine new items ( $t(21)=8.58, p<0.001$ ), but no significant difference between conditions for target or non-target items.

**Table 13 – Probabilities of correct responses (accuracy) and reaction times (RT) for targets, non-targets and new items split by target designation (imagine/perceive) for Experiment Three. Standard deviations (SD) are in parentheses**

	Imagine (SD)		Perceive (SD)	
	Accuracy	RT	Accuracy	RT
Target (T)	0.88 (0.11)	1381 (241)	0.96 (0.09)	1300 (228)
Non-Target (NT)	0.88 (0.09)	1176 (203)	0.92 (0.06)	1158 (235)
New	0.96 (0.04)	1319 (239)	0.99 (0.02)	1087 (204)
<b>Pr(T Hit – NT FA)</b>	0.80 (0.17)		0.84 (0.11)	
<b>Pr(T Hit – New FA)</b>	0.83 (0.14)		0.86 (0.10)	

### Stroop Task

Response accuracies and reaction times for the Stroop task can be seen in **Table 14**. Only interference scores were reliable ( $>0$ ;  $t(21)=7.81, p<0.001$ ).

**Table 14 – Probabilities of correct responses (accuracy) and reaction times (RT) for congruent, incongruent and neutral stimuli in the Stroop Task for Experiment Three. Standard deviations (SD) are in parentheses**

	Accuracy	RT
Congruent (C)	0.99 (0.02)	1037 (314)
Incongruent (I)	0.96 (0.04)	1242 (301)
Neutral (N)	0.99 (0.02)	1043 (245)
<b>Facilitation (C RT-N RT)</b>	-6 (130)	
<b>Interference (I RT-N RT)</b>	199 (119)	

### Psychometric Measures

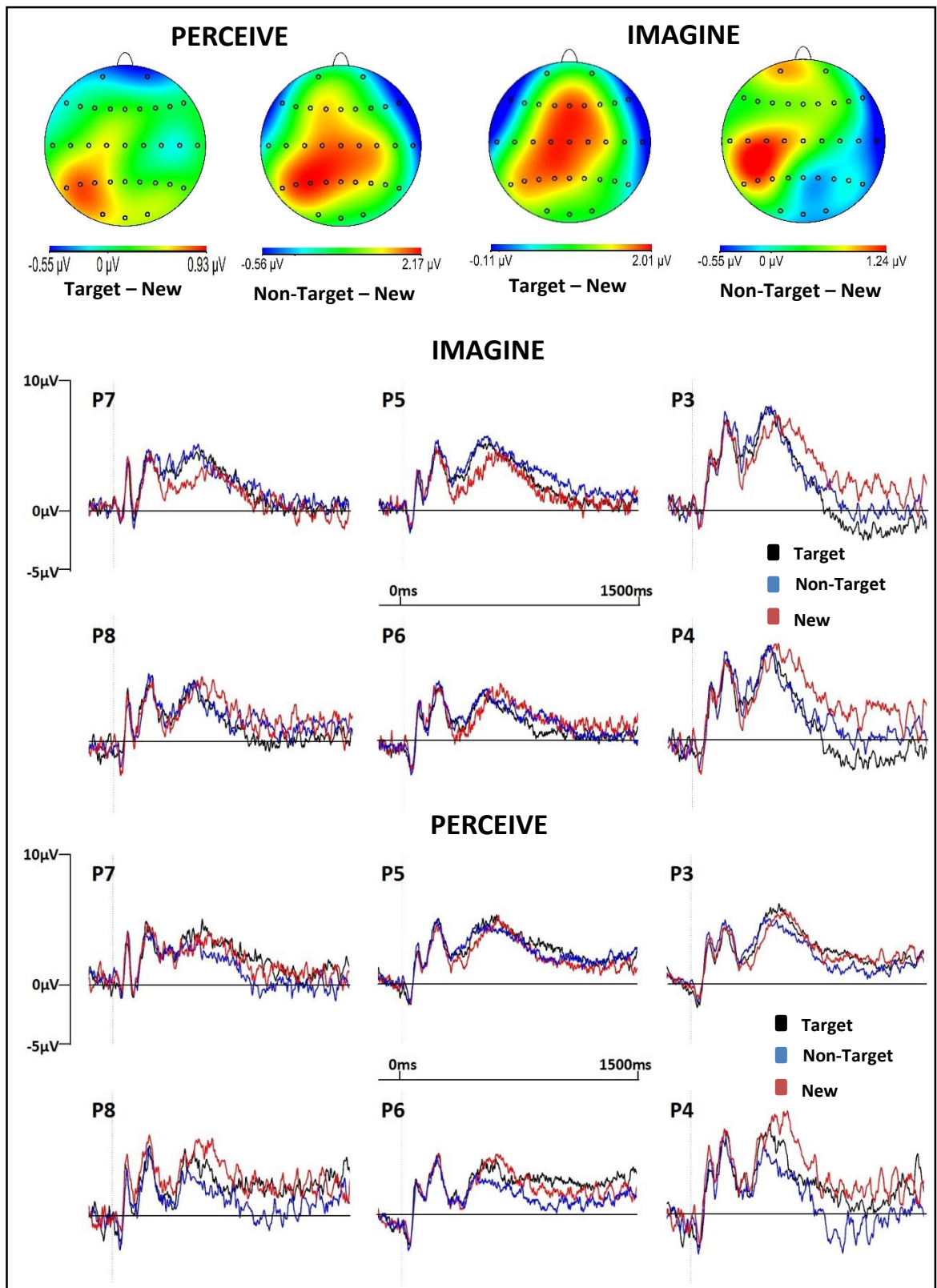
Mean scores for working memory, O-LIFE, PDI and LSHS-R for this sample as well as normative values (where available) can be seen in **Table 15**. Generally, the measures obtained from this sample are lower than the normative values for each measure (Mason et al., 1995; Peters et al., 2004; for O-LIFE and PDI respectively), even for the age corrected O-LIFE norms (Mason & Claridge, 2006). This is not necessarily unexpected however, given psychotic symptoms decrease with age (Jeste, Wolkowitz, & Palmer, 2011), and the age range of participants in this sample.

**Table 15 – Mean psychometric scores for Experiment Three. Standard Deviations (SD) are in parentheses. Values in bold represent the measures entered into initial analyses. Normative values are included where possible (Mason et al., 1995; Peters et al., 2004; for O-LIFE and PDI respectively). Normative values for O-LIFE for age range 31-40.**

Measure	Mean (SD)	Min	Max	Normative Value (SD)
<b>Working Memory</b>	<b>69.47 (10.53)</b>	<b>42</b>	<b>87</b>	
<b>O-LIFE</b>				
<b>UnEx</b>	<b>4.77 (3.66)</b>	0	16	8.39 (6.08)
<b>CogDis</b>	<b>7.82 (5.62)</b>	1	19	10.12 (6.15)
<b>IntAn</b>	<b>6.09 (4.72)</b>	0	15	6.32 (4.63)
<b>PDI Total</b>	<b>22.59 (14.75)</b>	0	49	58.90 (48.00)
<b>Yes</b>	3.09 (2.00)	0	7	6.70 (4.40)
<b>Dis</b>	5.05 (3.44)	0	12	15.50 (14.10)
<b>Pre</b>	6.18 (4.08)	0	14	15.40 (14.10)
<b>Con</b>	8.27 (6.48)	0	25	20.40 (16.00)
<b>LSHS-R Total</b>	<b>20.14 (4.46)</b>	15	32	
<b>VivTh</b>	5.09 (1.63)	3	9	-
<b>AudHal</b>	4.59 (1.14)	4	8	-
<b>VivDay</b>	4.50 (2.04)	3	12	-
<b>VisHal</b>	5.95 (1.17)	5	10	-

#### PRINCIPAL CORRELATIONS BETWEEN BEHAVIOURAL MEASURES AND SCHIZOTYPY

Reaction times, discrimination values, estimates of familiarity and recollection and Stroop interference scores were correlated with schizotypy measures. Analyses of reaction times revealed no significant correlations. Reaction times for correct responses to imagine non-target items approached significance with two measures of positive schizotypy ( $r(20)=0.42, p=0.054$  for both UnEx and LSHS-R Total) and RT for correct responses to imagine target items approached significance with one measure of positive schizotypy ( $r(20)=0.37, p=0.092$  for PDI Total). Similarly, when discrimination values were assessed no significant relationships were identified though Target – Non-Target discrimination in the perceive target designation approached significance with one measure of positive schizotypy ( $r(20)=0.42, p=0.051$  for PDI Total). Finally, analysis of estimates of familiarity and recollection and Stroop interference scores revealed no significant relationships.



**Figure 12 - Topographic maps showing old/new effects for targets and non-targets split by target designation (imagine/perceive) from Experiment Three for the 450-600ms epoch. The maps were computed from difference scores obtained by subtracting mean amplitudes for correct responses to new items from those associated with targets and non-targets respectively. ERP waveforms are from electrodes included in the left-parietal old/new effect analysis, with the exception of P1/P2. These sites have been excluded for consistency of presentation across Experiments.**

## PRINCIPAL ERP RESULTS

The mean number of trials (range in parentheses) contributing to each condition of interest were as follows: imagine target = 32 (20-39), perceive target = 31 (15-40), imagine non-target = 33 (21-40), perceive non-target = 33 (24-40), imagine new = 35 (26-40) and perceive new = 34 (19-40).

### Left-Parietal Old/New Effects

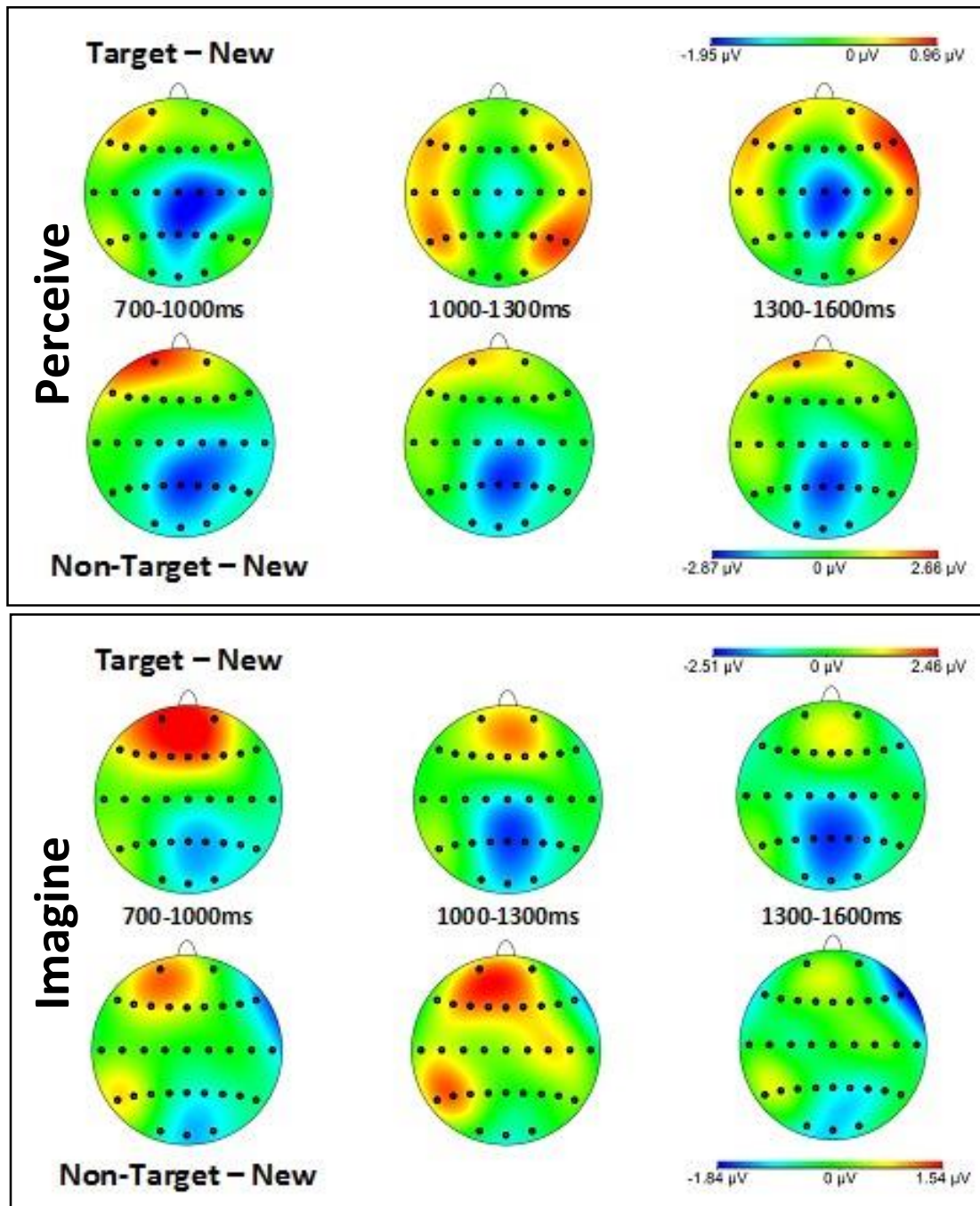
Figure 11 shows the target and non-target old/new effects for items presented in the imagine and perceive target designations. The figure shows the left-parietal old/new effects in this group have a somewhat different time course to those for the younger participants. There is an earlier divergence at parietal sites that does not differ between target designations. For this reason the data were analysed using 450-600ms.

Initial ANOVAs with factors of target designation (two levels; imagine and perceive), response category (three levels; correct responses to target, non-target and new), hemisphere (two levels; left and right) and site (four levels; inferior [P7/8], medial [P5/6], medial superior [P3/4] and superior [P1/2]) were conducted. The analysis revealed a significant main effect of response category ( $F(1.8, 38.1)=5.00, p=0.014, E=0.91$ ) and an interaction between response category and hemisphere ( $F(1.9, 40.7)=10.77, p<0.001, E=0.97$ ). Planned pairwise comparisons for each hemisphere revealed differences over the left only, where there were reliable and statistically equivalent old/new effects for targets and for non-targets items (smallest  $t(21)=3.33, p=0.003$ ).

## PRINCIPAL CORRELATIONS WITH SCHIZOTYPY AND STROOP PERFORMANCE

As no reliable differences were identified between target and non-target left-parietal old/new effects, one approach to analysis would be to not pursue further correlational analysis. The nature of the analyses however means individual differences between participants may not be reflected in the results of higher order analyses and thus it may still be fruitful to conduct correlation analyses. When target-non-target old/new differences were averaged across P7, P5, P3 and P1 electrode sites however no significant correlations were identified.

The alternative analysis strategy however would be to investigate whether the magnitudes of target and non-target old/new effects were related to measures of schizotypy and Stroop interference scores. Target and non-target old/new effects were averaged across P7, P5, P3 and P1 electrode sites and no significant correlations were identified.



**Figure 13 – Topographic maps showing old/new effects for targets and non-targets split by target designation (imagine/perceive) for Experiment Three for three epochs between 700 and 1600ms. The maps were computed from difference scores obtained by subtracting mean amplitudes for correct responses to new items from those associated with targets and non-targets respectively.**

## SUBSIDIARY ERP RESULTS

### Late Posterior Negativity

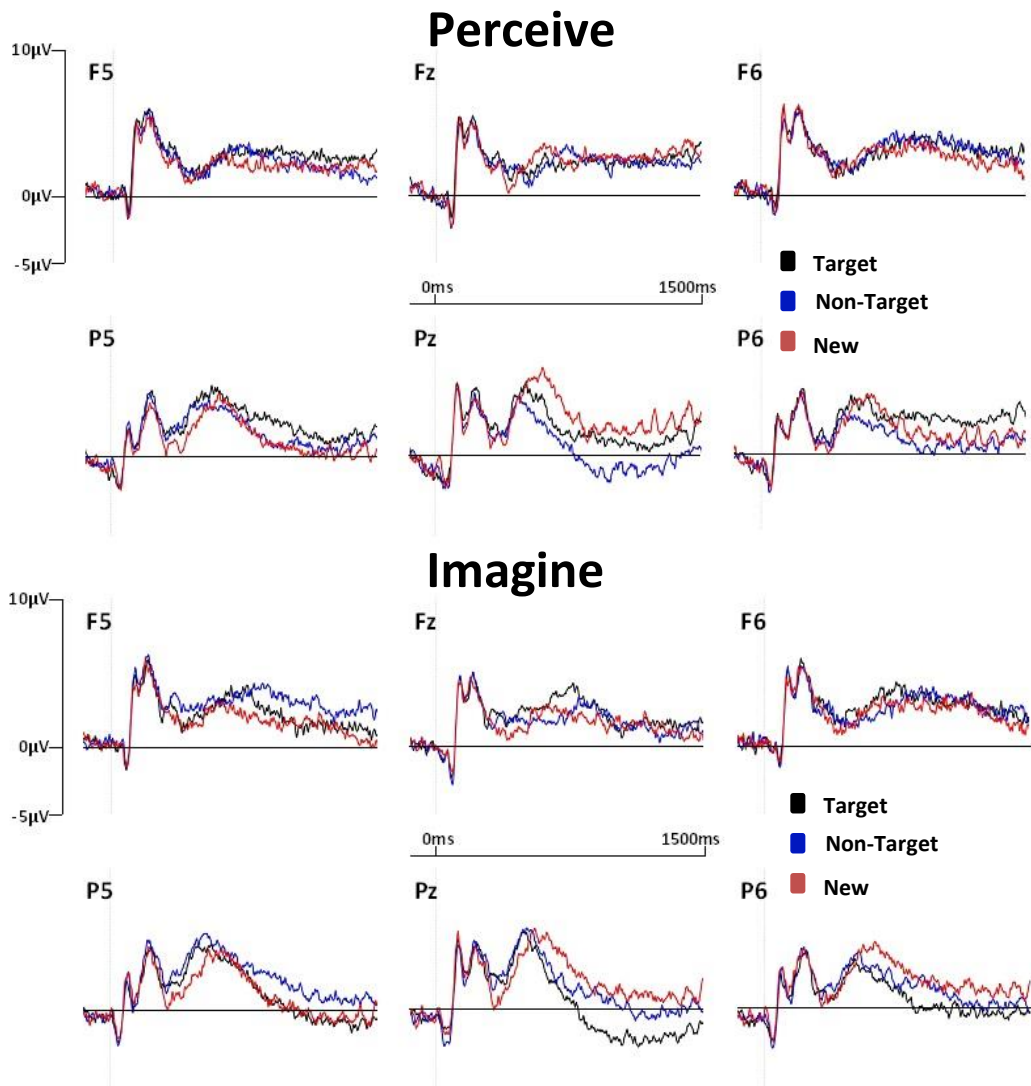
As can be seen in the scalp maps and waveforms in **Figure 13** and **Figure 14**, there is a late posterior negativity emerging from approximately 700ms post-stimulus presentation; earlier than reported for Experiment One and Two. The analysis epochs were therefore adjusted accordingly. Initial exploratory ANOVAs with the factors of target designation (two levels; imagine and perceive) and response category (three levels; correct responses to target, non-target and new items) and site (three levels; P3, Pz and P4) were conducted across three epochs (700-1000ms, 1000-1300ms, 1300-1600ms). In the 700-1000ms epoch, there was a significant main effect of response category ( $F(1.7, 36.6)=4.78, p=0.018, E=0.87$ ), indicating both target and non-target items were more negative going than new items (smallest  $t(21)=2.41, p=0.025$ ), but there was no significant difference between target and non-target items.

In the 1000-1300ms epoch, there were significant interactions between target designation and response category ( $F(1.4, 29.5)=5.00, p=0.023, E=0.70$ ) and response category and site ( $F(3.2, 68.2)=2.80, p=0.043, E=0.81$ ). In the 1300-1600ms epoch, no significant effects were identified. Following up the target designation by response category interaction in the 1000-1300ms epoch revealed that in both target designations, targets were more negative going than new items (smallest  $t(21)=2.11, p=0.047$ ). In the perceive target designation however non-target items were also more negative going than new items (smallest  $t(21)=2.18, p=0.041$ ). There was no significant difference between target and non-target items.

### Right-Frontal Old/New Effect

As can be seen in the scalp maps in **Figure 13**, in addition to the LPN, there is also a frontal ERP old/new effect. Further examination of the waveforms reveals this modulation appears from approximately 500ms and lasts until 1300ms post-stimulus presentation. An initial exploratory ANOVA with the factors of target designation (two levels; imagine and perceive), response category (three levels; correct responses to target, non-target and new), hemisphere (two levels; left and right) and site (four levels; inferior [F7/8], medial [F5/6], medial superior [F3/4] and superior [F1/2]) was conducted across two epochs: 600-900ms and 900-1200ms.





**Figure 14 – Grand average ERP waveforms elicited by targets, non-targets and new items attracting correct judgments from left and right hemisphere and midline sites at frontal (F5, Fz, F6) and posterior (P5, Pz, P6) electrode sites split by target designation (imagine/perceive) for Experiment Three**

No significant effects were identified in the 600-900ms epoch. In the 900-1200ms epoch, there was an interaction between target designation and site only ( $F(2.0, 42.7)=3.26, p=0.048, E=0.68$ ). As no significant effects involving response category were identified, it was not possible to pursue further analyses investigating how this index of post-retrieval monitoring varied with measures of schizotypy.

## SUBSIDIARY CORRELATIONS WITH SCHIZOTYPY

### Late Posterior Negativity

It was not possible to investigate how this ERP index of post retrieval monitoring was modulated by schizotypy scores, as no reliable differences were identified between target and non-target LPNs. It was possible however to investigate whether the magnitude of target and non-target old/new effects were related to measures of schizotypy. Target and non-target old/new effects were averaged across P3, Pz and P4 electrode sites for the epochs where reliable late posterior negativities were identified (700-1000ms and 1000-1300ms). Negative schizotypy (IntAn) was positively correlated with the target old/new effect in the imagine target designation in the 700-1000ms and 1000-1300ms epochs ( $r(20)=0.47, p=0.026$ ;  $r(20)=0.53, p=0.011$  respectively). Negative schizotypy was also positively correlated with the non-target old/new LPN effect in the perceive target designation in the 700-1000ms epoch ( $r(20)=0.51, p=0.016$ ). Finally, LSHS-R total was negatively correlated with the non-target old/new LPN effect in the imagine target designation in the 1000-1300ms epoch ( $r(20)=-0.48, p=0.025$ ).

### CORRELATIONS WITH WORKING MEMORY CAPACITY

Reliable differences between the ERPs elicited by targets and non-targets were not identified during analyses of the left-parietal old/new effects, however reliable non-target – new differences were identified. If people exert cognitive control when they have the capacity to do so, a negative relationship between the magnitude of the non-target – new difference and measures of working memory capacity would be expected, as those higher in working memory capacity would be expected to exhibit smaller non-target – new differences. Non-target differences were calculated from P7, P5, P3 and P1 from 450-600ms post stimulus presentation. No significant relationship was identified.

### EXPLORATORY ERP ANALYSES

As can be seen in Figure 10, in addition to the divergence from 450-600ms, there is a later divergence from 1000-1600ms that is more positive going for perceive items only, irrespective of target designation. Thus, initial ANOVAs with factors of target designation (two levels; imagine and perceive), response category (three levels; correct responses to

target, non-target and new), hemisphere (two levels; left and right) and site (four levels; inferior [P7/8], medial [P5/6], medial superior [P3/4] and superior [P1/2]) were conducted to investigate this effect. Analysis revealed significant interactions between response category and site ( $F(3.7, 77.3)=5.94, p<0.001, E=0.61$ ) and target designation, response category and site ( $F(4.0, 83.0)=2.74, p=0.035, E=0.66$ ). Follow up analyses within each target designation revealed significant interactions between response category and site for both target designations ( $F(3.6, 74.6)=4.07, p=0.007$ ;  $F(3.7, 78.6)=4.54, p=0.003$  for perceive and imagine target designations respectively). Following up this interaction within each target designation however revealed no significant differences between response categories at any site. This interaction probably arose because in the imagine target designation, amplitudes were numerically more negative going for targets over medial superior and superior electrode locations compared to non-target and new items. Whereas, over the same locations in the perceive target designation, target amplitudes were numerically more positive going compared to non-target and new items.

#### EXPLORATORY CORRELATIONS WITH SCHIZOTYPY

In light of these numerical differences, one approach to conducting correlations with schizotypy would be to calculate target – new and target – non-target ERP magnitude differences averaged across (medial superior) P3/4 and (superior) P1/2 electrode sites separately for each target designation, considering there is no interaction with hemisphere and these were the locations where the effects were numerically largest. These analyses revealed positive correlations between negative schizotypy (IntAn) and the magnitude of the target – new ( $r(20)=0.52, p=0.012$ ) and target – non-target ( $r(20)=0.51, p=0.016$ ) magnitude differences in the imagine target designation. Disorganised schizotypy (CogDis) was also positively correlated with the magnitude of the target – non-target magnitude difference in the imagine target designation ( $r(20)=0.43, p=0.048$ ).

## DISCUSSION

### PRINCIPAL ANALYSES

#### Left-Parietal Old/New Effects

One purpose of this investigation was to investigate whether retrieval control, as indexed by magnitude differences between target and non-target left-parietal old/new effects, is modulated by schizotypy scores in a non-university student sample. The time period used for the parietal analyses was not the same as in Experiments One and Two. Rather, mean ERP magnitudes were calculated from 450-600ms post stimulus presentation because this is the epoch in which the effects were largest. Reliable target and non-target left-parietal old/new effects were identified, though there were no significant attenuations of non-target relative to target effects. Two analysis strategies were explored: i) conducting correlations with target-non-target magnitude differences in the absence of finding higher order differences and, ii) conducting correlational analyses using target and non-target old/new effects respectively. The former could be justified given the nature of the analyses means individual differences between participants may not be reflected in the results of higher order analyses and thus it may still be fruitful to conduct correlation analyses. The latter could be justified considering robust old/new effects were identified in the absence of differences between target and non-target effects. When target and non-target ERP old/new magnitudes from 450-600ms were correlated with schizotypy and Stroop measures however, no significant relationships were identified using either strategy. Similarly, no correlations were identified between measures of schizotypy and behavioural performance.

The time course of parietal old/new effects reported in this study differed from that previously reported in both university and some older adult samples (e.g. Dywan et al., 2002; Wilding et al., 1995). As previously highlighted in Chapter Three (page 64), parietal old/new effects in university samples tend to be largest over left-parietal scalp locations from 500-800ms post-stimulus presentation. By contrast, old/new ERPs for older adults tend to be far less differentiated within this time window but with greater amplitude at frontal locations (e.g. Dywan et al., 2002). Given the present sample are substantially younger than those who participated in the study conducted by Dywan et al. (2002); 38.55 years compared to 68.10 years and substantially older than university samples,

including those recruited for Experiment One and Two however, it is not necessarily surprising that established patterns of ERP activity do not translate to the present sample.

One possible explanation for the earlier divergence in the present sample is that it indexes implicit memory. Rugg et al. (1998) previously identified that old relative to new items produced activity in three neuroanatomically and functionally dissociable neural populations. Two of these ERP effects were considered to correspond to item familiarity and recollection (for further details of these effects refer to 62 and 64 respectively). The third effect however was considered an index of implicit memory as parietal ERPs from 300-500ms for old items, irrespective of response accuracy or encoding manipulation, were more positive going than new items. Whilst the time course of the effects in the present data do not strictly correspond to the time course of the implicit and explicit memory effects reported by Rugg et al. (1998); 300-500ms and 500-800ms for implicit and explicit memory effects respectively, this could be due to the RT latency in the current sample compared to younger participants.

Rugg et al. (1998) were able to analyse ERPs elicited by misses in their experiment, and this was not possible here due to trial number restrictions. As a result, it is at least as plausible to argue that the parietally distributed effects that were of the same magnitude for targets and for non-targets are indices of recollection and their magnitude was influenced by the early onset of the large late posterior negativity which may have attenuated any lateral positivity occurring in similar time windows. This possibility will be discussed in greater detail in Chapter Nine (page 187).

Assuming that the parietally distributed effects are in fact indices of recollection, then the absence of evidence for control over recollection here is at odds with the findings in Experiments One and Two, and this is notable because the levels of Target – Non-Target discrimination in this experiment are superior to those obtained with the university samples (smallest  $t(68)=2.13, p=0.037$ ). Nonetheless, these results are in one sense consistent with the suggestion of Elward and Wilding (2010) that the likelihood of correct responses to targets is not the only determinant of when control over retrieval will be observed in the electrical record. These points will be addressed in greater detail in Chapter Nine (page 190).

Finally, given the absence of target – non-target ERP differences in the current study, it was difficult to assess the relationship between this proposed ERP measure of cognitive control and an established behavioural measure of cognitive control.

### Correlations with Schizotypy

Consistent with Experiments One and Two, there were no significant correlations between ERP measures of retrieval control and measures of schizotypy. The lack of behavioural correlations however is inconsistent with the results obtained in the first two experiments reported in this thesis. In the first experiment, reaction times were positively correlated with measures of positive schizotypy and in the second experiment estimates of familiarity for imagine items were positively correlated with measures of positive schizotypy. One reason for this could be that the present sample is substantially older and more heterogeneous (e.g. more variable in terms of age range, educational and/or work experiences etc) than those used for the first two experiments reported in this thesis. Furthermore, whilst the current sample has a similar range of schizotypy scores to that of the university samples, more of these scores fall to the lower end of the scales, as reflected by the reduced means for the present sample. Given symptoms of schizophrenia and schizotypy scores decrease with age (Jeste et al., 2011; Moritz et al., 2004), this latter outcome is not unexpected and could have contributed to the absence of effects.

## SUBSIDIARY ANALYSES

### Late Posterior Negativity

These analyses were conducted to gain a better understanding of how post-retrieval control processes may contribute to memory performance in schizotypy. The time periods used differed from those for the university samples. Mean ERP magnitudes were calculated from 700-1000ms, 1000-1300ms and 1300-1600ms post stimulus presentation. In the first two epochs, the general pattern was for reliable and statistically equivalent LPNs for targets and for non-targets. When target and non-target ERP old/new magnitudes were correlated with schizotypy measures however, target – new ERP differences for the imagine target designation were positively correlated with measures of negative schizotypy in the first and second epoch. Non-target – new ERP differences for the perceive target designation were positively correlated with measures

of negative schizotypy in the first epoch only. Furthermore, a measure of positive schizotypy was negatively correlated with the non-target – new difference in the imagine target designation in the second epoch only. Generally, this pattern of results suggests that those higher in schizotypy engaged more in post-retrieval monitoring of imagine items irrespective of target designation, though the negative correlation between positive schizotypy and the magnitude of the non-target – new difference in the imagine target designation is at odds with this account.

#### CORRELATIONS WITH WORKING MEMORY CAPACITY

These analyses were conducted to examine the generality of the association between the left-parietal target – non-target magnitude difference and working memory capacity identified by Elward and Wilding (2010). As no reliable target – non-target differences were identified, the magnitude of the non-target – new difference and measures of working memory capacity were entered into analyses as if people exert cognitive control only when they have the capacity to do so, a negative relationship would be expected. No significant relationship was identified however. This result could be considered unsurprising given the smaller ERP magnitudes in this sample compared to those of university students. Though given the minimal task difficulty (as demonstrated by the high level of behavioural performance) a relationship was anticipated as participants had the capacity to exert cognitive control.

#### EXPLORATORY ANALYSES

In addition to the divergence from 450-600ms over parietal electrode sites, there is a later divergence from 1000-1600ms that is more positive going for perceive items only, irrespective of target designation. Exploratory ANOVAs to investigate this effect revealed reliable differences between response categories as indicated by interaction between response category and site in each target designation. When ERP difference measures were correlated with measures of schizotypy negative schizotypy was positively correlated with both the target old/new effect and the magnitude difference between target and non-target ERPs in the imagine target designation. Disorganised schizotypy was also positively correlated with the magnitude difference between target and non-target ERPs in the imagine target designation. Given the similarities in both the epoch

(1000-1300ms vs 1000-1600ms) and electrode sites (P3,Pz,P4 vs P1/2 and P3/4) to those included in the correlation analyses with LPN however, the correspondence between the correlational outcomes here and those reported for the LPN are not surprising. These findings can most likely be attributed to the earlier emergence of late positive negativity, especially in light of the fact target items in the imagine target designation were numerically more negative going compared to non-target and new items.

## CONCLUSIONS

Taken together, the present results indicate that the time course of old/new effects is not comparable for university students and members of a community sample in the 19-59 age range, which is a group that is not commonly studied. Measures of schizotypy correlated with ERP measures of post-retrieval monitoring only, suggesting control processes acting on the products of retrieval, rather than during retrieval, are more crucial to memory performance in those higher in schizotypy. The final experiment of this thesis is an assessment of retrieval control in patients with schizophrenia, and how their behavioural and ERP data relate to those of the controls for whom the data has been reported in this chapter.



## CHAPTER EIGHT: EXPERIMENT FOUR

It is estimated that cognitive deficits affect 75-85% of schizophrenia patients (Reichenberg et al., 2006). These deficits are the strongest predictor of functional outcome (Green et al., 2000; Puig et al., 2008), adherence to medication (Burton, 2005) and treatment programmes more broadly (Prouteau et al., 2005). Furthermore, patients presenting with significant cognitive deficits show reduced living and social skills (Bowie & Harvey, 2005), in addition to an increased tendency for symptom relapse (Chen et al., 2005). These findings indicate cognitive deficits have a considerable impact on quality of life for schizophrenia patients, identifying alleviating cognitive dysfunction as an important treatment target.

Several studies using standard neuropsychological batteries have identified deficits across most cognitive domains (e.g. Braff, 1993; Hutton et al., 1998; Saykin et al., 1991), though meta-analyses of both first episode and chronic patients have revealed episodic memory to be one of the most profoundly affected domains (Aleman et al., 1999; Mesholam-Gately et al., 2009). Two important points emerge from such findings. First, memory dysfunction experienced by schizophrenia patients is severe and enduring, despite psychopharmacological intervention (Goldberg et al., 1993). Second, episodic memory encompasses several cognitive processes and most studies investigating cognition have used tasks tapping multiple cognitive processes, making it difficult to draw conclusions relating to specific processes.

The outcomes in some studies have led to the suggestion that the processes contributing to episodic memory performance are not equally affected in schizophrenia. For example, if patients are required to organise information during encoding, recall associations between items rather than individual items or complete recall rather recognition tests, memory performance is disproportionately compromised (Achim & Lepage, 2003; Iddon et al., 1998; Ranganath et al., 2008). This latter evidence particularly suggests schizophrenia patients may have selective deficits in recollection considering successful recall performance requires the retrieval of contextual details from the encoding phase. This is in contrast to recognition performance which can be based to a larger extent on item familiarity (Yonelinas, 2002).

Whilst many behavioural and fMRI studies have been conducted to assess process-specific impairments (e.g. Bonner-Jackson, Yodkovik, Csernansky, & Barch, 2008; Guillaume et al., 2007; Ragland, Blumenfeld, et al., 2012), very few have made use of ERP indices of memory processes. The findings from those that have are inconsistent (e.g. Guillaume et al., 2012; Tendolkar et al., 2002). However, a recent quantitative reanalysis of several studies led to the conclusion that recollection and familiarity are both compromised in schizophrenia (Libby et al., 2013). One of the most important conclusions of this reanalysis was that recollection is a potentially important therapeutic target for improving episodic memory performance in patients with schizophrenia (Libby et al., 2013). Therefore, by better understanding cognitive processes that contribute to recollection specifically, this could facilitate the development of new pharmacological and cognitive training procedures to address these deficits.

The importance of investigating cognitive mechanisms contributing to successful recollection is further emphasised by evidence suggesting individuals with schizophrenia have difficulty discriminating between particular encoding contexts, namely reality monitoring. Reality monitoring requires people to differentiate between self-generated and externally presented information (Johnson et al., 1988; Johnson et al., 1994; Rosburg et al., 2011b). Discrimination between such contexts may be more difficult for people with schizophrenia as one hypothesis for the occurrence of some positive symptoms (e.g. hallucinations) is that patients have a particular difficulty discriminating between internally and externally generated events (e.g. Ditman & Kuperberg, 2005; Frith, 1992; Johns et al., 2001). Together, this suggests that by understanding processes that contribute to successful recollection of contextual details, not only could the development of treatments alleviating cognitive deficits be facilitated but also those aimed at reducing positive symptoms.

One process that could facilitate discrimination between different contexts is cognitive control over what is retrieved and how information is prioritised. Control mechanisms allow us to modify our behaviour flexibly in accordance with task demands (Lesh et al., 2011) and previously it has been hypothesised that many of the deficits observed in schizophrenia patients arise at least in part due to failures in cognitive control operations (Cohen & Servan-Schreiber, 1992). Herron and Rugg (2003) were the first to identify an ERP marker of cognitive control during retrieval and the previous experiments reported

in this thesis investigated this index in relation to schizotypy, a dimensional correlate of schizophrenia. In doing so, this provided a starting point for investigating the mechanisms underlying memory problems in schizophrenia patients. No correlations however were identified between ERP indices of retrieval control and measures of schizotypy.

Importantly, this does not preclude investigations of cognitive control in patients with schizophrenia, considering schizotypy is not simply an analogue of schizophrenia but rather an indicator of liability (Lenzenweger, 2006). Under this view, whilst investigations using measures of schizotypy can provide invaluable insights into factors implicated in the development of schizophrenia, ultimately studies using measures of schizotypy, especially those employing psychometric assessments, will not invariably provide indicators that translate to patients with schizophrenia (Kwapil & Barrantes-Vidal, 2015). In light of this, it is important to examine how patterns of performance in schizotypy compare to those in schizophrenia to better understand the relationship between these constructs. In doing so it is possible to gain a better understanding of the distribution of schizophrenia spectrum phenotypes across the population (Ettinger et al., 2015). This purpose of this final experiment was therefore two-fold: i) to determine whether retrieval control is compromised in patients with schizophrenia and ii) to investigate the generality of findings obtained from healthy participants using measures of schizotypy to patients with schizophrenia.

## METHODS

### Participants

31 participants were recruited from a pre-existing database held by Dr. James Walters of patients who had previously consented to be approached about further research studies. Ethical approval was obtained from the Wales Research Ethics Committee 6. All participants spoke fluent English, reported to have normal or corrected-to-normal vision and hearing, and to be right-handed. Participants were excluded from participating if the care co-ordinator or participant reported a change/increase in medication within the past month, contact with the home treatment team or admission to hospital within the last three months, any clinically significant neurological conditions (e.g. stroke/epilepsy), any significant medication side effects that would interfere with the study session (e.g.

significant movement problems) or history of alcohol or drug dependence. Participants provided written informed consent prior to their participation, and were aware they could withdraw from the study at any point without reason or penalty. Participants received £40 for their participation. Data from fifteen participants were excluded due to poor behavioural performance (6), excessive EEG artefact (3) and insufficient trials in conditions of interest (6; >14 trials per condition of interest). For behavioural rejection criteria see the Exclusion Task section of Chapter Five: Experiment One (pages 87). Of the remaining 16 participants (mean age = 40.69, range = 24-59) eight were female. Of those included, participants met DSM criteria for schizophrenia (10), schizoaffective disorder (3 depressive and 2 bipolar subtype), or other psychotic disorder (1). All included participants were taking antipsychotic medication, though the types of medications varied widely (clozapine=4, olanzapine=3, aripiprizole=2, risperidone=2, amisulpride=1, depixol=1, haloperidol=1, quetiapine=1). To accommodate this variability, medications were converted to chlorpromazine equivalents (CPZE) using the tables provided by Danivas and Venkatasubramanian (2013) and Wulff, Dijk, Middleton, Foster, and Joyce (2012). CPZE is defined as the dose of a drug that is equivalent to 100mg of chlorpromazine (Danivas & Venkatasubramanian, 2013). Refer to **Table 16** for more detailed information about participant characteristics, including symptom ratings. Importantly, patients were matched to controls in terms of age, gender, Full Scale IQ, Parental Education, cigarettes per day as well as BAI and BDI scores. Significantly more patients identified as smokers compared to control participants however ( $t(36)=2.26, p=0.030$ ).

## OVERVIEW OF PROCEDURE

The order of tasks remained consistent for participants where possible. Typically, participants first completed the exclusion task used for Experiment Three whilst ERPs were acquired. Following this, participants were interviewed using the Structured Clinical Interview: Positive and Negative Syndrome Scale (SCI-PANSS; Opler, Kay, Lindenmayer, & Fiszbein, 1992) and the Functional Remission Scale for Schizophrenia (FRSS; Llorca et al., 2009). Then, participants completed the computerised working memory task as used in Experiment Three and the Vividness of Visual Imagery Questionnaire (VVIQ; Cui et al., 2007; Marks, 1973). Following this, participants completed the computerised classic Stroop task (Stroop, 1935) as used for Experiment Three. To finish, participants

completed the Beck Anxiety Inventory (BAI; Beck et al., 1988), the Beck Depression Inventory (BDI-II; Beck et al., 1996) and the learning task as used in Experiment Three (Haselgrove & Evans, 2010). Refer to EEG Acquisition and Analysis Procedures section of Chapter Seven: Experiment Three for details of EEG acquisition (page 135).

**Table 16 – Mean sample characteristics for Experiment Four. Characteristics included for control participants where possible. Standard Deviations (SD) are in parentheses.**

Measure	Mean (SD)	Min	Max	Control (SD)
Age	40.69 (10.53)	24	59	38.55 (
Onset of Illness	25.52 years (9.37)	7	44	
Duration of Illness	15.16 years (11.23)	3	34	
No. of Admissions	2.37 (1.75)	0	6	
Gender	8 female			10 female
Smoking Status	10 smokers			6 smokers
Cigarettes per day	15.80 (8.39)	6	30	8.50 (3.94)
Working Memory	59.96 (16.84)	23	93	69.47 (10.53)
Full Scale IQ	110.67 (7.18)	97	120	111.40 (4.17)
Parental Education	13.00 (2.04)	10	18	13.14 (3.32)
<b>SCI-PANSS</b>				
Positive	9.81 (2.54)	7	15	
Negative	12.19 (4.62)	7	23	
General	21.19 (5.71)	16	40	
<b>FRSS Total</b>	<b>76.94 (10.32)</b>	<b>47</b>	<b>85</b>	
CPZE	376.5mg (238.68mg)			
BAI	8.26 (6.00)	0	19	8.41 (4.66)
BDI	7.47 (4.22)	1	14	6.64 (4.17)

Structured Clinical Interview: Positive and Negative Syndrome Scale (SCI-PANSS; Opler et al., 1992)

The SCI-PANSS is a semi-structured interview based on the original Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987) and provides a measure of the severity of schizophrenia symptoms experienced by an individual. The SCI-PANSS assesses only the most pertinent 13 symptoms from the original 30 symptoms using specific questions and distinct criteria for rating responses to facilitate administration and reduce inter-rater variability (Opler et al., 1992). From this reduced assessment, scores for the full collection of symptoms can be derived. This measure produces scores for four basic scales: Positive, Negative, General Psychopathology and a Composite score. All items in the interview are scored using a 7-point scale, with 1 indicating the absence of a symptom and 7 indicating extremely severe symptomatology. Scale scores are produced

by summing the scores pertaining to relevant items. For more detailed information on the subscales that contribute to these four dimensions see Kay et al. (1987).

The SCI-PANSS has been shown to correlate well with other measures of schizophrenia symptoms including The Scale for the Assessment of Positive Symptoms (Andreasen, 1984), The Scale for the Assessment of Negative Symptoms (Andreasen, 1983) and The Brief Psychiatric Rating Scale (Bell, Milstein, Beam-Goulet, Lysaker, & Cicchetti, 1992; Norman, Malla, Cortese, & Diaz, 1996; Overall & Gorham, 1962). Despite this, SCI-PANSS has been shown to have reduced validity compared to PANSS, despite increased inter-rater reliability (Von Knorring & Lindström, 1994). Nonetheless, Von Knorring and Lindström (1994) concede that the improved accuracy of rating negative symptoms is of paramount importance given the emphasis placed on such symptoms in the diagnosis and treatment of schizophrenia. For the purposes of this experiment, only positive, negative and general scores were entered into analyses.

#### Functional Remission Scale for Schizophrenia (FRSS; Llorca et al., 2009)

FRSS was developed to evaluate functional remission in schizophrenia patients. This measure assesses functioning in five domains over the month preceding the assessment: Daily Life (5 items), Activities (3 items), Quality of Adaptation (3 items), Relationships (5 items) and Health/Treatment (3 items), via semi-structured interview. Daily life incorporates items assessing personal care and appearance, diet and housekeeping in addition to administrative/financial management. An individual's ability to engage in personal or social activities as well as work/studying is assessed in the Activities domain. Items assessing Quality of Adaptation address the individual's independence, as well as management of health and stressful circumstances. The Relationships domain incorporates items assessing the nature and quality of family, friend and intimate relationships in addition to the degree to which the individual exhibits antisocial or empathic behaviours towards others. Finally the Health and Treatments domain assesses the degree to which the individual takes responsibility for their health and respects biological rhythms (e.g. sleep/wake cycles), as well as the functional impact of any side effects of treatment (e.g. mood, cognition, metabolic function). Each item is rated on a 5-point scale with 1 responses indicating extreme impairment and 5 responses indicating little or no impairment. FRSS produces scores for each domain by summing the responses to relevant items, in addition to producing a total score. Whilst the five-factor structure

of this tool has not been validated (3 factors supported on replication; Llorca et al., 2009), the authors maintain that the total score is valid and can be used to assess a general construct of 'functioning'. Importantly, this measure provides a means of assessing functionality independently of psychopathological symptoms (Llorca et al., 2009). For the purposes of this experiment, only the total score was entered into analyses.

## ANALYSES PROCEDURES

The principal foci of this chapter are: i) to understand whether, and if so how, behavioural and ERP measures of memory performance differ between patient and control participants, ii) to understand the relationship between measures of behavioural performance and symptoms of schizophrenia or general functioning, iii) to investigate whether schizophrenia symptoms are associated with an ERP index of retrieval control, and iv) to investigate whether schizophrenia symptoms are associated with changes in post-retrieval processes indexed by ERPs.

In keeping with this, behavioural accuracy, reaction time, process estimates and discrimination performance for patients were contrasted with those for control participants, for whom the data were shown in the previous chapter. These measures were subsequently correlated with positive, negative and general symptoms. Initial examinations of the ERP data were restricted to parietal electrodes between 450-600ms and 1000-1600ms post-stimulus presentation, as this is where left-parietal old/new effects were reported for the control participants, and these time windows are a good fit for the analysis of the patient data, as Figure 15 shows. Once left-parietal old/new effects had been identified at the group level, correlational analyses were conducted to investigate whether the symptoms of schizophrenia were associated with the magnitude of these effects, in addition to the magnitude of the relative difference between these effects. These analyses were conducted on the average amplitudes across P7, P5, P3 and P1 electrode sites within the aforementioned epochs.

ERP analyses of late posterior negativity and right frontal old/new effects were restricted to parietal electrodes from 700-1600ms and frontal electrodes from 600-1200ms post-stimulus respectively, with selection of these windows having been guided by visual inspection (see **Figure 18**). Once old/new effects had been identified at the group level, correlational analyses were conducted to identify whether the three symptom

dimensions were associated with the magnitude of these effects, in addition to the magnitudes of the relative differences between these effects. The specific sites included in these analyses were dependent on the outcome of higher level analyses for each epoch.

As identified in Chapter One: Schizophrenia (page 38), there are several methodological issues associated with studying patient samples including, but not limited to; medication effects, smoking status, broader cognitive deficits and comorbid diagnoses. Once initial analyses had been conducted and significant effects identified, the aforementioned variables were included in further analyses to investigate whether these variables provide a better explanation for the pattern of data obtained.

## RESULTS

### PRINCIPAL BEHAVIOURAL RESULTS

#### Exclusion Task

Response accuracies and reaction times for each category of stimulus, split by target designation are presented in **Table 17**. Pr values were reliably above zero in each case (smallest  $t(15)=9.88, p<0.001$ ). A 2x2 repeated measures ANOVA of these discriminations by target designation revealed only that Target – New discrimination was superior to Target – Non-Target discrimination ( $F(1, 15)=16.95, p<0.001$ ).

When process estimation formulae were applied to the present data, estimates of recollection ( $pR$ ) were 0.73 and 0.65, and familiarity ( $pF$ ) were 0.24 and 0.55 for imagine and perceive target designations respectively. A 2x2 repeated measures ANOVA of these estimates by target designation revealed a main effect of estimate ( $F(1, 15)=20.00, p<0.001$ ) and an interaction ( $F(1, 15)=15.79, p=0.001$ ). Pairwise Bonferroni-corrected  $t$ -tests (adjusted alpha = 0.025) between target designations revealed estimates of familiarity for perceive items were significantly higher than those for imagine items ( $t(15)=3.37, p=0.004$ ), but there was no significant difference between the target designations in terms of estimates of recollection.



**Table 17 – Probability of correct responses (accuracy) and reaction times (RT) for targets, non-targets and new items split by target designation (imagine/perceive) for Experiment Four (Patient; top) and Experiment Three (Control; below). Standard deviations (SD) are in parentheses**

<b>Patient</b>				
<b>Proportion</b>	<b>Imagine (SD)</b>		<b>Perceive (SD)</b>	
	Accuracy	RT	Accuracy	RT
Target (T)	0.80 (0.17)	1562 (223)	0.84 (0.16)	1473 (221)
Non-Target (NT)	0.81 (0.13)	1405 (187)	0.93 (0.09)	1374 (221)
New	0.84 (0.16)	1610 (162)	0.95 (0.06)	1258 (203)
<b>Pr(T Hit – NT FA)</b>	0.64 (0.24)		0.65 (0.26)	
<b>Pr(T Hit – New FA)</b>	0.73 (0.25)		0.76 (0.18)	
<b>Control</b>				
<b>Proportion</b>	<b>Imagine (SD)</b>		<b>Perceive (SD)</b>	
	Accuracy	RT	Accuracy	RT
Target (T)	0.88 (0.11)	1381 (241)	0.96 (0.09)	1300 (228)
Non-Target (NT)	0.88 (0.09)	1176 (203)	0.92 (0.06)	1158 (235)
New	0.96 (0.04)	1319 (239)	0.99 (0.02)	1087 (204)
<b>Pr(T Hit – NT FA)</b>	0.80 (0.17)		0.84 (0.11)	
<b>Pr(T Hit – New FA)</b>	0.83 (0.14)		0.86 (0.10)	

A 3x2 repeated measures ANOVA of reaction times (RTs) for response category (correct responses to target, non-target and new items) and target designation (imagine and perceive) revealed significant main effects of target designation ( $F(1, 15)=17.54, p=0.001$ ) and response category ( $F(1.3, 19.7)=7.03, p=0.010$ ) as well as an interaction ( $F(1.3, 20.2)=6.03, p=0.016$ ). Pairwise Bonferroni-corrected  $t$ -tests (adjusted alpha = 0.006) between target designations revealed significantly faster RTs for perceive new items compared to imagine new items ( $t(15)=7.17, p<0.001$ ), but no significant difference between conditions for target or non-target items. Comparisons within the imagine target designation revealed RTs for non-target items were significantly faster than RTs for new items ( $t(15)=7.43, p<0.001$ ) only. Analogous comparisons for the perceive target designation revealed only that RTs to target items were significantly slower than to new items ( $t(15)=3.34, p=0.004$ ).

#### BEHAVIOURAL COMPARISONS WITH CONTROL PARTICIPANTS

A 2x2x2 repeated measures ANOVA of Pr values by target designation and group (patient and control) revealed significant main effects of discrimination value ( $F(1, 36)=27.47, p<0.001$ ) and group ( $F(1, 36)=6.47, p=0.015$ ) as well as a significant interaction

between discrimination value and group ( $F(1, 36)=9.88, p=0.003$ ). Following up the interaction between participants revealed Target – Non-target discrimination was superior for control compared to patient participants ( $t(22.3)=2.72, p=0.012$ ), though Target – New discrimination approached significance ( $t(36)=1.96, p=0.057$ ).

A 2x2x2 repeated measures ANOVA of estimates of recollection and familiarity by target designation and group revealed main effects of target designation ( $F(1, 36)=16.29, p<0.001$ ), estimate ( $F(1, 36)=62.22, p<0.001$ ) and group ( $F(1, 36)=8.62, p=0.006$ ), indicating patient estimates were lower, as well as an interaction between target designation and estimate ( $F(1, 36)=37.78, p<0.001$ ).

Finally, a 3x2x2 repeated measures ANOVA of RTs for response category (correct responses to target, non-target and new items), target designation (imagine and perceive) and group (control and patient) revealed significant main effects of target designation ( $F(1, 36)=39.22, p<0.001$ ), response category ( $F(1.4, 49.0)=23.42, p<0.001$ ) and group ( $F(1, 36)=13.96, p=0.001$ ), indicating patients responded slower, as well as a significant interaction between target designation and response category ( $F(1.5, 55.0)=15.10, p<0.001$ ). Follow up analyses were not conducted as there were no significant effects with the factor of group.

#### PRINCIPAL CORRELATIONS BETWEEN BEHAVIOURAL MEASURES AND SCHIZOPHRENIA SYMPTOMS AND GENERAL FUNCTIONING

Reaction times, discrimination values and estimates of familiarity and recollection were correlated with SCI-PANSS scores and FRSS total score to investigate whether behavioural performance was associated with symptoms of schizophrenia or general functioning. When discrimination values were assessed, negative SCI-PANSS score was found to be negatively correlated with Target – New discrimination value for the imagine target designation ( $r(14)=-0.67, p=0.005$ ) as well as the Target – Non-target discrimination value for the perceive target designation ( $r(14)=-0.59, p=0.017$ ). Regarding estimates of familiarity and recollection, negative SCI-PANSS scores were negatively correlated with estimates of recollection for imagine items ( $r(14)=-0.67, p=0.005$ ). Analysis of reaction times revealed several positive correlations (**Table 18**).

**Table 18 – Correlations between RTs and positive (Pos), negative (Neg) and general (Gen) symptoms of schizophrenia in Experiment Four. \* $p < 0.05$ , \*\* $p < 0.01$ , †  $p < 0.1$**

	SCI-PANSS		
Imagine RT	Pos	Neg	Gen
Target	0.18	<b>0.52 *</b>	<b>0.52 *</b>
Non-Target	0.03	0.23	0.20
New	0.14	0.20	0.15
Perceive RT			
Target	<b>0.54 *</b>	0.03	<b>0.53 *</b>
Non-Target	0.41	0.49 †	<b>0.50 *</b>
New	0.13	0.42	0.34

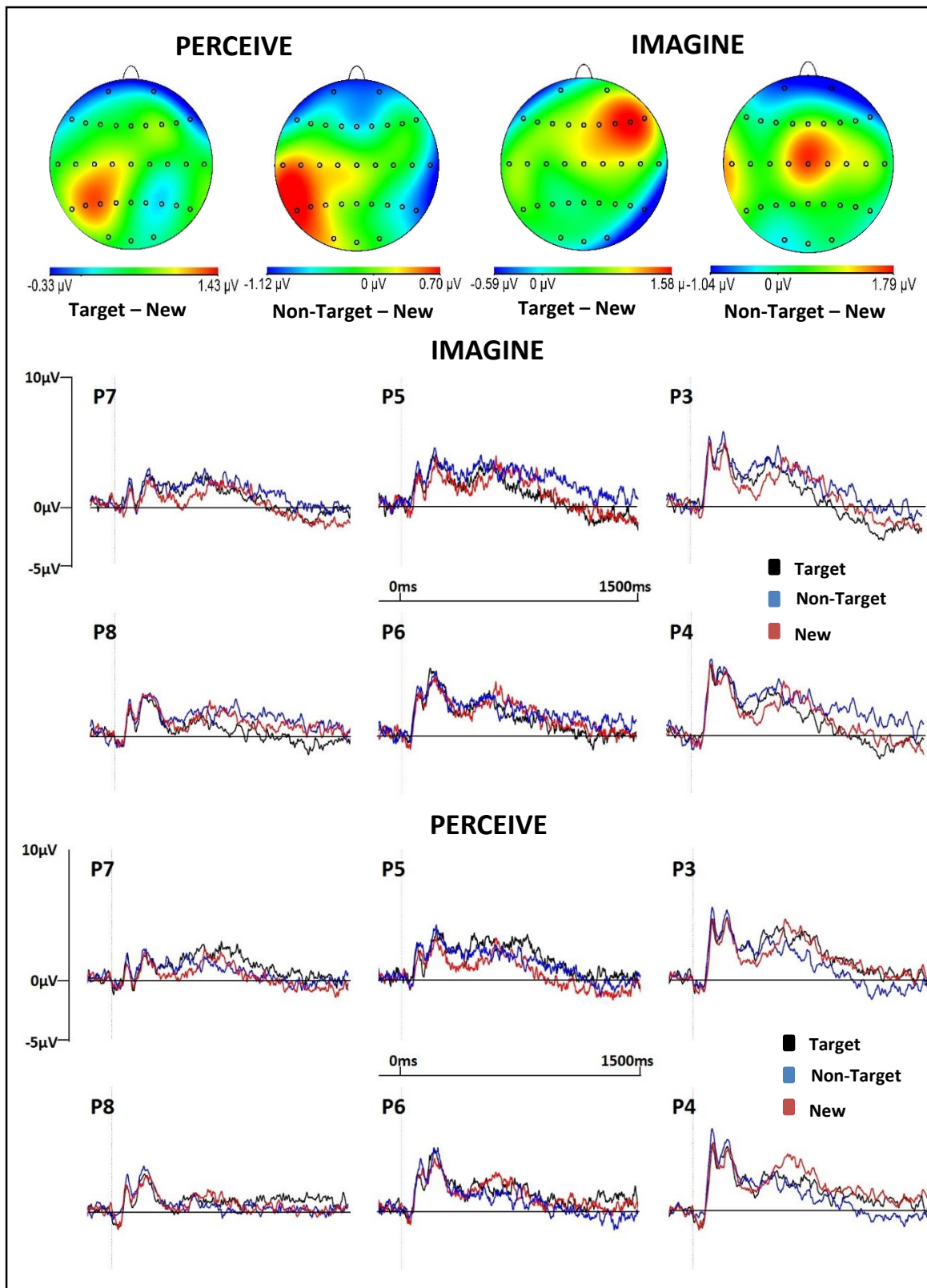
FRSS total score positively correlated with Target – New discrimination for imagine items ( $r(14)=0.52, p=0.041$ ), though the positive correlation between Target – Non-target discrimination also approached significance ( $r(14)=0.47, p=0.070$ ). In addition there was a positive correlation with Target – Non-Target discrimination value for perceive items ( $r(14)=0.57, p=0.021$ ), and the Target – New discrimination approached significance ( $r(14)=0.44, p=0.089$ ). For reaction times, only one significant negative correlation was found between FRSS total score and RT to imagine targets ( $r(14)=-0.53, p=0.034$ ). Finally, the estimate of recollection for imagine items was positively correlated with FRSS total score ( $r(14)=0.51, p=0.042$ ).

#### PRINCIPAL ERP RESULTS

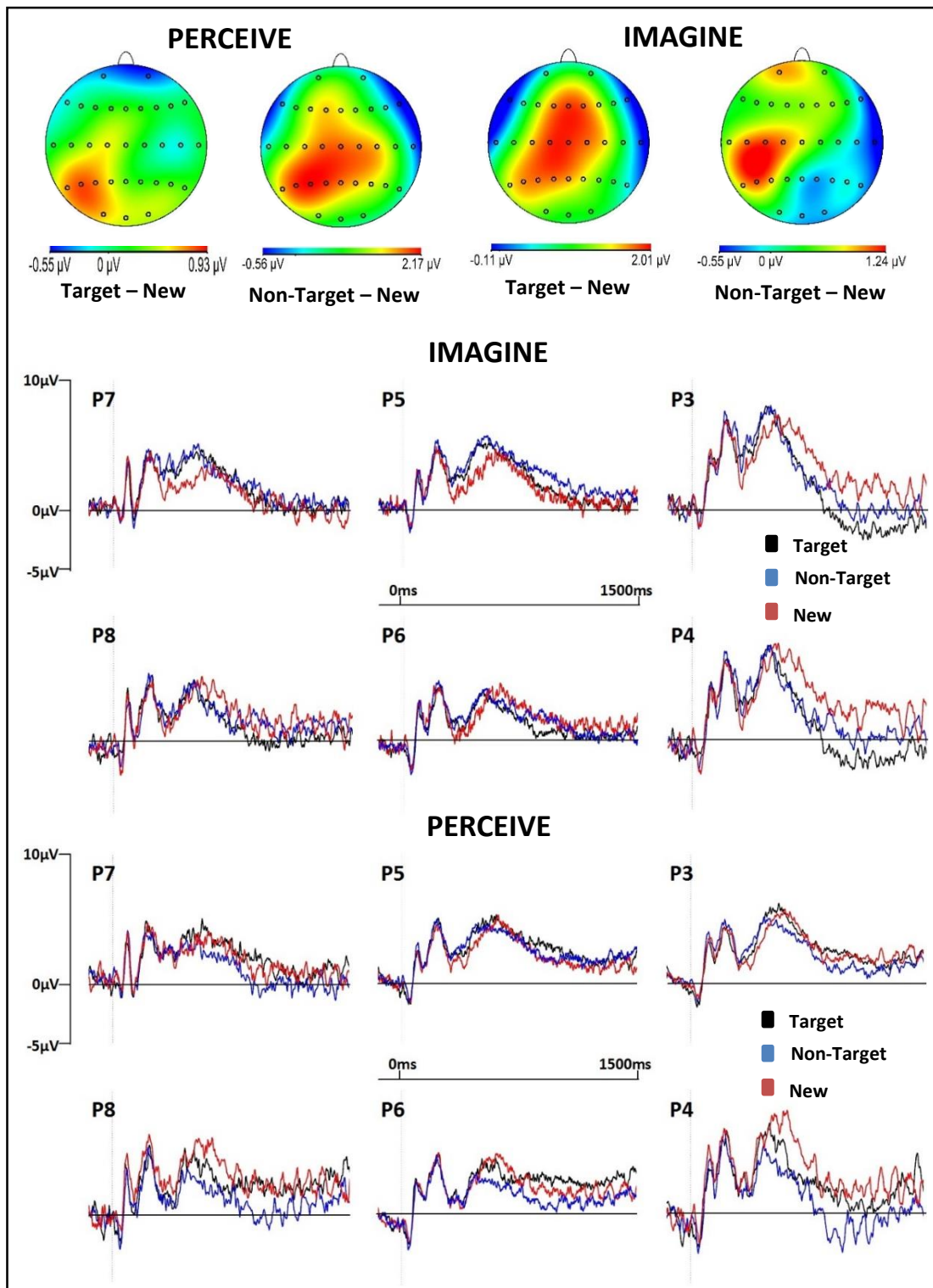
The mean numbers of trials (ranges in parentheses) contributing to each condition of interest were as follows: imagine target = 28 (18-38), perceive target = 30 (17-38), imagine non-target = 31 (22-37), perceive non-target = 30 (14-37), imagine new = 32 (19-39) and perceive new = 35 (24-39).

#### Left-Parietal Old/New Effects

Comparable to the data from control participants, there is an earlier divergence between response categories (450-600ms; as can be seen in *Figure 15*). An initial ANOVA with factors of target designation (two levels; imagine and perceive), response category (three levels; correct responses to target, non-target and new), hemisphere (two levels; left and right) and site (four levels; inferior [P7/8], medial [P5/6]



**Figure 15 – Topographic maps showing old/new effects for targets and non-targets split by target designation (imagine/perceive) from Experiment Four for the 450-600ms epoch. The maps were computed from difference scores obtained by subtracting mean amplitudes for correct responses to new items from those associated with targets and non-targets respectively. ERP waveforms are from electrodes included in the left-parietal old/new effect analysis, with the exception of P1/P2. These sites have been excluded for consistency of presentation across Experiments.**



**Figure 12 (reproduced for comparison) – Topographic maps showing old/new effects for targets and non-targets split by target designation (imagine/perceive) from Experiment Three for the 500-800ms epoch. The maps were computed from difference scores obtained by subtracting mean amplitudes for correct responses to new items from those associated with targets and non-targets respectively. ERP waveforms are from electrodes included in the left-parietal old/new effect analysis, with the exception of P1/P2. These sites have been excluded for consistency of presentation across Experiments.**

medial superior [P3/4] and superior [P1/2]) revealed significant interactions between response category and hemisphere ( $F(1.7, 25.0)=5.19, p=0.017, E=0.84$ ), target designation, hemisphere and site ( $F(2.4, 36.6)=3.23, p=0.042, E=0.81$ ) and target designation, response category, hemisphere and site ( $F(4.2, 62,3)=2.78, p=0.033, E=0.69$ ). Following up the four-way interaction within the right hemisphere revealed no significant effects. By contrast, follow up analyses within the left hemisphere revealed a main effect of response category only ( $F(2.0, 29.4)=3.50, p=0.044, E=0.98$ ), indicating target and non-target items were significantly more positive going than new items (smallest  $t(15)=2.40, p=0.03$ ), but there was no significant difference between target and non-target items.

#### PRINCIPAL ERP COMPARISONS WITH CONTROL PARTICIPANTS

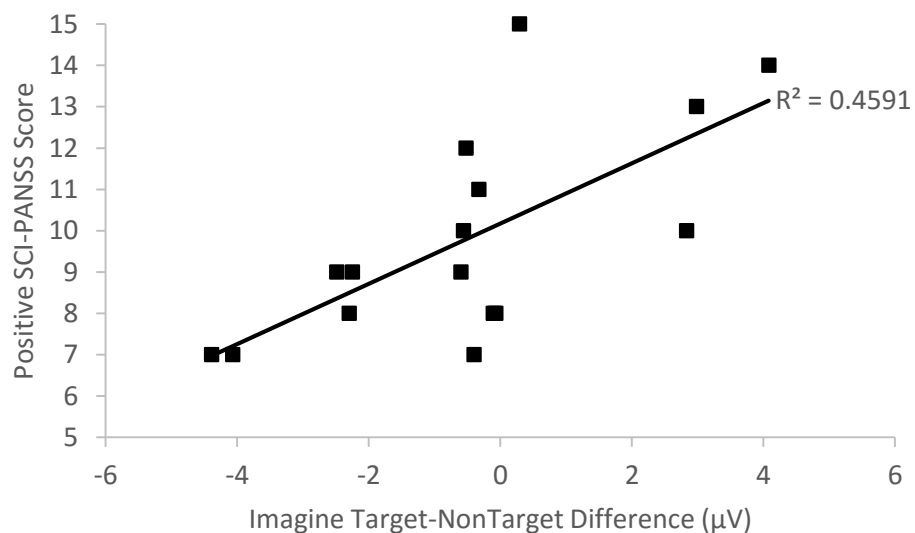
As reliable target and non-target old/new effects were identified from 450-600ms for both patient and control participants, comparisons between these groups were conducted. An initial ANOVA with factors of group (two levels; controls and patients), target designation (two levels; imagine and perceive), response category (three levels; correct responses to target, non-target and new items), hemisphere (two levels; left and right) and site (four levels; inferior [P7/8], medial [P5/6], medial superior [P3/4] and superior [P1/2]) revealed a main effect of response category ( $F(1.9, 69.6)=5.82, p=0.005, E=0.97$ ) as well as significant interactions between response category and hemisphere ( $F(1.8, 66.4)=14.94, p<0.001, E=0.92$ ) and target designation, response category, hemisphere and site ( $F(4.2, 149.7)=2.64, p=0.034, E=0.69$ ). As no significant effects involving the factor of group were identified, follow up comparisons were not conducted as effects within each group have previously been reported.

#### PRINCIPAL CORRELATIONS WITH SYMPTOMS OF SCHIZOPHRENIA AND GENERAL FUNCTIONING

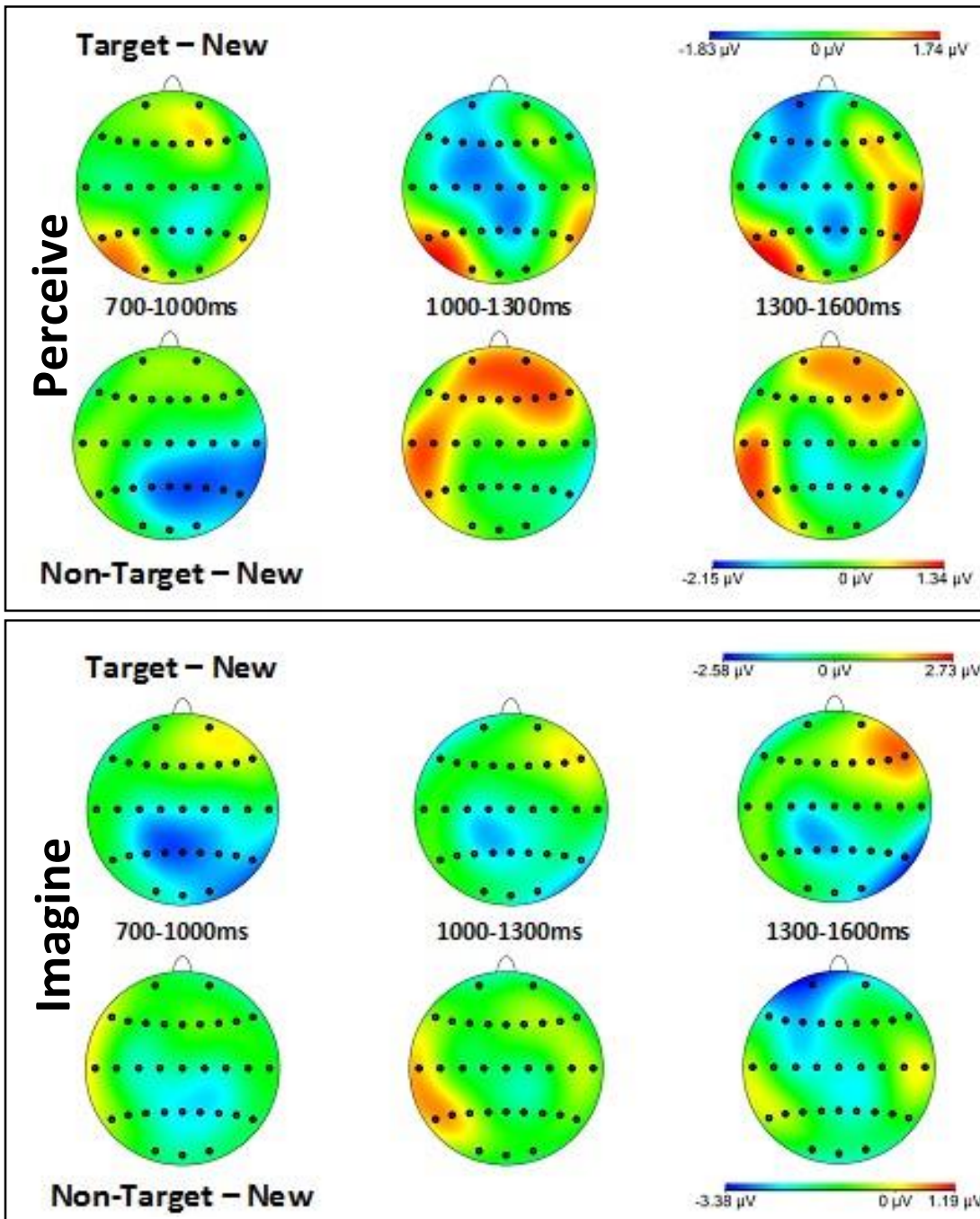
Comparably to the analysis strategy utilised in Chapter Seven: Experiment Three (page 139), considering no reliable differences were identified between target and non-target left-parietal old/new effects, it may still be fruitful to investigate how the ERP index of cognitive control was modulated by schizophrenia symptoms or general functioning. Target-non-target old/new differences were averaged across P7, P5, P3 and P1 electrode sites for the 450-600ms epoch. One significant positive correlation was identified

between positive SCI-PANSS scores and imagine target-non-target magnitude differences ( $r(14)=0.68, p=0.004$ ). On closer inspection of the data however, as can be seen in **Figure 15**, 50% of the data points centred around zero difference between target and non-target magnitudes. This raises significant concerns about the clinical relevance of this correlation.

In light of this and further consistent with the strategy employed in Chapter Seven: Experiment Three (page 139), another analysis strategy that was explored was examining correlations in relation to target and non-target old/new effects respectively. Target and non-target old/new effects were averaged across P7, P5, P3 and P1 electrode sites for the 450-600ms epoch. The magnitude difference between imagine target and new items was negatively correlated with general SCI-PANSS score ( $r(14)=-0.56, p=0.024$ ) and positively correlated with FRSS total score ( $r(14)=0.59, p=0.016$ ). To better understand the relationship between these two measures and the magnitude of target old/new effects in the imagine target designation a regression was conducted. The model predicted 39% of the variance ( $R^2=0.39, F(2, 13)=4.18, p=0.04$ ), though neither FRSS total nor general symptoms were significant predictors.



**Figure 15 – The relationship between Positive SCI-PANSS score and the difference in magnitude between target and non-target old/new effects averaged across left parietal electrode sites (P7, P5, P3, P1) in the imagine target designation for Experiment Four.**



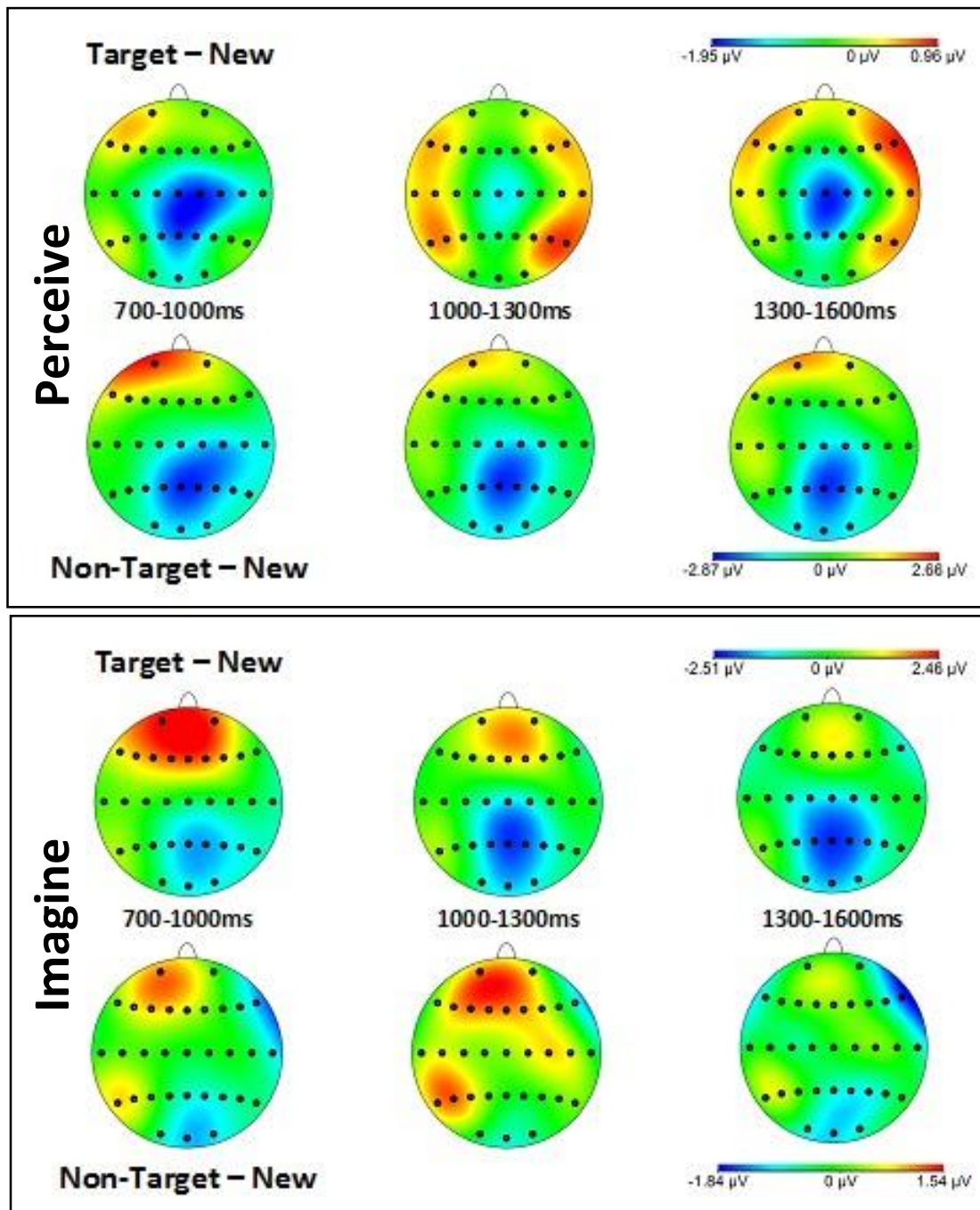
*Figure 16 – Topographic maps showing old/new effects for targets and non-targets split by target designation (imagine/perceive) for Experiment Four for three epochs between 700 and 1600ms. The maps were computed from difference scores obtained by subtracting mean amplitudes for correct responses to new items from those associated with targets and non-targets respectively.*

#### SUBSIDIARY ERP RESULTS

##### Late Posterior Negativity

As can be seen in the waveforms and scalp maps in **Figure 16** and **Figure 18**, there is a late posterior negativity emerging from approximately 700ms post-stimulus





**Figure 17 (reproduced for comparison) – Topographic maps showing old/new effects for targets and non-targets split by target designation (imagine/perceive) for Experiment Three for three epochs between 700 and 1600ms. The maps were computed from difference scores obtained by subtracting mean amplitudes for correct responses to new items from those associated with targets and non-targets respectively.**

presentation. Initial ANOVAs with the factors of target designation (two levels; imagine and perceive) and response category (three levels; correct responses to target, non-target and new items) and site (three levels; P3, Pz and P4) were conducted across three epochs (700-1000ms, 1000-1300ms, 1300-1600ms). Only one significant interaction between target designation and response category was identified, and this was in the

1300-1600ms epoch ( $F(1.7, 25.7)=3.91, p=0.039, E=0.86$ ). Following up this interaction within each target designation however revealed no significant effects. This interaction probably arose from the tendency of target and non-target items in the perceive target designation to be more negative going than new items, compared to only target items in the imagine target designation.

#### Right-Frontal Old/New Effect

As can be seen in the scalp maps in **Figure 16**, in addition to the LPN, there is a positive right frontal modulation present. To confirm the presence of this effect an initial ANOVA with the factors of target designation (two levels; imagine and perceive), response category (three levels; correct responses to target, non-target and new), hemisphere (two levels; left and right) and site (four levels; inferior [F7/8], medial [F5/6], medial superior [F3/4] and superior [F1/2]) was conducted for two separate epochs: 600-900ms and 900-1200ms. No significant effects were identified in either epoch of interest.

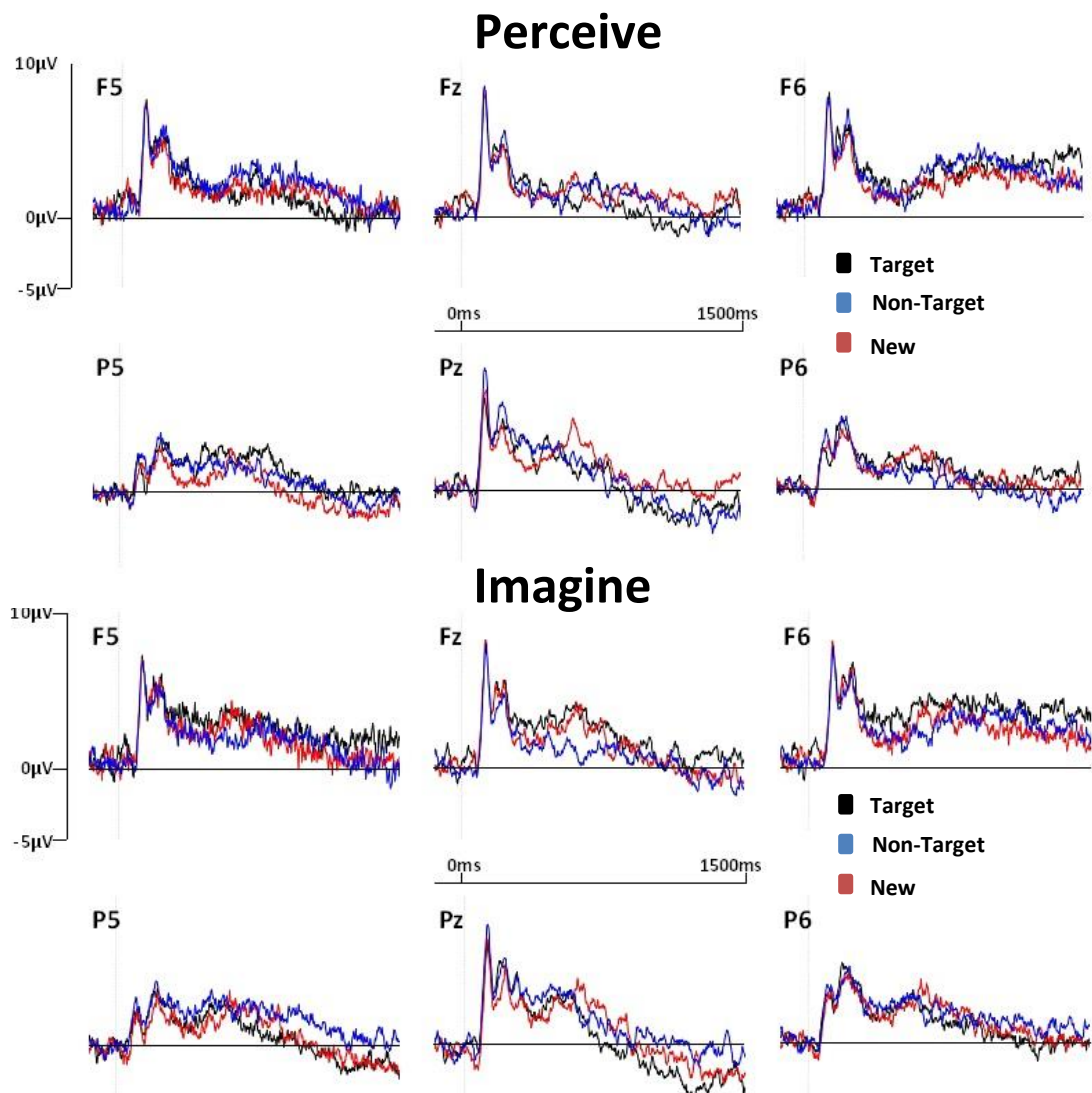
Given no significant differences between response categories were identified in analyses of right frontal old/new effects, it was not possible to pursue the question of how this index of post-retrieval monitoring varied with symptoms of schizophrenia. Furthermore, given no significant effects involving response category were identified for either control or patient participants during analyses of right-frontal old/new effects, subsidiary ERP comparisons between these groups were not pursued.

#### SUBSIDIARY ERP COMPARISONS WITH CONTROL PARTICIPANTS

##### Late Posterior Negativity

Initial ANOVAs with factors of group (two levels; control and patient participant), target designation (two levels; imagine and perceive), response category (three levels; correct responses to target, non-target and new items) and site (three levels; P3, Pz and P4) were conducted for the 700-1000ms and 1000-1300ms epoch only, considering neither group reported significant effects in the 1300-1600ms epoch. In both epochs, there were significant interactions between response category and site ( $F(3.0, 109.7)=3.51, p=0.017, E=0.76$ ;  $F(3.3, 117.1)=3.77, p=0.011, E=0.81$  for 700-1000ms and 1000-1300ms epoch respectively). In addition, there was a significant main effect of response category in the 700-1000ms epoch ( $F(1.8, 63.1)=5.88, p=0.006, E=0.88$ ). In

neither epoch were there significant effects involving the factor of group, therefore follow-up analyses were not pursued.

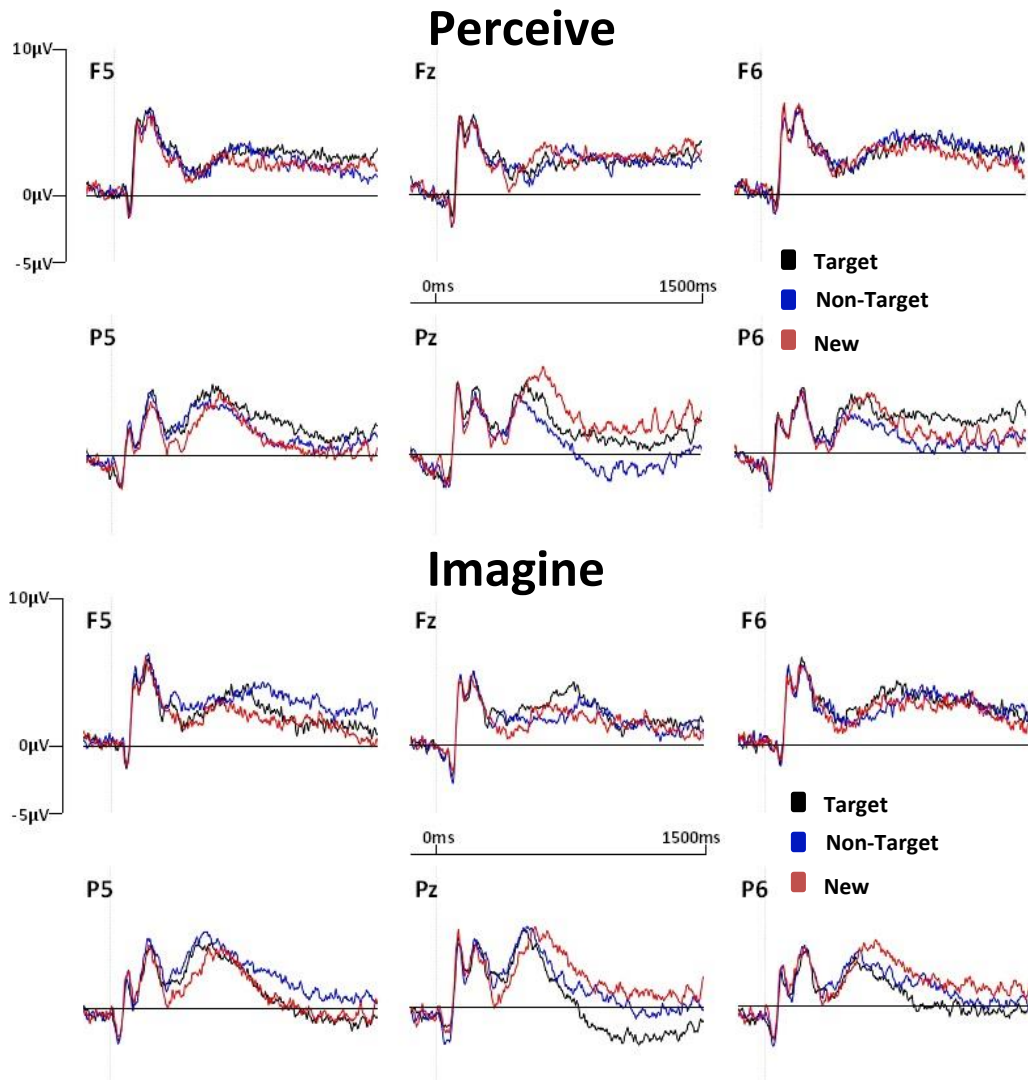


**Figure 18 – Grand average ERP waveforms elicited by targets, non-targets and new items attracting correct judgments from left and right hemisphere and midline sites at frontal (F5, Fz, F6) and posterior (P5, Pz, P6) electrode sites split by target designation (imagine/perceive) for Experiment Four**

#### SUBSIDIARY CORRELATIONS WITH SYMPTOMS OF SCHIZOPHRENIA AND GENERAL FUNCTIONING

In light of the reliable interaction between target designation and response category as well as the numerical differences between response categories in the 1300-1600ms epoch of the analyses of LPN, correlational analyses with symptoms and schizophrenia and general functioning were conducted. Target and non-target old/new effects were calculated for the perceive target designation and target old/new effects were calculated

for the imagine target designation averaged across P3, Pz and P4 electrode sites. General symptoms were negatively correlated with the magnitude of the target old/new LPN effect in the imagine target designation ( $r(14)=-0.58, p=0.018$ ).



**Figure 19 (reproduced for comparison) – Grand average ERP waveforms elicited by targets, non-targets and new items attracting correct judgments from left and right hemisphere and midline sites at frontal (F5, Fz, F6) and posterior (P5, Pz, P6) electrode sites split by target designation (imagine/perceive) for Experiment Three**

#### METHODOLOGICAL CONSIDERATIONS

When CPZE were entered into correlational analyses with behavioural and ERP measures, CPZE was only found to positively correlate with RTs to imagine target and non-target items ( $r(14)=0.67, p=0.004$ ;  $r(14)=0.65, p=0.007$  for target and non-target items respectively). Regression analyses were therefore conducted to better understand

the relationship between RT, CPZE, symptom dimensions of schizophrenia and general functioning.

Because RT to imagine targets were positively correlated with negative symptoms and negatively correlated with FRSS total score, imagine target RT was entered into regression analyses with CPZE, negative symptoms and FRSS total score as predictors. The model explained 72% of the variance in RTs ( $R^2=0.72$ ,  $F(3, 12)=10.35$ ,  $p=0.001$ ). Only CPZE significantly predicted RTs to imagine targets ( $\beta = 0.62$ ,  $t(14)=3.91$ ,  $p=0.002$ ).

RT to non-targets in the perceive target designation were entered into regression analyses with CPZE and general symptoms and the model explained 61% of the variance in RTs ( $R^2=0.61$ ,  $F(2, 13)=10.27$ ,  $p=0.002$ ). Both CPZE and general symptoms significantly predicted RTs to imagine non-target items ( $\beta = 0.60$ ,  $t(14)=3.47$ ,  $p=0.004$ ;  $\beta = 0.44$ ,  $t(14)=2.56$ ,  $p=0.024$  for CPZE and general symptoms respectively).

When Full Scale IQ (FSIQ) score was entered into correlational analyses with behavioural and ERP measures, significant positive correlations were identified for all discrimination values and estimates of recollection for both target designations. As some of these measures were significantly correlated with measures of negative symptoms and general functioning, regression analyses were conducted to better understand the relationship between these factors.

Target – New discrimination for the imagine target designation was entered into regression analyses with FSIQ, negative symptoms and FRSS total score as predictors and the model explained 60% of the variance ( $R^2=0.60$ ,  $F(3, 12)=6.00$ ,  $p=0.01$ ) with negative symptoms being the only significant predictor ( $\beta = -0.47$ ,  $t(14)=2.20$ ,  $p=0.048$ ). The same predictors were entered into regression analyses for perceive Target – Non-Target discrimination and this model explained 67% of the variance ( $R^2=0.67$ ,  $F(3, 12)=8.20$ ,  $p=0.003$ ), however FSIQ was found to be the only significant predictor ( $\beta = 0.53$ ,  $t(14)=2.89$ ,  $p=0.014$ ). When the estimate of recollection for imagine items was entered into regression analyses with the same predictors, the models explained 60% of the variance ( $R^2=0.60$ ,  $F(3, 12)=5.96$ ,  $p=0.01$ ). Negative symptoms, but not FSIQ or FRSS total score, significantly predicted estimates of recollection ( $\beta = -0.47$ ,  $t(14)=2.19$ ,  $p=0.049$ ).

Measures of anxiety were negatively correlated with the target old/new LPN effect from 1300-1600ms in the imagine target designation ( $r(14)=-0.67$ ,  $p=0.006$ ). Regression

analyses were conducted to better understand the relationship between general symptoms, measures of anxiety and the magnitude of this ERP effect. General symptoms and BAI were entered as predictors and the model explained 49% of the variance ( $R^2=0.49$ ,  $F(2, 14)=5.70$ ,  $p=0.018$ ), though neither variable was a significant predictor.

Finally, no significant correlations were identified between cigarettes per day, measures of depression and any measure of behavioural performance or ERP differences for this sample of patients.

### EXPLORATORY ERP ANALYSES

Comparably to control participants, there is a later divergence from 1000-1600ms that is more positive going for non-target items in the imagine target designation. Conducting an analogous ANOVA for the 1000-1600ms epoch as to that conducted for the 450-600ms epoch revealed a significant interaction between response category and site ( $F(2.5, 37.9)=3.72$ ,  $p=0.025$ ,  $E=0.42$ ). Following up this interaction revealed no significant differences between response categories at any site. This interaction probably arose because in the perceive target designation, target amplitudes were numerically more positive going compared to non-target and new items over inferior and medial electrode sites. By contrast, in the imagine target designation over the same electrode locations, non-target amplitudes were numerically more positive going compared to target and new items.

### EXPLORATORY CORRELATIONS WITH SYMPTOMS OF SCHIZOPHRENIA AND GENERAL FUNCTIONING

As there was a reliable interaction between response category and site as well as numerical differences between response categories in the 1000-1600ms epoch, correlational analyses were conducted. ERP magnitudes for non-target and new items were subtracted from those for target items in the perceive target designation and target and new amplitudes were subtracted from those for non-target items in the imagine target designation. Magnitudes were averaged across (inferior) P7/8 and (medial) P5/6 electrode sites separately for each target designation, considering there is no interaction with hemisphere and these were the locations where the effects were numerically largest. Only positive symptoms were negatively correlated with the magnitude ERP

difference between target and new items in the perceive target designation ( $r(14) = -0.50, p = 0.049$ ).

## DISCUSSION

### PRINCIPAL ANALYSES

#### Left-Parietal Old/New Effects and Behavioural Analyses

The principal purpose of this experiment was to investigate whether retrieval control, as indexed by magnitude differences between target and non-target left-parietal old/new effects is modulated by symptoms of schizophrenia. Comparably to matched control participants, ERP divergences exhibited a different time course to those obtained from the university samples reported in this thesis. There was an earlier divergence (450-600ms). Reliable target and non-target old/new effects were identified, though there was no significant difference between these effects. Nonetheless, comparably to Chapter Seven: Experiment Three (139), it was still considered fruitful to investigate the potential correlations with target-non-target magnitude differences. This analysis revealed one significant positive correlation between positive SCI-PANSS scores and the magnitude difference between target and non-target items in the imagine target designation. This correlation is in the opposite direction to what was hypothesised. On closer inspection of the data, it was found that 50% of the data centred around zero difference between that magnitude of target and non-target items. This raises considerable concerns around the clinical relevance of this correlation and consequently this finding was not considered further. In light of this and comparably to the strategy employed in Chapter Seven: Experiment Three (page 139), the magnitude of target and non-target old/new effects respectively from 450-600ms were correlated with symptoms of schizophrenia and general functioning scores. The magnitude of target old/new effects in the imagine target designation were positively correlated with general symptoms and negatively correlated with general functioning. In addition, there were several correlations with measures of behavioural performance and symptoms of schizophrenia. When left-parietal old/new ERP effects for patient and control participants were contrasted, no significant effects involving the factor of group were identified. By contrast, comparisons of behavioural performance revealed Target – Non-

Target discrimination was poorer, estimates of recollection and familiarity were lower and response times were longer for patient compared to control participants.

If this early divergence from 450 to 600ms is interpreted as an implicit memory effect as in Chapter Seven: Experiment Three (page 146), these results could be considered in contrast to those obtained by Matsuoka et al. (1999). Matsuoka et al. (1999) used an implicit memory task design and compared ERPs elicited from two semantic categorisation tasks with different non-target stimuli. In one task, participants were presented with words, pronounceable pseudowords and unpronounceable foreign letters. In the other task, participants were presented with meaningful words, half of which were re-presented once. These representations occurred immediately or after 4-6 words. Semantic processing effects on ERPs were observed for both patient and control participants from 200 to around 600ms, though these effects continued until around 700ms for patients. Immediate repetition effects on ERPs however were almost absent for patient compared to control participants from 300 to around 700ms. The authors suggested this latter difference reflected the failure of patients to utilise the information from the preceding words or context. It is important to acknowledge however that the results of this study contradict the common view that implicit memory is relatively spared in patients with schizophrenia (e.g. Bazin & Perruchet, 1996; Clare, McKenna, Mortimer, & Baddeley, 1993; Gras-Vincendon et al., 1994).

Assuming this parietally distributed effect is an index of recollection, the lack of group differences between control and patient participants is at odds with the behavioural data which indicates patients have deficits in recollection. Unlike the data for control participants, the present pattern of data are not easily explained by late posterior negativity attenuating parietal positivity, given the negativity onsets later in the patient sample (1300-1600ms). Rather, the ERP evidence indicates that processes acting on the contents of retrieval may contribute to the memory problems observed in patients with schizophrenia.

The present pattern of ERP results can be considered partially consistent with the results obtained by Guillaume et al. (2012). In that study, the process-dissociation procedure was applied and participants were presented with faces where intrinsic (facial expression) perceptual information was manipulated. When ERP data from the inclusion task were analysed, patient and control participants exhibited left-parietal old/new



effects for items with no facial expression changes. This is in contrast to items with intrinsic manipulations where patient participants exhibited no left-parietal old/new effects. Some of the most important comparisons with this study however arise from the behavioural data as both studies indicate patients with schizophrenia have deficits in both recollection and familiarity. The strength of the present data over that obtained by Guillaume et al. (2012) however is that residual concerns about the equivalence in processing on inclusion and exclusion tasks do not apply to the present data as estimates were derived from two exclusion tasks.

Behavioural comparisons with control participants were in the expected direction. Patient participants were worse at discriminating between target and non-target items compared to controls. This is consistent with previous work suggesting patients with schizophrenia find it more difficult than controls to differentiate between internal and external sources of information (e.g. Ditman & Kuperberg, 2005; Frith, 1992; Johns et al., 2001). Patients also had lower estimates of recollection and familiarity compared to controls, providing further support for recent findings indicating patients with schizophrenia experiences deficits in both recollection and familiarity (Libby et al., 2013). Finally, patient participants responded more slowly than control participants. These latter results are consistent with the general finding that RT are generally longer for patients compared to controls (e.g. Guillaume et al., 2007; Guillaume et al., 2012; Matsuoka et al., 1999; Tendolkar et al., 2002). Taken together, this pattern of data is consistent with previous reports of memory problems in patients with schizophrenia (e.g. Aleman et al., 1999; Libby et al., 2013).

#### Correlations with Measures of Schizophrenia Symptoms and General Functioning

Symptom scales and general functioning scores were correlated with the magnitude of target and non-target old/new effects separately for 450-600ms and revealed the magnitude of imagine target old/new effect was positively correlated with general functioning but negatively correlated with general symptoms. All correlations with behavioural measures were in the expected direction, in that those experiencing more symptoms demonstrated poorer discrimination performance and took longer to respond.

The observed correlation between the magnitude of imagine target old/new effect and symptoms of schizophrenia was in the expected direction in that those that were more symptomatic exhibited smaller old/new effects. The specific symptom dimension however, was less expected. Previous research has suggested those higher in positive (e.g. Brébion et al., 2000; Frith, 1992) or negative symptoms (e.g. Aleman et al., 1999) were negatively correlated with memory performance, thus correlations were expected with these dimensions rather than general symptoms. The present pattern of data suggests that the magnitudes of old/new differences are associated with more general psychopathology, rather than symptoms of schizophrenia specifically. This will be discussed in greater detail in Chapter Nine (page 181) By contrast, the correlation between the magnitude of imagine target old/new effect and general functioning was anticipated given cognitive deficits are the strongest predictor of functional outcome (Green et al., 2000; Puig et al., 2008). It is important to acknowledge however that neither general symptoms nor general functioning were significant predictors of imagine target old/new magnitudes, suggesting further research is required to better understand the relationship between these variables.

Measures of negative symptoms were negatively correlated with Target – New discrimination in the imagine target designation and Target – Non-Target discrimination in the perceive target designation. Negative symptoms were also negatively correlated with estimates of recollection for imagine items. These results are consistent with the findings of both Frith (1992) and Brébion et al. (2000), where patients were found to make more source attribution errors for self-generated than for externally presented information. Furthermore, these findings are consistent with those of Aleman et al. (1999), where a small but significant negative association was identified between negative symptoms and memory performance, as determined from a range of battery of standardised neuropsychological tests. These results are even more striking in light of the outcomes from regression analyses with FSIQ and general functioning where negative symptoms were the only significant predictor of target – new discrimination and estimates of recollection in the imagine target designation. These latter findings provide evidence for the independent contribution of negative symptoms to specific memory processes, namely the recollection of imagined information.

Positive correlations were identified between RT to target and non-target items and several symptom dimensions. Negative symptoms correlated with RT to imagine target items, positive symptoms correlated with RT to perceive target items and general symptoms were correlated with RT to target and non-target items in the perceive target designation and targets only in the imagine target designation. These mixed results echo the general discrepancies in the literature regarding which symptom clusters are most strongly associated with cognitive deficits (see the Relationship of Cognitive Dysfunction to Symptom Dimensions in Schizophrenia section in Chapter One for further information, page 36). Given the number of correlations with general symptoms, it may be the case that slower RTs are indicative of speed of processing deficits that are non-psychosis specific. This will be addressed in greater detail in Chapter Nine (page 184). This interpretation does however receive some support from the regression analyses where CPZE, but not negative symptoms or FRSS total, significantly predicted RT to imagine targets and both CPZE and general symptoms significantly predicted RT to imagine non-targets. The former findings suggests the observed relationships between negative symptoms, FRSS total and RT to imagine targets is more accurately explained in terms of medication effects, with those on higher doses of medication taking longer to respond. The latter findings indicate that CPZE may have contributed to the observed relationship between general symptoms and RT to imagine non-target items, with those on higher doses of medication taking longer to respond but general symptoms also independently contribute to RTs to imagine non-targets, with those higher in general symptoms taking longer to respond.

Finally, measures of anxiety and general symptoms were negatively correlated with the target old/new LPN effect from 1300-1600ms in the imagine target designation. When these factors were entered into regression analysis, the model was significant, but neither factor was found to be a significant predictor. These findings indicate that non-psychosis specific factors are likely responsible for the observed relationship, though further research would be required to better understand these factors.

#### EXPLORATORY ANALYSES

Similar to control participants, a later divergence from 1000-1600ms that was numerically more positive going for items in the perceive target designation, irrespective

of response category was observed. When target and non-target old/new measures were correlated with symptoms of schizophrenia and general functioning, positive symptoms were negatively correlated with target old/new effects in the perceive target designation. Unlike the control participants, these effects cannot be easily accounted for by LPN given the lack of correspondence in electrode locations. Nonetheless, the influence of the LPN on more lateral parietal effects cannot be ruled out considering the possibility for overlap between parietal old/new effects and LPN as previously discussed by Herron (2007). Thus, further investigation would be required to understand the functional significance and relationship of this ERP effect to symptoms of schizophrenia

## CONCLUSIONS

Taken together, reliable old/new ERP effects were identified from 450-600ms post-stimulus presentation for patients with schizophrenia. Whilst the imagine target old/new effect was positively correlated with general functioning and negatively correlated with general symptoms, neither of these factors were identified as significant predictors of the magnitude of this ERP effect. By contrast, negative symptoms were the only significant predictor of target-new discrimination and estimates of recollection for imagine items, indicating memory processes in patients with schizophrenia are not equally affected. These latter findings provide further support for the importance of understanding the relationship between symptoms and memory processes. In doing so we may be able to develop interventions to alleviate specific memory problems in people with schizophrenia.

## CHAPTER NINE: GENERAL DISCUSSION

### OVERVIEW

Approximately 75-85% of patients with schizophrenia have cognitive deficits (Reichenberg et al., 2006), with episodic memory being one of the most profoundly affected cognitive domains (Aleman et al., 1999; Mesholam-Gately et al., 2009). The functional basis for these problems however is not well understood. One parsimonious explanation for multiple cognitive deficits in patients with schizophrenia is that these problems arise in whole or in part, because of impaired higher-order processes such as cognitive control (Cohen & Servan-Schreiber, 1992; Kraepelin, 1919/1971). In work to date however, this possibility has not been explored in detail. The experiments in this thesis were designed to investigate whether deficits in cognitive control during retrieval contribute to memory problems in people with schizophrenia.

In pursuit of this, a combination of behavioural and ERP measures were utilised and multiple measures were collected from healthy individuals and patients with schizophrenia. Behavioural assessments were intended to probe the memory processes affected by schizophrenia. Individual difference and neural measures were employed to examine the mechanisms underlying any deficits identified.

The following sections are broken down as follows. First, summaries of the key behavioural and electrophysiological results obtained from the experiments reported in this thesis. Second, in separate sections, there are interpretations of these results. Subsequent sections discuss some of the limitations associated with the approaches adopted in pursuit of the aforementioned research questions, before addressing broader theoretical considerations raised through the course of this investigation and considering future directions.

### SUMMARY

Healthy university students (Experiments One and Two, pages 86 and 112), older adult community residents (Experiment Three, pages 130) and patients with schizophrenia or schizoaffective disorders (Experiment Four, pages 153) were recruited for the experiments reported in this thesis. In all experiments, participants completed a reality

monitoring exclusion task while ERP data were acquired. Participants were presented with words followed by either a picture of the object denoted by the word or a blank screen where participants were encouraged to imagine a picture of the object. In a subsequent test phase, these words were re-presented, interspersed with unstudied words. Participants made binary responses; one for studied words from a 'target' context, another for unstudied words and studied words from the alternate 'non-target' context. In addition, participants completed a battery of psychometric and neuropsychological assessments including a working memory capacity task and measures of schizotypy, which is a dimensional correlate of schizophrenia (university and community participants only).

An exclusion task was chosen as previous research has shown that under some circumstances the recovery of target information can be prioritised over that of non-target information (e.g. Herron & Rugg, 2003). The magnitude difference between target and non-target left-parietal old/new effects has been interpreted as an ERP index of control processes exerted during memory retrieval (e.g. Herron & Rugg, 2003; Rosburg et al., 2011b). A reality monitoring version of this task was chosen as there is evidence to suggest patients with schizophrenia have particular difficulty discriminating self-generated from externally presented information (e.g. Brébion et al., 2000; Frith, 1992).

The principal aims of the experiments reported in this thesis were: i) to understand whether, and if so how, behaviour and ERP measures of memory processes differ between patients with schizophrenia and control participants, and ii) to understand the relationship between symptoms of schizophrenia and/or dimensions of schizotypy and measures of behavioural performance and ERP indices of retrieval and post-retrieval control. In keeping with this, reaction times, discrimination values and estimates of familiarity and recollection were contrasted between patients with schizophrenia and matched control participants. These measures were correlated with symptoms of schizophrenia and assessments of schizotypy. Once left-parietal old/new effects, LPNs and right-frontal old/new effects for target and non-target items were identified at the group level, the magnitudes of these ERP effects as well as, where possible, the differences between them were correlated with symptoms of schizophrenia and schizotypy dimensions.

## Behavioural Results

The tasks were designed with a view to words associated with both study contexts being equally memorable. This was broadly achieved, although the estimates of recollection and familiarity derived from the process-dissociation procedure (PDP) differed in some cases. Most importantly, patient estimates of recollection and familiarity were lower than those of matched controls. Moreover, the controls performed comparably to the university students. For reaction times, there was a tendency in Experiments One and Two for faster responses for words studied in the perceive condition.

When measures of recollection and familiarity were correlated with measures of schizotypy there was no overall consistency between the experiments reported in this thesis. In Experiment One, estimates of familiarity in the perceive target designation were negatively correlated with a positive measure of schizotypy (PDI Total). In Experiment Two an estimate of familiarity was also found to correlate with a measure of schizotypy, though unlike Experiment One this was a *positive* correlation between the estimate for *imagine* items and a positive measure of schizotypy (UnEx). No significant correlations involving recollection and familiarity were identified in Experiment Three. When correlations were conducted with symptoms of schizophrenia however (Experiment Four), negative symptoms were negatively correlated with Target – New discrimination in the imagine target designation and Target – Non-Target discrimination in the perceive target designation. This symptom dimension was also negatively correlated with estimates of recollection in the imagine target designation. Finally, analyses with RT revealed several positive correlations across all symptom dimensions. Moreover, in Experiment One, RT for target items in both target designations, as well as new items in the imagine target designation, were also positively correlated with positive measures of schizotypy (UnEx and LSHS-R Total).

There are a number of confounds associated with conducting patient work (e.g. medication effects, comorbid diagnoses). To investigate whether some of the correlations between behavioural performance and symptoms of schizophrenia could be wholly or partially accounted for by these variables regression analyses were conducted. Full Scale IQ (FSIQ) was positively correlated with all discrimination values and estimates of recollection for both target designations. Subsequent regression analyses revealed negative symptoms were the only significant predictors of Target – New discrimination

and estimates of recollection in the imagine target designation. However, FSIQ, but not negative symptoms significantly predicted Target – Non-Target in the perceive target designation. Chlorpromazine equivalents (CPZE) were positively correlated with RT to imagine target and non-target items. CPZE, rather than negative symptoms, significantly predicted RTs to imagine targets, though both CPZE and general symptoms significantly predicted RTs to imagine non-target items. Finally, comorbid symptoms of depression and anxiety were not correlated with any behavioural measures in the patient sample.

### Principal ERP Results

Analysis of the left-parietal ERP old/new effects in Experiment One indicated participants could prioritise recovery of target information at the expense of non-target information, as indicated by the greater positivity for target old/new effects relative to non-target old/new effects from 500-800ms. There was, however, no correlation between schizotypy scores and the ERP evidence for the extent of retrieval prioritisation. One potential explanation was that the likelihood of retrieving target information was high, enabling participants to easily apply retrieval control strategies.

Experiment Two was designed to assess this possibility by increasing task difficulty and consequently reducing the likelihood of successfully retrieving target information. To achieve this, participants were presented with additional foil items during the study phase. Furthermore, a one hour retention interval between study and test was introduced. Levels of response accuracy were significantly lower in this experiment than in Experiment One. Despite the increased task difficulty, ERP measures indicated participants could prioritise recovery of target information at the expense of non-target information. There was still, however, no correlation between schizotypy scores and the ERP evidence for the extent of retrieval prioritisation. Given the sample of university students used in this experiment, it was considered these data may not be broadly representative of the way in which retrieval control strategies are utilised. That is, examining control processes in university students alone can be regarded as a conservative approach to this topic, given this population is usually associated with a number of protective factors that may minimise the impact of experienced problems (Lenzenweger, 2006).



To investigate this possibility, in Experiment Three participants were recruited from the general community. It was assumed this manipulation would reduce the likelihood participants would be versed in learning strategies, and thus be more likely to reveal any memory control deficits in people high in schizotypy. Left-parietal old/new effects demonstrated a different time course for participants in this experiment, as well as in Experiment Four. Consequently, target and non-target ERP old/new effects were analysed from 450 to 600ms. Despite superior levels of accuracy on the exclusion task to those exhibited by the university students, in this sample there was no evidence of prioritisation of retrieval of some contents over others.

Importantly, the absence of correlations with schizotypy measures in the aforementioned studies does not preclude investigations of these processes in patients with schizophrenia. Rather, by examining patterns of performance in both schizotypy and schizophrenia it is possible to gain better understanding of the relationship between these constructs. Comparably to control participants, although reliable target and non-target old/new effects were obtained from 450-600ms post-stimulus presentation, patients with schizophrenia did not demonstrate evidence for the prioritisation of some contents over others. As there was no significant difference between target and non-target old/new effects, symptoms of schizophrenia were correlated with the magnitude of target and non-target old/new effects respectively. General symptoms were negatively correlated with the magnitude of the imagine target old/new effect. The magnitude of this effect was also positively correlated with measures of general functioning. To better understand the relationship between these dimensions regression analyses were conducted. The model predicted 39% of the variance, though neither FRSS total nor general symptoms were significant predictors. CPZE, FSIQ and BDI scores were not significantly correlated with these ERP measures or those resulting from subsidiary ERP analyses. Finally, when ERPs from patients and older adult community participants were contrasted no significant effects involving the factor of group were identified.

#### Subsidiary ERP Results

These analyses were conducted to gain a better understanding of how post-retrieval control processes may contribute to memory in schizotypy. Two ERP effects were investigated: the Late Posterior Negativity (LPN) and the right frontal old/new effect. Both effects are assumed to index control processes that are engaged downstream or at

least in parallel with memory retrieval (see Chapter Three: Memory, Models and Frameworks for details, page 73), and therefore offer a means of assessing links between memory monitoring, schizotypy and schizophrenia.

#### Late Posterior Negativity

The first reliable correlations with schizotypy were obtained in Experiment Three, where the analyses were conducted on target and non-target old/new effects separately, rather than the differences between these effects. Measures of negative schizotypy were positively correlated with target old/new LPN effects in the imagine target designation and non-target old/new LPN effects in the perceive target designation. Patients in Experiment Four also exhibited reliable LPN effects. Finally, general symptoms and measures of anxiety were negatively correlated with the magnitude of the LPN from 1300-1600ms.

#### Right Frontal Old/New Effects

In Experiment Two, several positive correlations were identified between measures of positive and disorganised schizotypy and the magnitude of right frontal target old/new effects in the imagine target designation. Positive correlations were also identified between measures of positive schizotypy and non-target old/new effects in the perceive target designation. This is in contrast to Experiment One where no significant correlations were identified between this ERP measure of post-retrieval control and measures of schizotypy. Finally, as no reliable target or non-target old/new effects were identified in either Experiment Three or Four, it was not possible to pursue further analyses investigating how this index of post-retrieval monitoring varied with measures of schizotypy or symptoms of schizophrenia.

### INTERPRETATION OF RESULTS

#### Behavioural Results

The comments here are directed primarily at findings from the patient sample. Crucially, negative symptoms were the only significant predictor of Target – New discrimination and estimates of recollection in the imagine target designation. These findings are consistent with previous reports indicating patients with schizophrenia have greater difficulty discriminating between internal and external sources of information compared

to control participants (e.g. Ditman & Kuperberg, 2005; Frith, 1992; Johns et al., 2001). Moreover, the correlations between these aforementioned measures and the negative symptom dimension are consistent with findings from Aleman et al. (1999) who identified a relationship between memory performance and negative symptoms.

The lower estimates of recollection and familiarity are also important because of disparate findings across studies. Whilst there is general agreement that patients with schizophrenia experience deficits in recollection, this is not the case with familiarity. Libby et al. (2013) proposed two principal reasons for the mixed results for familiarity. First, there may be substantial variation in the extent to which schizophrenia affects familiarity compared to recollection. Alternatively, differences may arise as an artifact of the manner in which estimates of familiarity are derived across studies. This latter point is particularly pertinent to studies using the Remember-Know paradigm; one of the most commonly used paradigms for investigating memory in patients with schizophrenia (Libby et al., 2013).

Many studies deriving estimates of familiarity using this method simply compare proportions of Know responses between control and patient participants (Libby et al., 2013). This is problematic as the proportion of Know responses does not take into account that a degree of familiarity may also be associated with Remember responses, unless it is assumed that the processes are mutually exclusive (Yonelinas & Jacoby, 1995). Furthermore, old items only receive a Know response if they do not receive a Remember response. Thus, when proportions of Remember responses are low, potentially as a result of conservative response criteria, proportions of Know responses may be inflated (Libby et al., 2013). Together, this suggests that by using this method, estimates of familiarity may be under- or over-estimated. As estimates of familiarity in the present data were derived using the process-dissociation procedure (Jacoby, 1991), some of these criticisms have been avoided. Refer to the Behavioural Paradigms subsection of Chapter Three: Memory, Models and Frameworks however, for the limitations of this approach (page 58).

Importantly though, one of the underlying assumptions of this procedure is the invariance of familiarity. Toth et al. (1995) emphasised that if participants were to utilise familiarity differentially across conditions (e.g. alter their response criterion) this would be reflected in different false alarm rates, which should be reported in every paper using

the process-dissociation procedure and used to inform any conclusions drawn. When false alarm rates were evaluated for the experiments reported in this thesis however, there was evidence to suggest participants utilised familiarity to a greater extent for items presented in the imagine target designation compared to those presented in the perceive target designation (See Appendix Chapter D for data, page 249). Whilst this violates the assumption of invariance, these findings are consistent with interpretations of the ERP data in that together they provide evidence for content-specific retrieval processes. For further details of this interpretation refer to Appendix Chapter B and the Left-Parietal Old/New Effects subsection of this chapter, pages 246 and 178 respectively.

Turning to the correlational outcomes across Experiments One, Two and Three, it may be that the lack of consistency has arisen as a consequence of conducting multiple correlations with no correction for multiple comparisons (see the subsection on Sensitivity Issues later in this chapter for more details, page 195). However, it is interesting that in the university samples positive symptom dimensions seem to be implicated, whereas in the older, patient sample negative symptoms are implicated to a great extent. One possibility is that these differences are indicative of neurodevelopmental changes to the mechanisms underlying memory deficits in patients with schizophrenia.

The positive correlations between reaction times and multiple symptom dimensions potentially indicate general speed of processing deficits in patients who are more symptomatic. These outcomes are consistent with the findings of Aleman et al (1999) who found attention-processing speed to be the second most profoundly affected subdomain of cognition behind immediate verbal memory, and is consistent with the findings of many other research groups (e.g. Blanchard et al., 2010; Braff & Saccuzzo, 1982; Cadenhead et al., 1997; Schatz, 1998). Whilst it could be that higher doses of medication produce greater latencies in motor responding, given that CPZE is a significant predictor of RTs to imagined but not perceived items, this provides evidence against delay in general motoric responding. Rather, it suggests that there is a slowing for cognitive processes related to imagined information only. Further support for differential processing of imagined compared to perceived information can be found in the ERP analyses reported in Appendix Chapter B, page 246. To anticipate, the data reported in the appendix demonstrate that the recovery of imagined information is

associated with more frontally distributed old/new effects compared to the recovery of perceived information.

The current data suggest smoking status or number of cigarettes smoked has not influenced the observed findings. It is notable however that some researchers have suggested patients with schizophrenia extract more nicotine per cigarette compared to the general population (Strand & Nybäck, 2005), and this cannot be ruled out here.

The absence of relationships between behavioural measures and symptoms of anxiety and depression in patients with schizophrenia is surprising, especially considering the present sample included people diagnosed with schizoaffective disorders. Most patients were also taking mood stabilising medication however, so this may have influenced the correlational analyses in the patient sample.

Overall, the present pattern of data highlights the benefit of using specific measures of behavioural performance to better understand cognitive problems in patients with schizophrenia. Furthermore, there is evidence to suggest that the processing of imagined information specifically is most adversely affected in patients with schizophrenia relative to controls.

#### Left-Parietal Old/New Effects

Although attenuations of non-target left-parietal old/new effects (relative to targets) were observed in Experiments One and Two, where university students were recruited as participants, this was not the case in Experiments Three and Four, where older adults from the community and individuals with schizophrenia participated. These findings are important because levels of response accuracy for patient and control participants were at least as high as performance for university students.

The fact that ERP changes suggesting retrieval prioritisation are evident only in the young participants under these conditions suggests strongly that the likelihood of recovering information about targets is not the only determinant of when a strategy of prioritising some contents over others will be adopted. These data therefore converge with those of Elward and Wilding (2010). In that study, working memory capacity predicted the extent to which prioritisation of target retrieval occurred. It may be that the data reported here

converge on the same conclusions because one factor common to the patient and control participants is that they were older than the university participants.

Numerous researchers have documented the negative correlation between age and working memory capacity (e.g. Light & Anderson, 1985; Mattay et al., 2006; Wingfield, Stine, Lahar, & Aberdeen, 1988), and as already noted, working memory capacity has been found to be positively correlated with the magnitude difference between target and non-target left-parietal old/new effects (Elward et al., 2012). Different measures of working memory capacity were adopted across the experiments reported in this thesis, and as a result it is difficult to assess the correspondences between the findings in Experiments One and Two, and those in Experiments Three and Four. Age, as a proxy for working memory capacity does, however, provide a parsimonious account of the results in this thesis regarding electrophysiological evidence for when prioritisation does and does not occur.

There are other considerations, however. Another factor associated with age that could account for the present pattern of results across experiments is the ability of participants to distinguish the study contexts. There is much evidence to suggest the contexts utilised in these experiments are distinct for specific reasons. For example, Mintzer and Snodgrass (1999) proposed pictures are distinctive due to the sensory processing and semantic features which are activated when these stimuli are presented. In contrast, imagined material is distinctive due to self-generation processes which are necessarily activated during task performance (Cornoldi, De Beni, & Pra Baldi, 1989). Furthermore, there is evidence to suggest source memory declines with age (e.g. McIntyre & Craik, 1987; Schacter, Osowiecki, Kaszniak, Kihlstrom, & Valdiserri, 1994), possibly as a result of declining frontal function in older adults (Glisky, Rubin, & Davidson, 2001). The importance of frontal function to recovering context-specific information receives support from neuroimaging studies.

Increased anterior prefrontal cortex activation, as indexed by Functional Magnetic Resonance Imaging (fMRI), has been associated with the recovery of self-generated, compared to externally presented information (e.g. Simons, Henson, Gilbert, & Fletcher, 2008; Simons, Owen, Fletcher, & Burgess, 2005; M. S. Turner, Simons, Gilbert, Frith, & Burgess, 2008). ERP old/new effects have also indicated a degree of sensitivity to the contents of what is retrieved. For example, faces but not words have been found to

exhibit anteriorly extended old/new effects during the same time window as left-parietal old/new effects (Yick & Wilding, 2008). The authors proposed this anterior projection reflected the on-line recovery of content associated with faces but not with words (which does not of course necessitate that the effect is specific to faces). The differential topographic distribution between contents suggests not entirely overlapping neural networks were involved in the recovery of these different memory contents. Refer to Appendix Chapter B (page 246) for analyses using broader electrode arrays to examine content-specific effects across all experiments reported in this thesis.

Crucially however, despite the smaller parietal old/new effects in Experiments Three and Four, compared to Experiments One and Two, which could reflect impoverished recovery of contents, behavioural performance for older adults and patients is still high. Thus, rather than being unable to distinguish between the study contexts, it may be more difficult for older adults and individuals with schizophrenia to capitalize on these differences to guide subsequent strategic retrieval. Cohen and Servan-Schreiber (1992) have previously emphasised the importance of contextual cues to memory problems in patients with schizophrenia. This interpretation however, begs the questions as to why prioritisation might occur in the first place. In principle, it could be argued that it will always be better to attempt to recover information about targets and non-targets. However, as highlighted by Bridger, Herron, Elward, and Wilding (2009) it may be that by attempting to recover both, the possibility of recovering information about either is reduced. Thus, under this latter assumption by using cognitive control to prioritise the recovery of information from one study context, overall behavioural performance may be improved.

Other researchers have proposed that bottom-up, rather than top-down cognitive control mechanisms, may actually drive the retrieval of non-target information, in that the presentation of non-target cues reactivates this information (Rosburg et al., 2011b). The authors nonetheless emphasised that these mechanisms may be complemented by top down mechanisms under certain circumstances (e.g. low task difficulty). Whilst the present pattern of data and aforementioned account does not preclude bottom-up mechanisms, the attenuated non-target old/new effects in light of the behavioural accuracy strongly suggest top-down mechanisms contributed, consistent with most

interpretations of this pattern of results (e.g. Elward & Wilding, 2010; Herron & Rugg, 2003).

Finally, the time course of parietal old/new effects reported in Experiment Three and Four differed from that previously reported in both university and older adult samples (e.g. Dywan et al., 2002; Wilding et al., 1995). In earlier chapters, the possibility that the earlier parietally distributed effect indexes implicit memory was considered, alongside the possibility that it is in fact a parietal old/new effect that indexes recollection, with the effect being truncated perhaps by the overlapping onset of the LPN. Both of these accounts are in principle possible, and perhaps the most important element of these data is the fact that age might reasonably be identified as the determinant of the changes across experiments: Broadly, the ERP data from Experiments Three and Four are similar to each other and differ from the data from Experiments One and Two. These outcomes highlight the need for baseline data across age groups and common tasks to understand the effects that are typically observed, as well as their time courses. Support for this view also stems from studies with young populations (children and adolescents) where substantive differences in ERP morphologies and effect sizes are sometimes seen (e.g. Sprondel, Kipp, & Mecklinger, 2011).

It may also be the case that with increasing age comes increasing variability within and across individuals in the time course of cognitive processes. As ERPs are typically averaged over several trials of the same kind, and grand average figures are averaged over groups, it is difficult to assess this, and certainly at the level of individual trials very difficult to select time periods that might accurately reflect a process of interest. Alternatively, and consistent with the outcomes of the other experiments reported in this thesis, exerting cognitive control during retrieval is not necessarily problematic for people with schizophrenia and does not necessarily contribute to observed memory deficits in these patients.

#### Late Posterior Negativity

Johansson and Mecklinger (2003) proposed that under conditions of low response conflict, the LPN reflects attempts to retrieve contextual information and to reconstruct the study episode by retrieving and evaluating attribution conjunctions. This interpretation is consistent with data from Herron (2007) who suggested that a



subcomponent of the LPN emerging 1200-1900ms post-stimulus presentation reflected retrieving and/or evaluating attribution conjunctions. The proposed time course of this subcomponent is consistent with the effect identified in the present investigations. Notably, there is possibly greater scope for there to be multiple attributes associated with imagined relative to perceived information, as a result of the presumably greater variability in the images generated by individuals during encoding. Support for this can be found in **Table 19** in Appendix Chapter C (page 248), where there are large individual differences in the ability of participants to imagine events as measured by the Vividness of Visual Imagery Questionnaire (VVIQ; Cui et al., 2007; Marks, 1973). Thus it is possible that engaging post-retrieval processes of the kind indexed by the LPN helps the accuracy of judgments for imagine items for certain individuals.

The ERP data provide some support for this. The ERP target – non-target differences in the perceive target designation for Experiments One and Two from 900-1200ms post-stimulus presentation were positive-, rather than negative-going. It could be that this activity reflects latency in the left-parietal old/new effect, a positive going effect, rather than the LPN, which as the name suggests is a negative-going effect. The possibility of overlap between parietal old/new effects and LPN was previously discussed by Herron (2007). This interpretation seems at odds with the ERP literature however as longer latencies for various ERP components have previously been reported for patients with schizophrenia compared to control participants (e.g. Guillaume et al., 2007; Niznikiewicz et al., 1997), but not in young control participants. Moreover, this interpretation does not seem to be supported by the behavioural data as shorter RTs were reported for young, control participants compared to older adults and those with schizophrenia. Thus, latencies in ERP effects would be expected in Experiments Three and Four, rather than One and Two. Nonetheless, Herron (2007) identified a subcomponent of LPN from 600-1200ms post-stimulus presentation that may index the search for episodic information, though granted the old/new difference reported in this paper were negative going in nature, rather than positive-going as in the present data. The multiple differences in experimental design between the experiments reported here and those by Herron (2007) however, may have contributed to these differences.

For Experiments One and Two, whilst it appears post-retrieval control mechanisms were differentially engaged between target designations, the extent to which these processes

were engaged was not modulated by schizotypy scores. Although this suggests schizotypy may not be related to post-retrieval control mechanisms, it is important to acknowledge there were correlations between another ERP index of post-retrieval monitoring and measures of schizotypy in Experiment Two.

Johansson and Mecklinger (2003) proposed that under instances of high response conflict, LPNs may reflect response monitoring processes. Given the length of the test phases and the fact response instructions change only once, it is unlikely there is high response conflict in Experiment One or Two. In Experiments Three and Four however, given the greater number of study-test phases, and the fact that each is shorter than in the preceding experiments, the response requirements change more frequently which may have produced more response conflict for participants. Thus, it may be the case that LPNs in Experiment Three reflect response monitoring rather than monitoring of the contents of retrieval, and those higher in schizotypy needed to engage in greater response monitoring to maintain performance. This interpretation however, does not necessarily explain the presence of late posterior negativity effects mostly for imagine items across all experiments. This difference between target designations suggests that LPN in the present data does also reflect monitoring of the contents of retrieval, but that response monitoring may be more important in relation to schizotypy. Importantly though, whilst response monitoring may not seem immediately relevant to cognitive control, response monitoring is reliant upon the maintenance of external goals (or rules), and thus reflects a core component of cognitive control.

Finally, the correlations observed in Experiment Three involved negative symptom dimensions. Negative symptoms have previously been associated with memory performance and measures of cognitive control as measured by standard neuropsychological tests (e.g. Aleman et al., 1999; Nieuwenstein et al., 2001). Similar correlations with ERP measures in the Experiment Four however revealed general symptoms and anxiety were implicated, suggesting non-psychosis specific mechanisms may determine the extent to which post-retrieval processes are engaged. It is important to acknowledge however, that correlations with schizotypy in Experiments One and Two, for both the behavioural and ERP analyses, implicated measures of positive schizotypy. Considering the significant differences in age between the samples recruited in

Experiments One and Two and those in Experiments Three and Four, it could be that symptoms differentially modulate cognitive performance throughout the life span.

#### Right Frontal Old/New Effects

Cruse and Wilding (2009) proposed that the right-frontal old/new effect indexes processes involved in the monitoring of retrieved information in service of task goals. Evans et al. (2010) similarly proposed that the right-frontal activity that emerged 800ms post-stimulus presentation in a variant of an exclusion task for target items relative to new items could be explained in terms of monitoring processes involved in the evaluation of recovered information, in service of task-relevant goals (see also Rugg et al., 2000). Given the time course of the effects and the pattern of data reported in Experiment One and Two, this interpretation suggests that monitoring processes were engaged to a greater extent when imagine items were designated as targets compared to when perceive items were designated as targets.

No significant right frontal old/new effects were identified in either Experiment Three or Four. This might be seen as raising a question about the utility of this ERP marker as an index of post-retrieval monitoring in samples beyond healthy, university participants. Researchers investigating right frontal old/new effects in relation to older adults have obtained mixed results. For example, Trott, Friedman, Ritter, and Fabiani (1997) compared younger and older adults on tests of item and source memory. Older adults, relative to younger adults, showed a greater source compared to item memory decrement. Furthermore, whilst both younger and older participants exhibited posteriorly distributed parietal old/new effects, only younger adults displayed late frontal old/new effects. By contrast, Mark and Rugg (1998) whilst also demonstrating greater source relative to item memory deficits in older compared to younger adults, reported older adults exhibited parietal and frontal old/new effects that were comparable to younger adults in terms of both magnitude and topography. The latency of these effects differed between groups though, with effects emerging after longer latencies for older adults. Mark and Rugg (1998) proposed the poor source accuracy of older adults recruited by Trott et al. (1997) may have contributed to the absence of late frontal old/new effects: older adults made correct source judgments only 55% of the time, whereas in the study conducted by Mark and Rugg (1998) the figure approached 90%.

More recently, Swick, Senkfor, and Van Petten (2006) compared healthy older and younger adults to patients with prefrontal cortex (PFC) lesions. Patients with PFC lesions exhibited item and source memory deficits compared to both older and younger adults. Furthermore, older adults exhibited decrements in both item and source memory relative to younger adults. Interestingly, right frontal old/new effects were absent for younger adults. By contrast, older adults exhibited a left frontal negativity from 600ms for old relative to new items. This left frontal negativity was dramatically reduced in patients with PFC lesions. The authors suggested the pattern of ERP activity for older compared to younger adults indicated that qualitatively distinct neural processes supported retrieval in these two groups, with older adults recruiting frontal brain regions to maintain performance in a task that did not require extensive frontal engagement from younger adults given their high level of source accuracy (> 97%). It is important to acknowledge however that the mean ages of the older adults recruited for the above studies were substantially greater than those of the current sample (>60years vs ≈39years).

The absence of correlations with schizotypy measures for these ERP effects in Experiment One was initially interpreted in terms of task difficulty. Given the high behavioural discrimination, it was thought that participants could easily exert post-retrieval control processes or did not need to, and thus any difficulties experienced by those higher in schizotypy were not necessarily detected. This possibility was subsequently tested in Experiment Two where task difficulty was increased (refer to page 182 for details of how this was achieved). The pattern of results in Experiment Two provided evidence to support this interpretation as behavioural discrimination was significantly lower and significant positive correlations were identified with measures of positive and disorganised schizotypy. Together this suggests that post-retrieval monitoring as measured by this ERP index is modulated by schizotypy measures under conditions of increased task difficulty.

The results from analyses of right frontal old/new effects in Experiment Two, in light of the absence of correlations with magnitudes of later posterior negativity, raise questions regarding the relationship between other ERP indices of post-retrieval monitoring and right frontal old/new effects. Detailed investigations using both stimulus- and response-locked ERP analyses strategies have been conducted for LPN (e.g. Herron, 2007;

Johansson & Mecklinger, 2003), and have identified dissociable subcomponents of which one was related to post-retrieval monitoring. It may be that right frontal old/new effects are similarly comprised of subcomponents, and broadly attributing the overall functional significance to post-retrieval monitoring is inaccurate.

Finally, consistent with the hypothesis that positive symptoms would be associated with memory performance, the correlations between this ERP index and schizotypy involve the positive dimension. This is consistent with previous work suggesting individuals with schizophrenia have difficulty differentiating internal and external sources of information, with people being more likely to misattribute imagined information to external sources (e.g. Ditman & Kuperberg, 2005; Frith, 1992). Correlations with the disorganised dimension were also observed however. Nieuwenstein et al. (2001) found a positive correlation between perseveration scores on the Wisconsin Card Sorting Task and disorganised symptoms in patients with schizophrenia. Perseveration scores reflect the number of errors made following a card sorting rule change. Lower perseveration scores therefore reflect greater cognitive flexibility in rule maintenance, and thus could be considered an index of cognitive control. In the same study however, no significant correlations with positive symptoms were identified. This previous research in relation to the present pattern of data highlights the need for further investigation into the relationship between symptom dimensions and specific indices of cognitive control. The present data however demonstrate the utility of at least some ERP markers in pursuit of these research questions.

## LIMITATIONS

### Sensitivity Issues

ERPs have been shown in multiple domains and tasks to provide useful ways of examining cognitive processes. First, the temporal precision of this technique provides insight into the time course of cognitive processes (Hillyard & Kutas, 1983; Luck, 2005). Through understanding the time course and order in which processes are engaged during cognitive activities, it is possible to make inferences about the nature of their relationships (Hillyard & Kutas, 1983). Second, certain ERP measures are strongly associated with particular cognitive processes (for a review in the context of memory processes see Wilding & Sharpe, 2003), and by using these neural indices it is possible to

ascertain the degree to which these processes are engaged depending on specific experimental manipulations. It is important to acknowledge however that there are also limitations associated with this technique.

Most importantly, only a proportion of neural activity is recorded by electrodes on the scalp, since asynchronous and/or activity from randomly orientated cells will not be propagated to the scalp. Consequently, interpreting null findings from ERP studies is particularly difficult as the absence of differential ERP effects does not necessarily mean experimental conditions did not produce divergent effects on brain activity. Rather, there may have been brain regions that responded vigorously to these manipulations, but this activity was simply not propagated to the recording sites. For more in depth discussion of the strengths and limitations associated with this technique refer to Appendix Chapter A (page 236).

This aforementioned limitation however only applies if there have been no previous reports of significant ERP effects when particular manipulations are used and/or effects were not identified in the present study. Since the effects examined in this thesis have been previously reported and identified in the present data, on one hand this suggests sensitivity is not necessarily problematic for these data. On the other hand however, the general lack of correlations between the ERP effects of interest and measures of schizotypy and symptoms of schizophrenia could reflect a lack of sensitivity. Nonetheless, some correlations were identified between some ERP measures and measures of schizotypy, notably measures of positive and disorganised schizotypy were positively correlated with measures of right frontal old/new effects in Experiment Two, negative schizotypy was positively correlated with LPN effects in Experiment Three and general symptoms were negatively correlated LPN effects in Experiment Four. Some researchers however have questioned the validity of correlating behavioural and neural measures.

Schaworonkow, Blythe, Kegeles, Curio, and Nikulin (2015) highlighted that by correlating neural and behavioural measures this method treats individual trials as independent events, rather than respecting the fact data are acquired in a temporal order. Both neural and behavioural measures have already been shown to exhibit power-law dynamics (e.g. He, Zempel, Snyder, & Raichle, 2010; Rhodes & Turvey, 2007), where processes vary systematically over a range of time scales. This demonstrates trials are not in fact

independent. Crucially, Schaworonkow et al. (2015) emphasise that through ignoring the long-range temporal dependencies between such measures, spurious correlations may be identified.

In the present data, no systematic pattern of correlations was identified between ERP and schizotypy measures. Furthermore, multiple exploratory correlations have been conducted and no correction for multiple comparisons has been applied. Taken together, these considerations suggest that the correlations must be treated cautiously. Schaworonkow et al. (2015) have a number of suggestions to help prevent identifying spurious correlations, such as adjusting the significance level in accordance with the estimated number of independent observations. It is important to acknowledge however, that these estimates are unreliable and may still overestimate the extent of relationships between variables (Schaworonkow et al., 2015). This unreliability arises in part as a result of the variance in power-law dynamics from certain experimental manipulations or groups of participants, such as those with Alzheimer's Disease (Montez et al., 2009). In the context of the experiments reported in this thesis, at present there is insufficient data from patients with schizophrenia or those from whom measures of schizotypy have been collected, thus making it difficult to apply the corrections as suggested by Schaworonkow et al. (2015).

### Sample Size

In order to determine how many participants would be needed for Experiments Three and Four power analyses were conducted. As no previous studies have examined cognitive control during memory retrieval in individuals with schizophrenia we examined effect sizes in i) memory experiments, and ii) cognitive control studies in this population to inform this decision. A recent review of memory for contextual information in schizophrenia found an average effect size of 0.99 (Libby et al., 2013) and a review of cognitive control found an average effect size of 0.93 (Dickinson et al., 2007). Based upon these figures, power calculations indicated minimum sample sizes of 28 and 32 individuals with schizophrenia, respectively as well as an equal number of control participants. As evidenced in relevant chapters (pages 86 and 112), these sample sizes were not achieved. Thus, it may be that the present data are underpowered to detect all effects of interest, although the most striking element of the ERP findings is the almost

complete overlap in the magnitudes of old/new effects at parietal locations in patients and in controls.

The smaller than ideal samples recruited for Experiments Three and Four in this thesis can be attributed to the challenges of recruiting patients. The relatively demanding protocol, 4 hours of testing on top of traveling into the university; in conjunction with the eligibility requirements, stable on medication for one month and consent to contact care co-ordinators, meant not all patients contacted were willing or able to participate. Furthermore, those who did participate represent a self-selected group of people who may not be representative of patients with schizophrenia more generally. This latter limitation is of course applicable to most patient research, not just the experiment reported in this thesis. Nonetheless, the numbers of participants are broadly comparable with some published patient studies (e.g. Guillaume et al., 2012; Tendolkar et al., 2002) and sufficient to regard trends, or the absence of trends, as indicative for subsequent investigations. Moreover, the power calculations were applied in respect of the ERP data and these concerns do not apply in the same way to behaviour alone, and notably the important finding that estimates of recollection and familiarity are down in patients relative to their matched controls.

For Experiments One and Two, sample size was based on previous experiments that have correlated individual difference measures with the magnitude difference between target and non-target left-parietal old/new effects (e.g. Elward & Wilding, 2010). It could be that the effect size is smaller for correlations between schizotypy and the aforementioned ERP difference and thus the sample is underpowered, though this is hard to conclude on the basis of null results. Alternatively, the effect size of the correlations reported by Elward and Wilding (2010) may have been inflated by chance. Button et al. (2013) proposed that occasionally low-powered studies will detect significant effects through a combination of sampling variation, random error and thresholds of statistical significance. Evidence to support this interpretation comes from the outcomes of Experiment One, Two and Three, where only one correlation was identified (Experiment One) between working memory capacity and the attenuation of non-target relative to target left-parietal old/new effects across all three experiments. It is important to acknowledge though that Experiments Two and Three did not represent direct replications of Experiment One and thus experimental manipulations and/or



participant characteristics may have contributed to the absence of effects in these experiments. However, as highlighted by Tversky and Kahneman (1971), a common misconception when conducting replication studies is that by using similar sample sizes there will be sufficient power to detect the initial finding. However, Button et al. (2013) suggested when studies use the same sample size to replicate effects that closely achieved nominal statistical significance (e.g.  $p \approx 0.05$ ) approximately only 50% power will be achieved. To avoid this, researchers are encouraged to determine their sample sizes through conducting formal power calculations rather than relying on historical precedent (Button et al., 2013).

## BROADER THEORETICAL CONSIDERATIONS

### Validity of the Schizotypy Context

Despite the current pattern of data being consistent with some previous findings, the pattern of correlations differs between experiments. In the first two experiments, behavioural measures correlate with measures of positive schizotypy, though in opposite directions. By contrast, no significant relationships were identified in Experiment Three, and negative symptoms were implicated in Experiment Four. This might be considered to raise questions about the suitability of using measures of schizotypy to investigate cognitive problems in people with schizophrenia, or at least in the domain of memory.

Schizotypy is a personality trait present to varying degrees throughout the population (Claridge et al., 1996). Confirmatory factor analysis has revealed schizotypy has the same tripartite factor structure that is reported in schizophrenia, comprising positive, negative and disorganised dimensions (Vollema & van den Bosch, 1995). These factors correspond to various behaviours or beliefs required for a diagnosis of schizophrenia (Bentall et al., 1989; Mason et al., 1997). Furthermore, people with a diagnosis of schizophrenia have higher scores on schizotypy dimensions than those without a diagnosis (Nettle, 2006). Finally, cognitive and electrophysiological impairments that correlate with schizotypy scores are also apparent in individuals with schizophrenia (Evans et al., 2005, 2007). Therefore, proposed similarities between schizotypy and schizophrenia imply that it is possible to investigate the mechanisms underlying symptoms of schizophrenia using non-clinical samples (Claridge, 1997), whilst avoiding confounds associated with using

clinical populations (e.g. anti-psychotic medication, comorbid diagnoses; for a discussion see Lenzenweger, 2011).

Some researchers have argued however that whilst the limitations of current categorical diagnostic systems are well recognised, the putative value of a continuous approach has not been conclusively demonstrated (Lawrie, Hall, McIntosh, Owens, & Johnstone, 2010). One of the principal arguments for a continuous approach is that there is evidence to suggest psychotic symptoms are distributed throughout the general population (e.g. Kendler et al., 1996; Sidgwick et al., 1894), though as highlighted by Lawrie et al. (2010), this does not mean schizophrenia and other psychoses are qualitatively comparable to normal experience. In fact, psychotic symptoms may be epiphenomenal to the true nature of psychosis (Lawrie et al., 2010). Another strong argument against symptom-focused approaches, such as those adopted by continua to psychoses, is that individual symptoms are less reliably elicited than multidimensional diagnoses that vary across time and environmental contexts (Lawrie et al., 2010). For example, a mood congruent delusion may share more biological similarities to other mood disturbances rather than other delusions. Thus, through reducing multiple symptoms to more general severity scores, the possibility of examining aetiopathogenetic similarities and differences is lost (Lawrie et al., 2010). Most importantly, Lawrie et al. (2010) highlighted that diagnostic categories were first introduced to regulate and facilitate diagnosis and treatment. These categories are based on replicated clinical trials and arguably these concepts are easier to communicate than continua (Lawrie et al., 2010). Whilst Lawrie et al. (2010) agree there are equally valid claims for a continuous approach, the authors proposed that sufficient research has not been conducted to indicate which model of psychosis best accounts for the distribution of symptoms in the general population, and prematurely adopting one approach over another may jeopardise scientific and clinical advancement.

Despite these criticisms, there are still several advantages to using continuous approaches to psychoses, such as schizotypy. First, it is hoped that through replicating deficits observed in patients with schizophrenia in non-clinical samples this helps provide evidence that the deficits can be attributed to the condition, rather than to any confounding variables. Second, measures of schizotypy may provide a useful tool to investigate liability to develop schizophrenia-spectrum disorders as well as protective mechanisms. Finally, through investigating relationships between schizotypy and

cognitive processes and/or neural function, it is possible to develop and refine hypotheses that can go on to be assessed in patients (Kwapil & Barrantes-Vidal, 2015). This latter approach was adopted in the experiments reported in this thesis. Nonetheless, Kwapil and Barrantes-Vidal (2015) have suggested the utility of schizotypy has been undermined by the conflicting identities in the literature, as this construct is often used interchangeably with other descriptors (e.g. schizotypal personality disorder, psychosis-proneness).

To move forward Kwapil and Barrantes-Vidal (2015) proposed that a clear operationalization of schizotypy, incorporating characterisations of etiological, developmental and phenomenological constructs, should be developed. Such theoretical models could then provide the basis for measurement and construct validation. The necessity for this clear operationalization is exemplified in the present data as different symptom dimensions were implicated in Experiments One and Two compared to Experiments Three and Four. Ultimately, as suggested by researchers on both sides of this debate, further research is required to better understand the relationship between schizotypy and schizophrenia.

## FUTURE DIRECTIONS

### Alternative Memory Paradigms

The exclusion paradigm was chosen for the experiments reported in this thesis as previous work has demonstrated ERPs acquired during these tasks can index cognitive control over memory retrieval. There are other tasks however, that are considered to involve strategic processing of test items. For example, the memory for foils procedure (Jacoby, Shimizu, Daniels, & Rhodes, 2005) and switching between tasks with different retrieval demands is also assumed to limit the opportunity exert control over retrieval (Swainson et al., 2003). The exclusion task is attractive because the instructions are simple and item and context judgments are combined in a binary judgment. These appeals do not mean, however, that the task is going to be a useful tool for investigating retrieval control in some or all populations (although see Sprondel et al., 2011), hence consideration of other kinds of tasks is worthwhile.

Using the memory for foils paradigm, Jacoby, Shimizu, Velanova and Rhodes (2005) collected data from two groups: young and healthy older adults and participants completed one of two study tasks. In one study context, participants made pleasantness judgments (deep condition), and in another context, participants made vowel judgments (e.g. does the word contain an O or a U; shallow condition). Subsequently, participants completed a recognition memory task where the old items were either from the deep condition or the shallow condition, depending on the initial study task. For both recognition memory tasks, different new items were presented (foils). Following these tasks, participants completed a memory for foils task where the new items presented in the deep and the shallow recognition memory tasks were presented as old items (deep and shallow foils respectively), in conjunction with new (not previously presented) items. Young participants who completed the test for deep foils were better able to recognise old items in comparison to participants who completed the test for shallow foils, suggesting participants constrained memory retrieval differentially based on prior processing of target items. By contrast, healthy older participants demonstrated no significant difference in memory for deep or shallow foils.

Considering the similarities between the ERP data for patient and control participants in light of the behavioural performance differences, it would be interesting to see if similar behavioural divergences are obtained using other paradigms. Estimates of familiarity and recollection cannot be explicitly derived from this procedure however, which would make comparisons with the present pattern of data difficult. A further potential concern with the memory for foils procedure is the small effect size. Larger samples of patient and control participants would be required and this may be a barrier to using this paradigm with patient participants.

Another possibility would be a task switching paradigm, such as that used by Richter and Yeung (2012). During study, participants were required to switch between making decisions about objects (natural or man-made) and decisions about words (abstract or concrete; randomised presentation). Two thirds of trials consisted of bivalent stimuli (word superimposed over an object), and one third of trials were univalent stimuli (word substituted for character strings e.g. #?!£%, or object substituted for scrambled object picture). Participants subsequently completed a surprise recognition test where participants were required to rate their confidence on a 6-point scale of whether the

object was new (sure, 1), or old (sure, 6). During the recognition test, each block consisted of either words or objects with the order of blocks conforming to an ABBA pattern. The presentation of items within each block was randomised. Task switching impaired memory for task-relevant information but improved memory for task irrelevant information. Together, this suggests control demands reduce the selectivity of memory encoding, rather than a general decline in memory performance.

The advantage of this procedure over the memory for foils procedure is the addition of confidence intervals, which enable receiver operating characteristics (ROCs), and thus estimates of recollection and familiarity, to be calculated. By examining the effect of response criteria on hit and false alarm rates, it is possible to estimate the contributions of recollection and familiarity (Yonelinas, 2002). However, to effectively derive stable ROCs, it is necessary to collect a large number of responses from participants, which may make this approach unsuitable in the context of patient research (Yonelinas, 2002). Furthermore, task-switching paradigms have challenges associated with separating switching processes from retrieval processes. Nonetheless, establishing comparable patterns of deficits in patient relative to control participants across different paradigms using the same stimuli would provide strong evidence to support the claims made in this thesis.

### Subsequent Memory Effects

The ability to focus on task-relevant contents during encoding is a determinant of successful retrieval (e.g. Bridger & Wilding, 2010; Otten & Rugg, 2001). Considering the ability to use contextual cues to organise information during encoding, as well as retrieval, has been shown to be reduced in schizophrenia patients (Cohen & Servan-Schreiber, 1992; O'Reilly, Braver, & Cohen, 1999), investigating the efficacy of encoding mechanisms in the context of these experiments could provide useful insights into precisely how such processes may be deficient in schizophrenia.

Accuracy at test was the driver for how the tasks were constructed, and as a result, the opportunities for observing subsequent memory effects would only be those that came about serendipitously. Nonetheless, EEG was recorded during both study and test phases of the exclusion task for most experiments reported in this thesis in case examination of these effects were possible. Cognitive control at encoding may well be linked to memory

problems in schizophrenia, but that conclusion would have held irrespective of the pattern of findings observed at the time of retrieval.

Indices of successful encoding are typically assessed using subsequent memory contrasts (Paller, Kutas, & Mayes, 1987; Paller & Wagner, 2002). These involve splitting the neural activity recorded for items during the study phase according to the responses these items receive during the subsequent test phase, with the most common contrast being between items that are correctly identified as being previously presented, and items that are forgotten. Differences revealed in contrasts of this kind are considered to index processes that contribute to subsequent accurate memory judgments (Bridger & Wilding, 2010; Sprondel et al., 2011).

Subsequent memory effects vary depending on the nature of the encoding task. Otten and Rugg (2001) conducted an experiment in which participants were required to make either animacy or letter-order judgments to visually presented words, prior to completing a surprise recognition memory test where participants were also asked to rate their confidence in old/new responses. Words previously presented in the animacy condition that subsequently received confidently recognised responses were associated with a more positive going ERP modulation compared to forgotten items from the same condition. This is in contrast to the letter-order condition where confidently recognised items were associated with a more negative going ERP modulation compared to forgotten items. Otten and Rugg (2001) interpreted their findings as indicating that qualitatively different encoding operations contributed to the subsequent memorability of items in each condition.

Other researchers have also revealed that subsequent memory effects vary depending on the content-type participants are required to retrieve. Bridger and Wilding (2010) presented participants with words either to the left or right of a fixation cross, and asked them to make a drawing difficulty or pleasantness judgment to each item. During separate test phases, participants were required to make study-location or study-task judgments. For study-location items, subsequent memory contrasts revealed a more positive going ERP modulation from 900ms post-stimulus presentation, whereas for the study-task condition contrasts revealed a more negatively going ERP modulation. The authors interpreted the findings in terms of qualitatively different encoding processes being engaged in the two tasks. Furthermore, it was suggested that variations in the

activation levels of the neural networks supporting these processes are at least partially independent.

Whilst it would be important to investigate the aforementioned contrasts in relation to the experiments reported in this thesis, there are complications associated with this form of analysis. Given the high level of behavioural performance exhibited by participants across tasks, there are relatively few participants that contribute sufficient ERPs to critical response categories (e.g. missed targets and non-targets for both imagine and perceive target designations). Therefore, traditional subsequent memory contrasts would not be advised as interpreting the results would be difficult given the small sample size. One possible approach could be to examine the neural activity at study associated with items subsequently recalled during the free recall task in Experiments One, with items that were not. However, in order to conduct such analyses, it would be necessary to collapse across encoding condition (e.g. imagine and perceive). Given the previously described studies suggest activity at encoding can vary depending on both encoding operations at time of study and the type of content that is subsequent retrieved, by analysing the data in this way, it would be difficult to draw conclusions regarding specific encoding operations that serve to facilitate subsequent retrieval. Consequently, investigating these effects is not possible in the present data. Nonetheless, future studies would benefit from manipulating task difficulty to achieve sufficient trials numbers in critical response categories. This could be achieved through using a task design similar to that adopted in Experiment Two, but collecting data both during encoding and test phases.

### Oscillatory Activity

Numerous human and animal studies have demonstrated that when performing cognitive tasks, neural activity becomes highly co-ordinated, in that neurons align oscillatory phase to achieve highly synchronous action potential discharges (e.g. Fries, 2009; Hormuzdi et al., 2001). This synchrony is considered to play a critical role in coordinating cerebral activity (Uhlhaas, Roux, Rodriguez, Rotarska-Jagiela, & Singer, 2010). In particular, theta (4-7Hz) and gamma (30-200Hz) rhythms have been thought to contribute to coherent concept construction through the strengthening and weakening of synaptic connections (Buzsaki, 2006), and the integration of neural activity within and between brain regions associated with higher cognitive functions including perception,

attention, episodic memory and working memory respectively (e.g. Gruber, Tsivilis, Montaldi, & Müller, 2004; Singer, 1999; Varela, Lachaux, Rodriguez, & Martinerie, 2001); virtually all cognitive domains known to be deficient in schizophrenia. Furthermore, other researchers have proposed that alpha (8-12Hz) rhythms, in conjunction with theta, underlie the long-range co-ordination of local high frequency activity (Von Stein, Chiang, & König, 2000). This is in contrast to beta (13-30Hz) which, similar to gamma oscillations, are believed to be implicated in the synchrony of local cortical networks and the maintenance of cognitive sets (Engel & Fries, 2010; Gray, König, Engel, & Singer, 1989).

Given the growing literature characterising the functional significance of oscillatory patterns, increasing research attention has been paid to how such synchrony may be aberrant in clinical populations. Haenschel et al. (2009) investigated the effects of evoked and induced oscillatory activity on the various components of working memory (encoding, maintenance and retrieval) using EEG in both control participants and early-onset schizophrenia patients. Patients demonstrated altered oscillatory activity in all three subcomponents of the working memory task. For control participants, evoked alpha, beta and theta activity during the encoding subcomponent predicted the number of items successfully encoded. Furthermore, control participants exhibited reductions in theta and beta activity with increasing working memory load during encoding: this is in contrast to schizophrenia patients who demonstrated no changes. Considering the maintenance subcomponent, patients demonstrated increasing changes in oscillatory activity with longer maintenance intervals. Specifically, between working memory loads two and three, control participants exhibited increases in induced gamma oscillations, whereas patients exhibited increases in such activity between working memory load one and two, but decreases between loads two and three. Haenschel et al. (2009) suggested that during longer maintenance periods, additional processes relating to active rehearsal are engaged to a greater degree, but that such processes are more sensitive to disruption in schizophrenia. Finally, during retrieval, patients showed reduced evoked and induced theta and gamma oscillatory activity compared to controls. Considering induced theta activity has been found to be larger for old compared to new items during recognition memory tasks (Klimesch, Doppelmayr, Schimke, & Ripper, 1997), Haenschel et al. (2009) interpreted these findings as indicating that patients, in contrast to controls, were more likely to treat old items as novel. However, the fact that no relationship was found between amount of induced gamma activity during retrieval and successful recognition



for patients weakens this claim. Nonetheless, the authors argued that the lack of relationship between oscillatory activity and task performance during both encoding and retrieval phases in schizophrenia patients highlights the importance of early evoked oscillatory impairments during the encoding, that could contribute to later process abnormalities (Haenschel et al., 2009).

Importantly, differences in oscillatory activity have also been reported in those high, compared to those low in schizotypy, using the same working memory task as that used by Haenschel et al. (2009). Koychev, Deakin, Haenschel, and El-Deredy (2011) calculated two measures of oscillatory activity: signal power and phase-locking factor (PLF). The first measure provides information regarding the magnitude of the oscillatory signal whilst the second measure provides information regarding the synchronisation of neural activity, regardless of power (Roach & Mathalon, 2008). The value obtained by PLF analysis indicates the consistency of synchronisation to stimulus presentation across trials, such that zero indicates random phase distribution and a maximum score of one represents exact alignment of neural signalling; thus this measure can indicate the variability of neural responding. Reductions in PLF have previously been interpreted as indicating increased cortical noise (Winterer et al., 2004; Winterer et al., 2000). Results from Koychev et al. (2011) indicated that participants high in schizotypy, compared to those low in schizotypy, exhibited reduced PLF values for beta and gamma bands at two correlated sets of electrodes: fronto-central and central-occipital sites, suggesting that high schizotypes do not exhibit co-ordinated neural activity to the same degree as those lower in this dimension. Because the activity at these two sites was correlated, the authors proposed two interpretations: i) that disturbed activity at the occipital electrodes drives higher-order cortical abnormalities (a similar conclusion was also drawn by Butler et al., 2007); ii) that top down processes drive the occipital abnormality by biasing the processing of incoming sensory information (similar to ideas proposed by Engel, Fries, & Singer, 2001). The authors favoured the latter interpretation in light of the large body of literature suggesting deficits in control mechanisms in schizophrenia populations (e.g. Kerns, 2007; Rass et al., 2011; Schlösser et al., 2008).

In order to further characterise the dysfunctional nature of oscillations in schizophrenia, other researchers have examined activity in relation to specific symptom clusters. Suazo et al. (2012) examined noise power in relation to performance on an auditory odd-ball

task across both control participants and schizophrenia patients. Noise power refers to the amount of scalp-recorded activity showing no temporal relation to stimulus presentation, quantified as the difference in each band between the mean power of single trials and the power magnitude in the averaged potential (Winterer et al., 2000). Compared to controls, schizophrenia patients exhibited significantly higher gamma noise power across P3, P4, T5 and Fz electrode sites. Gamma noise power for patients was found to positively correlate with negative symptom scores (as measured using PANSS; Kay et al., 1987), in addition to demonstrating a negative correlation with verbal memory scores (as measured by the Spanish Version of the Brief Assessment in Cognition in Schizophrenia Scale [BACS]; Segarra et al., 2011). Since EEG activity is thought to be dominated by synaptic currents as opposed to action potentials, Suazo et al. (2012) proposed that the increased gamma noise power observed in patients in this study could reflect inefficient and/or disorganized excess of excitatory activity, potentially resulting from deficient top-down control of response-inhibition.

Taken together, this literature suggests that in the context of the experiments reported in this thesis it may be advantageous to conduct noise power and PLF analyses, focusing particularly on gamma band activity, for both encoding and retrieval phases, in order to fully understand how synchronised oscillatory activity contributes to memory performance. Furthermore, based on evidence reported by Suazo et al. (2012), it may be that negative schizotypy scales are particularly relevant to examine when considering correlations with the aforementioned measures. Whilst the electrode density represented in the present data may be sufficient for conducting group-level comparisons (Kayser & Tenke, 2006), higher density electrode arrays may be necessary for understanding the individual differences that contribute to variations in these measures (Srinivasan, Tucker, & Murias, 1998). However, the utility of low- versus high-density EEG recordings has been determined using: i) source localisation analyses and/or, ii) robust ERP effects with large effect sizes (e.g. P300); markedly different approaches to those employed in pursuit of the research questions examined in the present experiments. Thus, the utility of low- compared to high-density electrode recording arrays in relation to memory effects remains unclear. Nonetheless, future research would benefit from conducting initial investigations using larger arrays before comparing these results to those obtained from smaller electrode arrays.

## CONCLUSIONS

The ERP measures indicated healthy, young participants could prioritise recovery of target over non-target information, though the extent of retrieval prioritisation was not correlated with measures of schizotypy. There was evidence however to suggest that post-retrieval control mechanisms are engaged to a greater extent in those higher in schizotypy. This pattern of results was not replicated in older, healthy volunteers and patients with schizophrenia where there was no evidence indicating target information was prioritised relative to non-target information. This finding is potentially important, given that accuracy of responding did not vary markedly across the university population or community sample. Previously target accuracy has been considered a key determinant of the degree of retrieval control exerted. The present pattern of results however suggests age, or an age related confound such as working memory capacity or source memory performance, is a more crucial factor.

Alongside the insight from the ERP data that factors other than response accuracy govern when control will be exerted (and the concomitant implications that has for resource availability in the community sample and the patient group), the data in Experiments Three and Four provide strong evidence supporting the view that recollection as well as familiarity are impaired in schizophrenia. This outcome converges with the claims in a recent meta-analysis, but represents one of the strongest individual data points of this kind. Moreover, several behavioural correlations were identified in patients with schizophrenia. Importantly, these were in the expected direction, with those experiencing greater symptoms experiencing greater difficulties. Patients higher in negative symptoms had greater difficulty discriminating imagined items from other items. Estimates of recollection for imagined items were also negatively correlated with negative symptoms. This pattern of findings was not replicated in young or older healthy participants. One possible explanation is that symptoms differentially modulate cognitive performance throughout the life span. Alternatively, this pattern of results might be considered to raise questions about the utility of schizotypy as a model for investigating cognitive problems in patients with schizophrenia.

Whilst further work is needed to better understand how cognitive control operates in people with schizophrenia these results do indicate memory processes are differentially

affected in patients with schizophrenia, with those involved in recovering imagined information being disproportionately affected. Together, these results provide preliminary insights into potential treatment targets.

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## APPENDIX CHAPTER A: EVENT RELATED POTENTIAL TECHNIQUE

### ELECTROGENESIS

Neuronal activity is most commonly considered to reflect action potentials, which are brief disturbances ( $\approx 1\text{ms}$ ) of the resting membrane potential of neurons. Resting membrane potentials are approximately  $-70\mu\text{V}$  and this voltage is maintained via sodium/potassium pumps. Disturbances of this potential can be attributed to the influx of sodium ions through voltage-gated channels. This influx changes the electrochemical gradient of the membrane, which in turn propagates the reduction and eventual reversal of the membrane potential via other sodium ion channels along the membrane opening. When all available sodium ion channels are open, this produces an action potential which represents a membrane potential of approximately  $+40\mu\text{V}$ . Membranes repolarise via voltage gated potassium channels, which open to allow the influx of potassium ions. The involvement of these channels typically results in the membrane becoming more negative than the initial resting potential and the electrochemical gradient is reinstated via sodium/potassium pumps (Barnett & Larkman, 2007).

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***Figure 20 – Taken from Bioninja (no date). A schematic representation of the mechanisms underlying action potentials. 1) Sodium/potassium pumps maintain the resting potential ( $-70\mu\text{V}$ ). 2) Sodium channels open to allow influx of sodium ions which eventually reverse the membrane potential. 3) Potassium channels open to allow potassium ions to leave, causing hyperpolarisation of the membrane. 4) Resting potential re-established via sodium/potassium pumps.***

Importantly, action potentials can result in post-synaptic potentials, when cells release neurotransmitters into the synaptic cleft and initiate either inhibitory or excitatory effects in neighbouring neurons. Post-synaptic potentials are much slower in comparisons to action potentials (>10ms), but both of these potentials contribute to electrical potentials in the extracellular fluid, which are generated as a result of ionic currents into and out of cell membranes (Woodman, 2010). These potentials generate electrical and magnetic fields when there is sufficient separation between the net outward ionic flow from the neuron (source) and the net inward flow (sink), which is achieved through neuronal structure and the specific location of activation (Picton, Lins, & Scherg, 1995). As indicated in

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***Figure 21***, the electrical field generated runs from source to sink and the related magnetic field runs perpendicular to this electrical field.

To generate electrical fields large enough to be detected extra-cranially, two principal conditions need to be met. First, large populations of neurons must fire synchronously. Second, these large populations need to be orientated so that: i) the dipoles of the field are perpendicular to the scalp, and ii) the dipoles of one field do not cancel out those of another field (Coles & Rugg, 1995). Individual potentials measure only a few  $\mu\text{V}$  in magnitude, therefore, for this signal to propagate to the scalp, this activity needs to be summated across multiple parallel neuronal ensembles. This makes cortical pyramidal neurons the most likely generators of ERPs, considering these cells have a columnar structure and are perpendicular to the cortical surface (Woodman, 2010). Pyramidal cells

constitute 70% of the neocortex and consequently it is thought that this region is the primary source of scalp recorded ERPs (Nunez & Srinivasan, 2006)

#### STRENGTHS AND WEAKNESSES OF THE EEG TECHNIQUE

A consequence of the foregoing description is that only a small proportion of neural activity occurring in the brain is recorded via EEG, since asynchronous and/or activity

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***Figure 21 – Taken from Baillet (2010). A schematic representation of electrical and magnetic fields surrounding a neuron. The large solid black arrow represents the current dipole. The subsidiary electric field is represented by the dark plain lines. The magnetic fields generated by both the current dipole and subsidiary electrical fields is represented by the dashed lines arranged in circles perpendicular to the electrical field.***

from randomly orientated cells will not be propagated to the scalp. This knowledge makes interpreting null findings in ERP literature particularly difficult as the absence of differential ERP effects would not necessarily mean that experimental conditions did not produce divergent effects on brain activity. Rather, there may have been brain regions that respond vigorously to these manipulations, but this activity was simply not propagated to the recording sites (e.g. hippocampal activity; Bullock et al., 1995; Menon et al., 1996). This implication does not however diminish the value of experimental outcomes where differential ERP effects are observed.

A further limitation of the EEG technique is that the ability to localise the neural generators is extremely limited. There are two main reasons why this is problematic with



EEG data. First, both the skull and the scalp are electrically conductive materials, meaning electrical fields reaching one recording location may also propagate to other recording sites. For example, a pattern of activity observed at the scalp may be equally well explained by a discrete, deep source as by a distributed, shallow source. Consequently, the exact location of neural generators cannot be determined since there are an infinite number of possible locations and distributions that could contribute to the observed scalp distribution of an effect (Kutas & Dale, 1997). Whilst there are many techniques that can be used to improve the spatial accuracy of this technique (e.g. Brain Electrical Source Analysis [BESA], Scherg & Berg, 1990; in conjunction with PET/fMRI data can constrain the estimated dipole location), it is still important to acknowledge that resulting locations need to be replicated and verified several times before such findings can be accepted. Second, the inter-individual variability in craniocerebral topography is greater than originally estimated (Jasper & Carmichael, 1935), especially for regions that are more remote from the relatively constant central and lateral fissures (Steinmetz, Fürst, & Meyer, 1989). Thus, the validity with which scalp-recorded EEG signals can be ascribed to specific sources is minimal at best, limiting the extent to which EEG data can be used to attribute functional significance to particular brain regions.

Despite these limitations, EEG remains a valuable technique considering it provides a direct measure of neural activity in real time (Wilding, 2001). This is in contrast to other neuroimaging measures such as Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET) which provide indirect measures of neural activity by tracking changes in regional cerebral blood flow (rCBF), a measure assumed to correlate with neuronal activity. Moreover, these techniques are only sensitive to event-related neural activity some 2-3 seconds post-event, and take a further 10-12 seconds to return to baseline. Nonetheless, this temporal limitation is offset by the spatial resolution offered by these techniques, whereby a relative increase in activity can be localised to a brain region with millimetre precision. For further strengths of the EEG technique, refer to the Cognitive Electrophysiology subsection of Chapter Three, page 61.

## RECORDING EEG

Electrode locations most commonly correspond to the International 10-20 system (Jasper, 1958). This system identifies the inion, nasion and pre-auricular points and

locates electrodes in terms of percentage (10%, 20% or 50%) distances along the lines connecting these reference points. By using percentages rather than raw measures, it is possible to take into account the varying size and shape of the human head. Within this system, electrode locations are described with reference to the general location on the scalp (e.g. Frontal pole [FP]; Frontal [F]; Central [C]; Temporal [T]; Parietal [P]; and Occipital [O]) and the lateral plane (odd numbers = left hemisphere; z = midline; even numbers = right hemisphere), where larger numbers indicate more lateral positioning. For research purposes, these locations are now usually pre-specified on elasticated caps in order to maintain relative consistency in locations across participants. Elasticated caps were used in the experiments described in this thesis.

In order for the signal from the scalp to propagate to the electrodes an electrolyte solution must be applied to the skin at each location (Picton et al., 2000). Low electrode impedance is imperative for the acquisition of quality data and abrading the skin can help reduce impedance. Some systems, generally referred to as active electrode systems, amplify the signal at each site and thus can produce high quality data with higher

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***Figure 22 – Taken from Jasper (1958). Illustration of the location of electrodes using the original international 10:20 system.***

impedances than passive systems. All acquisition approaches benefit from reducing impedance, though. Commonly, impedance is kept below 5k $\Omega$  for each recording site (Picton et al., 2000).

Voltage activity from each site is recorded relative to a reference, which might be a single location or some aggregated measure. Luck (2005) provides three guidelines for

selecting an appropriate reference site. First, it should be relatively comfortable and convenient for the participant. Second, the location should not be biased towards either hemisphere, since this will selectively attenuate the activity of the reference hemisphere. Third, this site should be consistent across experiments and laboratories conducting similar research, considering the location of the reference will influence the overall morphology of the waveforms and scalp distributions. The two most popular references are linked mastoids (Coles & Rugg, 1995) and an average reference. The mastoids are suitable considering they are relatively comfortable for the participant, not greatly influenced by brain activity and not biased to either hemisphere (Nunez & Srinivasan, 2006). The average reference similarly satisfies these guidelines by operating under the assumption that noise is evenly distributed over the head and the remaining signal is exclusive to particular electrodes. However, some researchers have identified issues with this latter method. Namely, Desmedt and Tomberg (1990) suggested that the average reference method is prone to spurious effects, such as ghost field potentials. These effects arise because the average reference is computed using a limited number of electrodes which do not survey the lower portion of the head. In keeping with the approach employed in the majority of ERP studies of memory, a linked mastoids reference was employed in the experiments reported in this thesis.

#### AMPLIFICATION, FILTERING AND A/D CONVERSION

Electrical potentials recorded from the scalp are typically  $1/100,000^{\text{th}}$  Volt, and therefore need to be amplified by a factor in the order of 10,000-50,000 before these differences can be measured accurately (Luck, 2005). However, the amplification process not only affects the neural activity, but also non-brain related activity as well electrical noise. To counteract the amplification of electrical noise, differential amplifiers can be used. These systems allow for the detection and elimination of activity that is equivalent across all electrodes (common mode rejection; Picton et al., 2000). Other sources of noise include large gradual shifts in voltage, such as those produced by skin potentials (Luck, 2005), making high bandpass filters particularly important during acquisition. High bandpass filters attenuate low frequencies, with higher frequency filters producing less drift in the signal. This is in contrast to low bandpass filters which attenuate high frequencies. Together, these filters enable frequencies outside of the specified bandwidth to be rejected by the amplifier (Picton et al., 2000), reducing the impact of noise on the data

signal. Typically, the high bandpass filters are set to between 0.01-1Hz and the low bandpass filters are between 30-100Hz (Luck, 2005). In the experiments described in this thesis data were filtered with a bandwidth of 0.03-40Hz, which captures a frequency range within which the majority of processes of interest are evident.

The analogue-to-digital (A/D) converter samples the ongoing EEG data at discrete time points and produces a digital signal (Picton et al., 2000). The rate of A/D conversion, or the sampling rate, refers to the time between each data point. Sampling rates are constrained by the Nyquist Theorem, according to which the highest frequency that can be captured accurately is half of the sampling rate (Luck, 2005). If the sampling rate is not calculated correctly, this will not only produce a loss of data at lower frequencies but could also induce artificial lower frequencies into the data, known as aliasing (Luck, 2005). The use of high and low bandpass filters can help reduce the impact of this problem, making it essential these filters are applied correctly. In the first two experiments described in this thesis, a sampling rate of 250Hz was used. In the latter two experiments a sampling rate of 2048Hz was used.

## ARTIFACT REJECTION AND CORRECTION

As previously described (page 234), EEG data consists of a signal embedded in noise. The signal of interest is often much smaller (5-10 $\mu$ V) than that produced by artifacts (50-100 $\mu$ V). Whilst procedures are available to minimise the influence of such artifacts offline, this does not eliminate the need for collecting clean, artifact free data in the initial instance.

One of the major sources of artifact in EEG recordings is eye movements and blinks. This is because the eyeball functions as a dipole with the cornea acting as the source (positive end) and the retina as the sink (negative end). Eye movements (e.g. saccades) cause this dipole to rotate, whereas blinks lead to the propagation of the current backwards across the head. In order to minimise the effect of these artifacts, electrodes can be placed above and below one eye (vertical electro-oculogram [VEOG]) and on the outer canthi (horizontal electro-oculogram [HEOG]). These electrodes facilitate the detection and elimination of both vertical and horizontal eye movements. One method for eliminating these artifacts involves simply removing trials containing such contaminants, however Gratton et al. (1983) identified three problems associated with this method. First,

discarding trials in this manner may lead to an unrepresentative sample of trials. Second, the use of this method with some groups of participants (e.g. children and psychiatric patients) may lead to insufficient trial numbers required for analysis. One possible solution to this is to ask people to fixate on a particular location of the screen and only blink at specified times, outside of the epoch of interest. However, this approach is not without complications. By asking people to control their eye movements, this manipulation may constitute a dual-task demand. Furthermore, this task may be more challenging for some groups compared to others and hence may influence performance and the emergence of subsequent ERP effects. Third, for some experimental designs these artifacts are integral to the task, making the elimination of such effects counterproductive. Consequently, several artifact correction algorithms have been developed to address this issue. These algorithms work on the principle of calculating the propagation factor between the EOG and the scalp electrodes, and subtracting the corresponding proportion of EOG activity from each recording site, reducing the need to reject excessive trials (Luck, 2005). The Gratton et al. (1983) algorithm was used to correct for ocular artifacts in all experiments reported in this thesis.

Other sources of artifact include muscular movement (e.g. jaw clenching), baseline drift (e.g. linear increase or decrease in voltage across the recording epoch) and A/D saturation (e.g. when the signal voltage exceeds that permitted by bandpass filters). Some data processing packages enable some of these artifacts to be detected automatically (e.g. baseline drift exceeding  $\pm 80\mu\text{V}$ ). Given the sporadic and variable emergence of artifacts of these kinds, however, it is not possible to develop correction algorithms to address these issues. It is therefore still necessary, to remove such trials from further analysis. For all experiments reported in this thesis, artifacts of this nature were detected using both automatic detection of deflections exceeding  $\pm 80\mu\text{V}$  and visual inspection of the electrical record. Trials including these artifacts were subsequently eliminated from further processing and analysis.

## SIGNAL AVERAGING

The aforementioned procedures provide some means for enhancing the EEG signal of interest. Unfortunately, these steps alone are not sufficient to differentiate this signal from the background noise. The most widely used method to achieve this is signal

averaging. This method is reliant on the assumption that signals of interest are invariant across trials, but sources of noise will vary randomly; and involves averaging across a sufficiently large number of individual, artifact-free epochs, time locked to the same event. Typically, this event of interest is preceded by 100-200ms of EEG recording. This period acts as the baseline and is averaged and subtracted from all post-event data points. This process, referred to as baseline correction, controls partially for the influence of pre-stimulus activity on post-stimulus activity. Together these processes produce averaged, baseline corrected ERP waveforms for each event of interest.

Despite the advantages of utilising this method, there are two main limitations associated with this procedure. First, by averaging across all trials associated with an event of interest any graded property in mental processing is lost. Second, the averaged waveform will not necessarily resemble those associated with individual trials. Where the signal of interest is invariant across trials, this will be accurately represented in the averaged waveform. This is in contrast to instances when the latency of the signal of interest differs between individual trials (referred to as latency jitter). In these cases, the resulting averaged ERPs will be distorted compared to the individual trials that contributed to the average (e.g. lower in amplitude; (Spencer, Abad, & Donchin, 2000). There are other averaging techniques available that minimise the impact of this variability (for a summary see Luck, 2005), however this variability and the potential loss of graded data quality is not usually problematic as the conclusions of most ERP experiments acknowledge that ERPs represent a measure of central tendency (Luck, 2005).

## DESCRIBING ERP DATA

Deflections in the ERP recording are often described in terms of their polarity and latency; where polarity is indicated with P for positive peaks and N for negative troughs, and the latency corresponds to the time point at which the deflections are maximal (Kutas & Dale, 1997). By labelling deflections using this system it becomes possible to communicate similar deflections across experiments and use these as a covert physiological marker for the engagement of cognitive processes (Otten & Rugg, 2004). However, some researchers have identified problems with labelling deflections in this way. For example, the latency of effects has been found to vary in accordance with

certain individual difference variables (e.g. age; Picton et al., 1995). In response to this, some authors advocate the use of sequential numbering to label deflections (e.g. P1, N1, P2; Picton et al., 1995). Whilst there is some inconsistency with regard to the nomenclature used to describe deflections, a more pressing issue with respect to interpreting ERP data is the issue of what constitutes a notable deflection, or an ERP component.

One approach to defining deflections is referred to as the physiological approach. This approach is concerned with defining components with respect to underlying neural generators and anatomical location (Näätänen & Picton, 1987). However, difficulties with this approach arise principally due to ERP scalp distributions being mathematically ill-defined, as already described, and hence could result from an infinite number of neural generators in one or multiple locations (Coles & Rugg, 1995). An alternative approach is referred to as the functional approach. This approach is based on the premise that subtracting waveforms associated with different experimental manipulations (Kutas & Dale, 1997) produces a difference waveform that can be considered to reflect the neural signature of the process of interest. However, this approach is strongly reliant on experimental manipulations only differing with regard to the degree to which a particular processes is engaged (Coles & Rugg, 1995), and as such has not gone unchallenged. For example, Friston et al. (1996) have stressed that multiple cognitive processes may occur simultaneously and interact to produce the observed ERP difference. Similarly, the observed difference waveforms may span multiple ERP components described by the previously discussed nomenclature (page 232). As a result of these criticisms, the most commonly adopted approach to defining ERP deflections combines both physiological and functional importance. This hybrid approach proposes that ERP components have both a circumscribed distribution and functional significance as evidenced by the behaviour of this deflection across experimental manipulations (Donchin, Ritter, & McCallum, 1978).

The use of changes in amplitude between measures, and the inferences available when scalp distributions differ, are fundamental to the way in which ERP data are used in this thesis. Qualitative differences, or differences between scalp distributions, are often interpreted as reflecting either the engagement of different brain regions or the differing degrees of activation among some of a set of brain regions (Urbach & Kutas, 2002). In

contrast, quantitative differences, or differences in magnitude between conditions in the absence of differing scalp distributions, are usually interpreted as indicating differences in the degree to which a particular process was (or set of processes were) engaged across conditions. In the experiments reported in this thesis, ERP waveforms associated with different experimental conditions and response categories were contrasted. By using inferential statistics it was possible to discern when and in what way the ERP waveforms associated with these different event-types reliably differed.

## APPENDIX CHAPTER B: CONTENT-SPECIFIC MEMORY EFFECTS

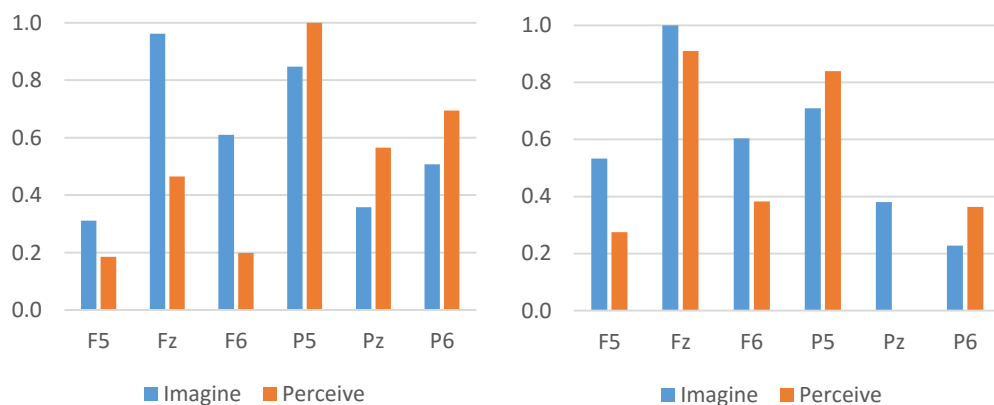
The analyses described here were designed to assess the sensitivity of ERPs to content-specific retrieval under circumstances where response accuracy was matched. The ERP analyses were restricted to the 500-800ms epoch for Experiments One and Two, because this is the time period in which ERP old/new effects have been shown to vary with content in samples of university students (MacKenzie & Donaldson, 2007, 2009; Yick & Wilding, 2008).

In separate initial ANOVAs for each target designation, the mean amplitudes associated with correct judgments to targets were contrasted with those associated with correct rejections. In both contrasts the factor of site was included (25 levels; FP1/2, F7/8, F5/6, F3/4, Fz, T7/8, C5/6, C3/4, Cz, P7/8, P5/6, P3/4, Pz, O1/2). Where reliable interactions between response category and site were obtained, indicating the presence of old/new effects, the sensitivity of ERP old/new effects to the contents of retrieval was then investigated by contrasting the mean amplitudes for difference scores. Difference scores were obtained by subtracting amplitudes associated with correct responses to new items from those associated with correct target judgments. Analysing the target old/new effects only permitted a more controlled assessment of the sensitivity of ERPs to contents of retrieval than if non-targets were also included. Given the nature of the response requirements in the exclusion task, correct responses to non-targets come about when a non-target is forgotten, as well as when a correct response is made on the basis of veridical information recovered from memory. Site was again included as a factor (levels as indicated above) along with target designation. Where reliable interactions were obtained follow-up analyses were conducted over data rescaled using the min-max method (McCarthy & Wood, 1985; Wilding, 2006).



For Experiments One and Two, in both target designations there were reliable interactions between response category and site (Experiment One:  $F(4.6, 215.1)=7.23, p<0.0001, E=0.19$ ;  $F(5.3, 251.2.4)=14.06, p<0.0001, E=0.22$ ; Experiment Two:  $F(4.3, 201.7)=7.04, p<0.0001, E=0.18$ ;  $F(4.2, 197.4)=8.41, p<0.0001, E=0.18$  for imagine and perceive items respectively). These interactions are evidence for the presence of old/new effects in each of the four cases.

When analyses were conducted on the ERP differences obtained when mean amplitudes for new items were subtracted from those for target items, a reliable interaction between target designation and site was obtained ( $F(4.6, 215.8)=8.51, p<0.0001, E=0.19$ ;  $F(2.9, 134.3)=3.21, p=0.027, E=0.199$  for Experiment One and Two respectively). Moreover, these interactions remained reliable when the analysis was conducted over data rescaled using the min-max method ( $F(4.4, 205.6)=6.90, p<0.0001, E=0.18$ ;  $F(4.1, 194.7)=8.27, p<0.0001, E=0.17$  for Experiment One and Two respectively; see McCarthy & Wood, 1985; Wilding, 2006).



**Figure 23 – Bar charts showing the rescaled target-new differences for Experiment One (left) and Experiment Two (right) for frontal (F5, Fz, F6) and parietal electrode sites (P5, Pz, P6) for the 500-800ms epoch. Difference scores were obtained by subtracting amplitudes associated with correct responses to new items from those associated with correct target judgments. Data were rescaled using the min-max method (McCarthy & Wood, 1985; Wilding, 2006).**

This provides evidence to suggest recovering imagined and perceived information elicit qualitatively distinct ERP distributions, indicating that not entirely overlapping neural mechanisms are involved in the recovery of these two types of information. The primary difference between the distributions is the somewhat more anteriorly distributed effect in the imagine target designation from 500ms onwards. This is broadly consistent with

fMRI data acquired during retrieval tasks where anterior prefrontal cortex activation has been associated with recovery of self-generated information (e.g. Simons et al., 2008; Simons et al., 2005; Turner et al., 2008). These findings extend the range of circumstances under which ERPs index retrieval in a content-sensitive manner. This finding is important because it broadens the opportunities that ERPs provide to investigate questions about retrieval control and content-specific retrieval impairments.

**APPENDIX CHAPTER C: RESULTS FROM VIVIDNESS OF VISUAL IMAGERY QUESTIONNAIRE (VVIQ; CUI ET AL., 2007; MARKS, 1973)**

*Table 19 – Mean scores from VVIQ for all experiments. Standard deviations (SD) in parentheses.*

	<b>Experiment One</b>	<b>Experiment Two</b>	<b>Experiment Three</b>	<b>Experiment Four</b>
<b>Eyes Open Total</b>	37.38 (11.34)	41.98 (10.07)	36.73 (14.21)	32.27 (14.30)
<b>Eyes Closed Total</b>	33.93 (14.11)	34.13 (11.01)	38.41 (15.72)	34.80 (14.08)
<b>Total Score</b>	71.30 (22.57)	76.10 (18.43)	74.68 (26.10)	63.73 (28.82)

## APPENDIX CHAPTER D: ANALYSES OF FALSE ALARM RATES AND BR VALUES

One of the underlying assumptions of the process dissociation procedure (Jacoby, 1991) is that the probability of correctly responding old to an item would be equal across both the inclusion and exclusion conditions, were it not for recollection. Toth et al. (1995) emphasised that if participants were to utilise familiarity differentially across conditions (e.g. alter their response criterion) this would be reflected in different false alarm rates, which should be reported in every paper using the process-dissociation procedure and used to inform any conclusions drawn. Whilst no inclusion condition was used in the experiments reported in this thesis, it is still possible to investigate whether familiarity was differentially used between target designations.

**Table 20 – Probability of incorrect responses for target, non-target and new items split by target designation (imagine/perceive) for each experiment. Standard deviations (SD) are in parentheses.**

Proportion	Experiment One		Experiment Two	
	Imagine	Perceive	Imagine	Perceive
Target	0.16 (0.12)	0.18 (0.13)	0.24 (0.12)	0.27 (0.15)
Non-Target	0.11 (0.08)	0.07 (0.05)	0.14 (0.07)	0.14 (0.08)
New	0.06 (0.15)	0.02 (0.04)	0.08 (0.08)	0.06 (0.07)

Proportion	Experiment Three		Experiment Four	
	Imagine	Perceive	Imagine	Perceive
Target	0.12 (0.11)	0.08 (0.09)	0.20 (0.17)	0.16 (0.15)
Non-Target	0.12 (0.09)	0.05 (0.06)	0.19 (0.13)	0.07 (0.09)
New	0.04 (0.04)	0.01 (0.02)	0.16 (0.16)	0.05 (0.06)

To establish differences between the criteria used for making an old response on the basis of familiarity new items are the most relevant to examine as these items should have the same range of familiarity scores in both target designations. For old items, however, that would not necessarily be the case. To examine this, false alarm rates were calculated for new items split by target designation within each experiment. As can be seen in **Table 20**, there appear to be discrepancies between target designations in terms of false alarm rates to new items across most experiments. This was confirmed using pairwise t-tests which showed there were significantly more false alarms to new items in the imagine target designation in Experiment One ( $t(47)=2.10, p=0.041$ ), Experiment Three ( $t(21)=2.44, p=0.024$ ) and Experiment Four ( $t(15)=3.68, p=0.002$ ), but not

Experiment Two. Arguably, out of the experiments recruiting healthy control participants Experiment Two provides the cleanest contrast, considering the low levels of false alarms exhibited across Experiments One and Three. The significant difference in Experiment Four however is more problematic and suggests participants may have used familiarity differentially across target designations. The higher false alarm rate for new items in the imagine target designation suggests patients may compensate for difficulties in recollecting imagined information by relying to a greater extent on familiarity (e.g. Moritz et al., 2004).

This possibility was further assessed using Br values. Br values refers to the probability of accepting an item when in an uncertain state (Snodgrass & Corwin, 1988). The rationale for examining these measures was that if familiarity was being used differentially between target designations, this may also be reflected in differential measures of response bias. As can be seen in **Table 21**, for most experiments more stringent response criteria seem to have been adopted for target items relative to non-target items, especially for items in the perceive target designation compared to those in the imagine target designation. To examine this, initial ANOVAs with factors of target designation (two levels; imagine and perceive) and response category (two levels; target and non-target) were conducted for each experiment. No significant interactions were identified in any experiment. Main effects of target designation were identified in Experiment One ( $F(1, 47)=14.12, p<0.001$ ), Experiment Three ( $F(1, 21)=9.35, p=0.006$ ) and Experiment Four ( $F(1, 15)=12.20, p=0.003$ ), indicating more liberal response criteria were adopted in the imagine compared to the perceive target designation. Main effects of response category were identified in Experiment One ( $F(1, 47)=45.92, p<0.001$ ), Experiment Two ( $F(1, 47)=63.97, p<0.001$ ) and Experiment Three ( $F(1, 21)=22.13, p<0.001$ ), indicating more liberal response criteria were adopted for non-targets compared to targets. The main effects of response category are unsurprising given the response demands of an exclusion task and the proportion of items associated with a non-target response key. The main effects of target designation provide further evidence to indicate differential retrieval processes contribute to the recovery of imagined compared to perceived information.

**Table 21 – Br values split by target designation (imagine/perceive) for each experiment. Standard deviations (SD) are in parentheses. T = target and NT = non-target.**

Proportion	Experiment One		Experiment Two	
	Imagine	Perceive	Imagine	Perceive
Br T Value	0.24 (0.22)	0.11 (0.16)	0.23 (0.18)	0.18 (0.16)
Br NT Value	0.43 (0.22)	0.31 (0.20)	0.37 (0.15)	0.34 (0.15)

Proportion	Experiment Three		Experiment Four	
	Imagine	Perceive	Imagine	Perceive
Br T Value	0.24 (0.31)	0.13 (0.25)	0.44 (0.17)	0.21 (0.28)
Br NT Value	0.57 (0.25)	0.32 (0.33)	0.44 (0.13)	0.27 (0.25)