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Nature of contribution by PhD candidate	Participant recruitment, running of the experiment, data analyses, writing up of the manuscript.
Extent of contribution by PhD candidate (%)	85%

CO-AUTHORS

Name	Nature of Contribution
Vanessa Lim	Experiment design and programming, equipment set up, and help with EEG data analyses.
Ian Kirk	Help with EEG data analyses, and editing of the manuscript.
Karen Waldie	Supervision of the study, help with statistical analyses, and editing of the manuscript.

Certification by Co-Authors

The undersigned hereby certify that:

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- in cases where the PhD candidate was the lead author of the work that the candidate wrote the text.

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Nature of contribution by PhD candidate	Participant recruitment, running of the experiment, data analyses, writing up of the manuscript.
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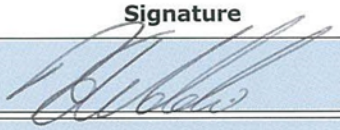
A/P Karen Waldie		25/03/2015
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Extent of contribution by PhD candidate (%)	90%

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Karen Waldie	Supervision of the study and editing of the manuscript.

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Nature of contribution by PhD candidate	Participant recruitment, running of the experiment, data analyses, writing up of the manuscript.
Extent of contribution by PhD candidate (%)	85%

CO-AUTHORS

Name	Nature of Contribution
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Karen Waldie	Supervision of the study and editing of the manuscript.

Certification by Co-Authors

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Preface

This section briefly describes the chapters in the current thesis. The four experimental studies (Chapters 3, 4, 5, and 6) are presented in manuscript style, which includes abstract, introduction, methods and materials, results, and discussion subsections.

Chapter 1 provides the relevant background literature into the cognitive and neural bases of schizotypy and schizophrenia. The history of the schizotypy construct, its development, and the overlap with schizophrenia are discussed, followed by a detailed review focusing on four separate aspects of schizotypy research. The thesis rationale is then outlined, which includes the aims and hypotheses of the current thesis.

Chapter 2 describes the general overview of the research design and methods from the four studies within the thesis. It provides detailed descriptions of the recruitment procedures, participants, tasks and stimuli, as well as the testing procedures. The behavioural and neuroimaging methods used to collect and analyse data are also outlined.

Chapter 3 presents the results from the first experiment, which uses electroencephalogram to investigate sensory level differences in high and low schizotypal participants by examining the P50 event-related potential.

Chapter 4 presents the results of two separate laterality experiments, whereby a behavioural dual-task and a functional magnetic resonance imaging lexical decision task are employed to further clarify the possible association between schizotypy and atypical language laterality.

Chapter 5 investigates the link between enhanced creativity and schizotypy by utilising a behavioural creativity task and a functional magnetic resonance imaging drawing task. First, a well-known behavioural measure is used to assess the levels of both verbal and figural creativity. This is then followed by examining the neural correlates of figural creativity, which is then correlated with schizotypal traits.

Chapter 6 reports findings from the last experiment, which uses structural magnetic resonance imaging to examine the association between schizoypy and regional neuroanatomical differences.

Finally, Chapter 7 provides a general discussion of the findings from the four studies reported in the current thesis. The main implications of this research, its limitations, and suggestions for future directions are also presented.

Chapter 1: General introduction

1.1 Introduction

Schizophrenia is a clinical mental disorder with a lifetime prevalence of 0.7%-1.1% and a peak onset age of early adulthood (McGrath, Saha, Chant, & Welham, 2008). It is a heterogeneous disorder comprising of three distinct types: positive; negative; and disorganised schizophrenia (5th Ed.; *DSM-5*; American Psychiatric Association, 2013). Positive symptoms include delusions, hallucinations, conceptual disorganisation, grandiosity and formal thought disorder, whereas negative symptoms consist of emotional and social withdrawal, anhedonia, attentional impairment, lack of empathy, and difficulty in abstract thinking. Disorganised schizophrenia is characterised by disorganised cognition and thinking, as well as atypical motor behaviour (Kay, Fiszbein, & Opler, 1987; Schultz & Andreasen, 1999). Because of its pervasive and detrimental effects on typical daily life functioning, it creates a large cost to both the individual and society, including costs of health and residential care, loss of quality of life for the individual, as well as the financial and emotional burden to the families and carers (Masters, 1997).

Due to these reasons, increasing amounts of effort have focused on developing early detection and intervention methods, with the aim of placing preventative measures prior to the first psychotic episode, and during the individual's 'prodromal' and 'critical' periods (Birchwood, Todd, & Jackson, 1998; Debbané et al., 2014). The 'prodromal' period indicates a change from a stable premorbid mode to an 'at-risk' mode before the onset of the first psychotic symptoms, whereas the 'critical' period represents the deterioration in functioning within the first 2-3 years of the diagnosis (Birchwood et al., 1998; Masters, 1997). Such progression of the disorder suggests that the development of the disorder lies on a spectrum, rather than being dichotomous with a sudden onset.

This developmental nature of the disorder was first observed over a century ago by Bleuler (1911/1950), who suggested a 'whole group of schizophrenias' to describe the variety of the different symptoms, which did not always progress to full manifestation of the disorder, and were often present in the relatives of patients (Fusar-Poli & Politi, 2008). This led to the idea of 'latent schizophrenia' referring to the nonpsychotic individuals displaying schizophrenia-like traits, gradually leading to the concept of a genetic liability and the dimensional nature of the disorder. It was further extended to include models of schizotypy in the 1950s and 60s by Rado (1953) and Meehl (1962), which provided a unifying contruct linking the spectrum of clinical and subclinical manifestations of symptoms (Debbané et al., 2014). Since the pioneering work of these early psychiatrists and scientists, schizotypy has become an increasingly studied construct with more than 1000 publications, with various behavioural, functional, and structural studies establishing a substantial overlap between schizotypy and schizophrenia. It provides an integrative framework due to its multidimensional nature that allows for investigations into the expression and progression of schizophrenia-spectrum psychopathology, without the confounding effects that frequently stem from patient studies (Kwapil & Barrantes-Vidal, 2014).

A major focus of current schizotypy research has been on the transition from subclinical schizotypy to clinical disorders by examining the at-risk states and cognitive functioning of high-risk individuals, with the aim of identifying presymptomatic criteria for early detection of psychopathology onset (e.g., Schultze-Lutter, Klosterkötter, & Ruhrmann, 2014). Although this is crucial step for the possible prevention of the disorder, a view of schizotypy as a trait (rather than a predisorder state) is also imperative in defining developmental pathways that link schizotypal personality traits to subclinical mental states to clinical psychopathology. In particular, research into the mediating role of schizotypy traits in *nonclinical* individuals is important as it has been speculated that only 10% of those with

schizotypal traits will transition into a clinical state, which gives rise to the big question of what differentiates this 10% from the rest of the schizotypal population (Lenzenweger & Korfine, 1992; Lenzenweger, 2006). In line with this, a continuous model of schizotypy may be a more appropriate approach (rather than treating schizotypy as an attenuated form of schizophrenia), which defines schizotypy as a group of normally distributed traits within the general population, that range from individual personality differences to dysfunctional states (Claridge & Beech, 1995). This view is particularly interesting as it offers insight into the possible 'healthy' manifestations of the construct, and may allow for the differentiation between maladaptive and adaptive schizotypy, where the former has a higher risk of conversion into schizophrenia-spectrum disorders compared to the latter.

Therefore, the main aim of the current thesis was to investigate and expand our understanding of schizotypy using neuroimaging methods. By defining schizotypy as a dimensional construct, we were interested in examining it both as a liability to schizophrenia *and* also as a part of individual personality differences. We were especially interested in the effect of schizotypy across multiple domains, as majority of the research has focused on the influence of schizotypy on a single task or a specific function. Therefore, we used a core sample of 35 participants across four separate experimental studies, taking into consideration the overall construct as well as the different dimensions of schizotypy. This chapter will provide a broad description of the construct and an introduction of the research which has been conducted thus far, with a focus on the overlap between schizotypy and schizophrenia, as well as the rationale behind the four studies.

1.2 What is schizotypy?

Schizotypy is defined as a cluster of nonclinical symptoms and personality traits within a healthy population, which may lead to a predisposition to schizophrenia and other

related disorders (Claridge, 1997; Jahshan & Sergi, 2007; Raine, Lencz, & Mednick, 1995). Due to the dimensional nature of schizotypy, this construct is used to describe a continuum ranging from normal behaviour and experiences to more extreme states that characterise psychosis and schizophrenia (Kravetz, Faust, & Edelman, 1998).

Schizotypal traits are seen to be especially prevalent in non-affected relatives of those with schizophrenia, who often display traits that are qualitatively similar to schizophrenic symptoms in the absence of psychosis (Koychev, El-Deredy, Haenschel, & Deakin, 2010; Snitz, MacDonald, & Carter, 2006). This observation was first made by two early psychiatrists, Kraepelin (1909-1913/1971) and Bleuler (1911/1950), who were the first to establish the concept of 'latent schizophrenia', used to describe a group of individuals who displayed dilute schizophrenic-like symptoms. They also noted that such affected individuals were often the biological relatives of those suffering from clinical schizophrenia, establishing a theoretical foundation for a possible schizophrenia liability (Kendler, 1985).

The term 'schizotype' was first introduced by Rado (1953), who used it to describe the alternate manifestations of such genetic liability. He proposed that an interaction between environmental factors and an inherited predisposition to schizophrenia resulted in a schizophrenic phenotype (or schizotype). He described schizotypal individuals as having a reduced capacity to experience pleasure and lacking in body awareness, and suggested that compensatory mechanisms to overcome such deficiencies resulted in the presentation of schizotypal traits. He further described these mechanisms as lying on a continuum (or as "developmental stages of schizotypal organisation"; p. 416) depending on the overt manifestations of schizotypal behaviour, ranging from stable compensated schizotypy to schizophrenic psychosis.

Leading on from Rado's observations, Meehl (1962, 1990) described four clinical signs of schizotypy (cognitive slippage, interpersonal aversiveness, anhedonia, ambivalence),

and put forward a neurodevelopmental model of schizotypy. This model posits that an aberration in a single dominant gene (or schizogene) results in a widespread defect in the synaptic control system of the central nervous system (CNS) at a neuronal level, resulting in a "ubiquitous CNS anomaly" (1990, p. 14), or schizotaxia. When combined with appropriate environmental influences and social learning history, the schizotaxic individual may develop schizotypal personality (or schizotypy). In agreement with Rado, he also emphasised that only a subset of schizotypes developed clinical schizophrenia depending on the amount of interaction between schizotaxia and genetically determined factors, named polygenic potentiators (see Figure 1.1). These potentiators include social introversion, levels of anxiety and aggression, hypohedonia, low overall energy, hypoarousal, and passivity (Meehl, 1990; Lenzenweger, 2006).

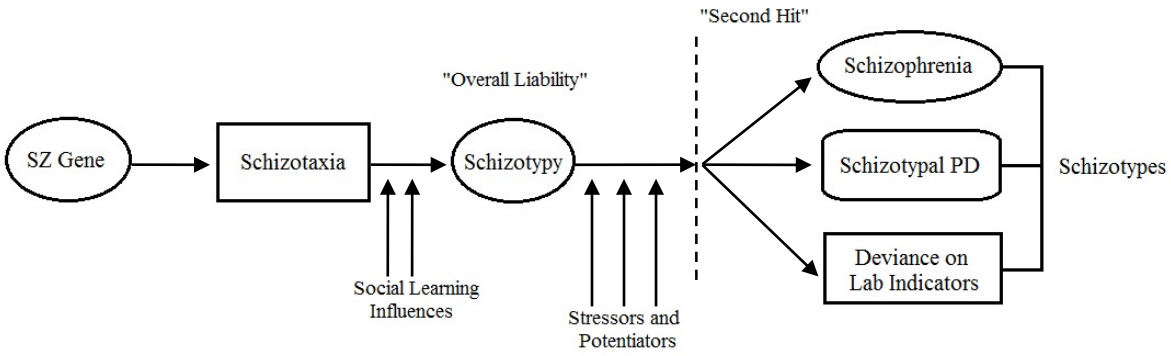

Figure 1.1 Causal relationship among schizotypy, social influences, and potentiators, leading to three possible outcomes: schizophrenia (SZ); schizotypal personality disorder (PD); and deviance on laboratory indicators. The broken vertical line represents the divide between nonclinical and clinical manifestations of schizotypy. Overall liability refers to the combination of all factors (schizotypy, social learning influences, stressors, and potentiators), which affect the likelihood of developing schizotypy. Second hit refers to the external agent which triggers the development of a clinical schizotype. Adapted from Lenzenweger (1998, p. 97).

In summary, Meehl's model of schizotypy (1962, 1990) posits that the likelihood of an individual developing clinical schizophrenia depends on the complex interaction between three crucial factors: 1) a schizotaxic vulnerability; 2) social learning influences mediated by the environment; and 3) the polygenic potentiators. A crucial component of this model is the requirement of the schizogene, which is necessary (but not sufficient) for the development of schizophrenia. Furthermore, he defined schizotypy as taxonic in nature, and estimated that approximately 10% of the general population to be schizotypal, with 10% of this subgroup eventually developing schizophrenia (for a review, see Lenzenweger, 2006). Although some studies have confirmed base rates of around 10% in nonclinical populations (e.g., Linscott, 2013), questions have been raised regarding the categorical nature of taxonic models, which are inconsistent with the view that psychopathology is the result of multiple factors and influences, both genetic and environmental (Widiger, 2001).

When taken together, Rado's (1953) and Meehl's (1962, 1990) models form the quasi-dimensional approach to schizotypy, which represents a view where schizotypy is seen to be an attenuated version of schizophrenia. A key feature of this model is that schizotypy is viewed as an underlying clinical process, which can manifest itself with varying levels of severity depending on the degree of expression of the underlying cause (the schizogene). However, the quasi-dimensional nature of the model does not account for the prevalence of psychotic-like experiences (such as hallucinations and/or delusions) that occur within the general population, especially among those who may not have the schizogene (e.g., Scott et al., 2008). Therefore, an alternative view that takes these issues into consideration is the fully dimensional model of schizotypy developed by Claridge and colleagues (Claridge & Beech, 1995), which takes a more personality-based approach. As well as including the quasi-dimensional model, this approach extends the spectrum to include schizotypal traits that are

part of typical personality differences, therefore defining schizotypy as both healthy individual differences and as a predisposition to schizophrenia (see Figure 2; Claridge, 1997).

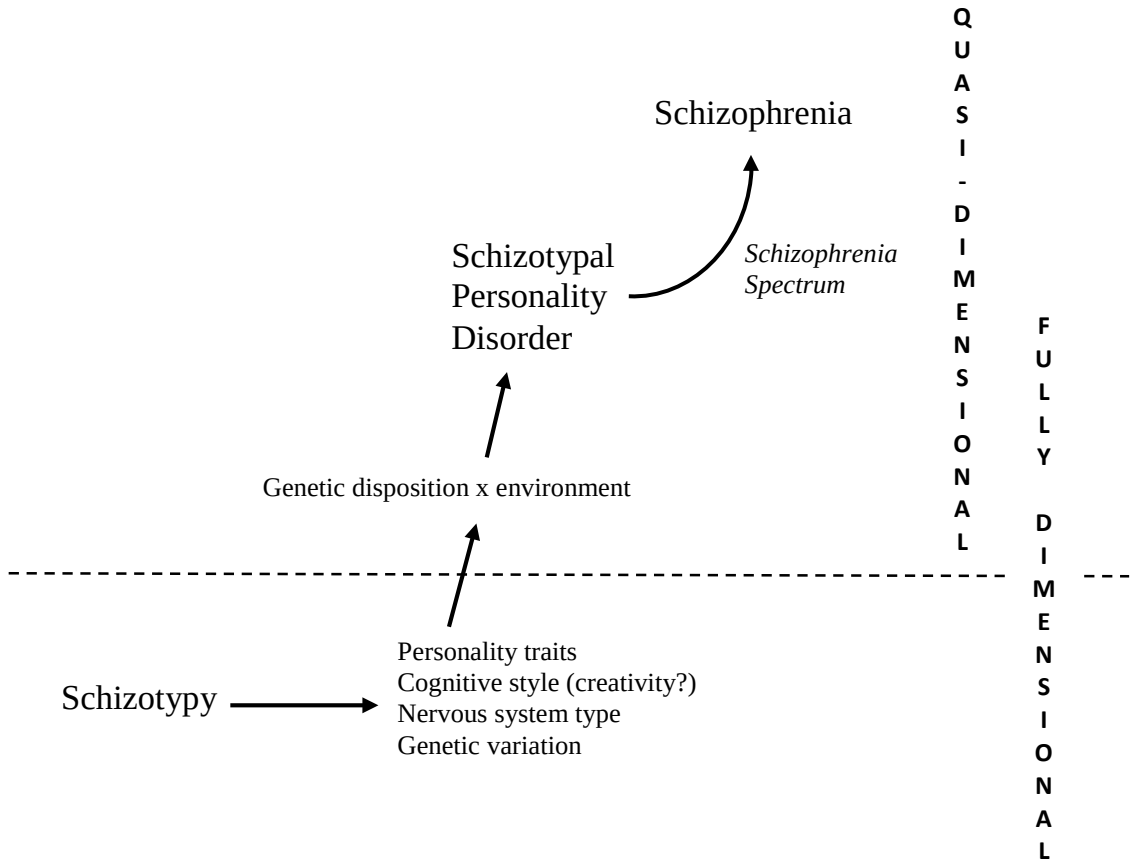

Figure 1.2 Two models of schizotypy as defined by Claridge (1997). The main difference between the two models is that the quasi-dimensional model is psychopathology-based, in contrast to the fully dimensional model which is more personality-based. The arrows represent the schizotypy spectrum, with the curved line indicating an increasing level of psychosis. The dotted line represents the divide between nonclinical and clinical schizotypal traits. Adapted from Claridge (1997, p. 12).

An important distinction between the two approaches is that, while the quasi-dimensional model only applies to a subset of the population, the fully dimensional model includes all members of the general population, with schizotypal traits ranging from low to high which result from a combination of genetic, environmental, and personality variations (Claridge & Beech, 1995). Although those with high levels of schizotypal traits may show

cognitive, emotional, behavioural, and psychophysiological alterations when compared to those with low levels of schizotypy, the model also emphasises that not all with high schizotypy will develop a clinical disorder, which may instead have adaptive effects such as enhanced creativity (Nelson & Rawlings, 2010; Raine, 2006). These traits are most commonly measured by psychometric schizotypy measures, which have been designed to incorporate the different types of schizotypal personality traits observed between individuals, as well as within.

1.3 The multidimensionality and assessment of schizotypy

Factor analytical studies of schizotypy measurement have shown it to be a multidimensional construct, usually consisting of three or four factors. Similar to schizophrenia, these factors include positive symptoms, which include magical ideation and unusual perceptual experiences, and negative symptoms, which include cognitive impairment, apathy, asociality, and affective flattening (Dinn, Harris, Aycicegi, Greene, & Andover, 2002). A third disorganised dimension is also commonly included in schizotypy measures, assessing the level of social anxiety, moodiness, and difficulties with concentration and attention, which is analogous to the disorganised type of schizophrenia (Mason, Claridge, & Jackson, 1995).

These dimensions have been found to be independent of age and gender, as well as existing across various cultures and religious affiliations, and therefore seem to be stable factors of the schizotypy construct (Fossati, Raine, Carretta, Leonardi, & Maffei, 2003; Reynolds, Raine, Mellingen, Venables, & Mednick, 2000). However, while some emphasise the overlap between these factors and symptoms of schizophrenia (e.g., Gruzelier, 1996), others argue that they do not fully parallel each other, and that clinical symptoms of schizophrenia are not direct manifestations of schizotypal traits (e.g., Mason, Claridge, &

Williams, 1997; Richardson, Mason, & Claridge, 1997). Furthermore, other factor analyses have identified a fourth schizotypy factor that is characterised by impulsive and nonconforming aspects of behaviour, which is not a part of the schizophrenia symptom subtypes (Claridge et al., 1996).

Psychometrically, schizotypy can be seen as a set of distributed personality traits and experiences which indicates the *degree of predisposition* to schizophrenia, although it needs to be stressed that a high degree of predisposition does not result in a definite progression into clinical psychopathology. Nonetheless, individuals who score high in self-report measures of schizotypal characteristics do seem to exhibit specific psychological and biological abnormalities, which are qualitatively similar to those observed in schizophrenia patients but less severe (Mohanty et al., 2005). Furthermore, these individuals may meet the criteria for schizotypal personality disorder (SPD; a clinically diagnosed disorder) which can either be observed as a distinct schizotype according to Meehl's model of schizotypy (Meehl, 1990), or as an attenuated form of schizophrenia (Raine, 2006). Therefore, if schizotypy and schizophrenia are part of the same extended psychosis spectrum, it is expected that they would share certain behavioural, perceptual, cognitive, and psychophysiological similarities albeit in a dose-related manner. This may be especially advantageous when examining the possible aetiology of schizophrenia, as those with high levels of nonclinical schizotypy usually consist of healthy individuals who do not need pharmaceutical treatment, which is one of the main confounding factors in schizophrenia research.

However, in order to make any inferences from schizotypy populations, this construct needs to be measured in a well-validated and reliable manner. Although many psychometric measures have been designed since the 1970s (for a review, see Fonseca-Pedrero et al., 2008), there are three main scales that have been used consistently within the literature and are widely-known: the Chapman scales (Chapman, Chapman, & Kwapil, 1995); the

Schizotypal Personality Questionnaire (SPQ; Raine, 1991); and the Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE; Mason, Linney, & Claridge, 2005; Mason & Claridge, 2006). The Chapman scales, which comprise of three separate 'true/false' scales (Perceptual Aberration Scale, Physical Anhedonia Scale, and Social Anhedonia Scale), were some of the earliest measures utilised in schizotypy studies, and are the bases of the more recently developed scales. Their psychometric properties have been researched since the 1980s and therefore are considered to be both reliable and valid. The SPQ (Raine, 1991) is a self-report questionnaire which consists of 74 'yes/no' items that are divided into 9 subscales, and incorporates DSM-III-R (American Psychiatric Association, 1987) criteria for SPD diagnosis. Subsequently, these scales have been found to load onto three factors: cognitive-perceptual (positive); interpersonal (negative); and disorganised (Raine et al., 1994). While it is a well-validated measure which has shown high internal reliability, sampling validity, and test-retest reliability, it has a broad scope designed to screen for SPD in the general population as well as measuring the level of subclinical schizotypal traits (Raine, 1991), and therefore may have more clinical applications compared to the other measures.

In contrast, the newer O-LIFE scale was developed to specifically measure schizotypal characteristics in healthy individuals (Claridge et al., 1996). It consists of 104 self-reported 'yes/no' items that load onto four factors: unusual experiences (which correlates to the positive symptoms of psychosis); cognitive disorganisation; introvertive anhedonia (similar to negative symptoms of psychosis); and impulsive nonconformity (which is not part of the SPQ); and was created through a factor analysis of fifteen pre-existing psychosis-proneness scales in over 1000 subjects (Mason & Claridge, 2006). Unusual experiences refer to items which describe perceptual and hallucinatory experiences, including magical thinking. Cognitive disorganisation measures the level of social anxiety as well as poor attention, concentration, and decision making. Introvertive anhedonia consists of items which describe

a lack of enjoyment from both physical and social sources, and intimacy avoidance. Lastly, impulsive nonconformity contains items that refer to impulse-driven, anti-social, and disinhibited behaviour, which often indicate lack of self-control (Mason & Claridge, 2006). As the O-LIFE is based on the fully dimensional model of schizotypy, rather than the quasi-dimensional, it is particularly suited to testing nonclinical populations, who may provide a more stable investigative opportunity. Due to these properties, the O-LIFE was utilised in the current thesis to measure the levels of schizotypy across all four dimensions in our sample of healthy, young adults.

1.4 The overlap between schizotypy and schizophrenia

As first noticed by Kraepelin and Bleuler, the initial link between schizotypy and schizophrenia was the observation of certain schizophrenia-like symptoms in non-affected relatives of patients, indicating a possible genetic inheritance. Such genetic overlap seems likely when family, twin, and adoption studies of schizophrenia are taken into account, which have shown strong evidence for a genetic component with high heritability estimates ranging from 70% and 84% (Cannon, Kaprio, Lonnqvist, Huttunen, & Koskenvuo, 1998; Lawrie, McIntosh, Hall, Owens, & Johnstone, 2008; Sullivan, Kendler, & Neale, 2003). Using admission records from the Maudsley and the Bethlem hospitals in London, Cardno et al. (1999) found that concordance for schizophrenia in monozygotic twins was 40.9% and 5.3% for dizygotic twins, lending considerable support for a genetic basis of the disorder. It has been further reported that the risk of developing the disorder increases to 9% when a sibling is affected, 16% when both a parent and a sibling are affected, and is the highest at 46% when both parents are affected (McGuffin, Owen, & Farmer, 1995).

In line with the concordance findings, higher levels of schizotypal personality traits have been observed in families with a history of schizophrenia, including individuals who do

not develop overt psychosis. This suggests that schizotypy may be a phenotypic expression of a biological-genetic vulnerability to schizophrenia (Mata et al., 2003; Mechri et al., 2010). In particular, correlations between specific dimensions of schizotypy and schizophrenia have also been found where schizophrenia patients with positive symptoms are related to those who display high levels of positive schizotypy, and vice versa, whereas those with negative schizophrenia symptoms have family members displaying negative schizotypal traits (Mata et al., 2000; Tsuang, 1993). Although this association is not always consistent, with some studies showing no differences in levels of schizotypy between relatives of schizophrenia patients and healthy controls (e.g., Kendler, Thacker, & Walsh, 1996), most studies have found that schizotypy and schizophrenia share some genetic heritability (for a review, see Nelson, Seal, Pantelis, & Phillips, 2013).

Behavioural and neurocognitive research indicate an overlap between clinical deficits in schizophrenia and cognitive abnormalities in schizotypal individuals. Recent studies indicate that these impairments in schizophrenia are a result of a failure to integrate local and distributed neural circuit activations (e.g., Andreasen et al., 1999; Benes, 2000; Lewis, Fish, Arion, & Gonzalez-Burgos, 2011; Mendrek et al., 2004) and similar, albeit less severe, performance deficits have also been found in schizotypy. Specific cognitive and perceptual impairments that are attributed to both schizotypy and schizophrenia include: poor working memory (Jansma, Ramsey, van der Wee, & Kahn, 2004; Matheson & Langdon, 2008; Park & McTigue, 1997); impaired facial discrimination (Brown & Cohen, 2010; Gur et al., 2002; Strauss, Jetha, Ross, Duke, & Allen, 2010); impaired emotional processing (Brown & Cohen, 2010; Kring & Moran, 2008); visual processing deficits (Ettinger et al., 2005; Kantrowitz, Butler, Schecter, Silipo, & Javitt, 2009); abnormal language processing (Cochrane, Petch, & Pickering, 2012; Marini et al., 2008; see for reviews, Covington et al., 2005; DeLisi, 2001); sustained attention deficits (Bergida & Lenzenweger, 2006; Liu et al., 2002); and impaired

sensory gating and inhibition (Braunstein-Bercovitz, Rammsayer, Gibbons, & Lubow, 2002; Potter, Summerfelt, Gold, & Buchanan, 2006; Takahashi et al., 2010).

In line with these findings, neuroimaging investigations have uncovered comparable neural activation patterns in schizotypal individuals to those observed in schizophrenia patients when completing specific tasks. These include reduced activations in the subcortical regions such as the striatum, thalamus, and cerebellum during an anti-saccade task (Aichert, Williams, Möller, Kumari, & Ettinger, 2012), and also in the insula, putamen, thalamus, parietal cortex, and fusiform and hippocampal gyri during early attentional processing (Kumari, Antonova, & Geyer, 2008). Other cortical regions have also shown different patterns of activation in highly schizotypal individuals compared to those with low levels of schizotypy when completing functional tasks, such as reductions in prefrontal activity during emotional processing (Modinos, Ormel, & Aleman, 2010), deactivation of the dorsal anterior cingulate cortex when viewing social rejection stimuli (Premkumar et al., 2012), and reduced activations in the inferior and medial frontal lobes during prospective memory task performance (Wang et al., 2014b).

Highly schizotypal individuals also show electrophysiological dysfunction measured by electroencephalography (EEG), which records electrical activity produced by the synaptic excitations of cortical neurons (a more detailed discussion of EEG and other neuroimaging methods is included in Chapter 2). Differences between those with high and low schizopty scores have been found in event-related potential amplitudes such as the P50 (Wang, Miyazato, Hokama, Hiramatsu, & Kondo, 2004), P100 (Koychev et al., 2010), P300 (Klein, Berg, Rockstroh, & Andresen, 1999), and N400 (Prévost et al., 2010), and in neural oscillations including beta and gamma bands (Koychev, Deakin, Haenschel, & El-Deredy, 2011). Such EEG alterations have also been found to be atypical in schizophrenia patients (e.g., Clementz, Geyer, & Braff, 1998; Sun et al., 2013), further adding to the functional

evidence that schizotypy and schizophrenia exist on the same spectrum of underlying traits and symptoms.

Moreover, some similarities in atypical brain structures have been observed across schizotypy and schizophrenia research. Structural differences found in schizophrenia patients when compared to healthy controls include both white and grey matter volume reductions (Honea, Crow, Passingham, & Mackay, 2005; Kawasaki et al., 2008; Kubicki, Westin, McCarley, & Shenton, 2005), as well as abnormal white matter integrity and connectivity (Burns et al., 2003; Pfefferbaum, Sullivan, & Carmelli, 2001), and enlarged ventricular volume (Gaser, Nenadic, Buchsbaum, Hazlett, & Buchsbaum, 2004). Although only a few studies have investigated structural differences in schizotypy so far, they again show some overlap with the abnormalities associated with schizophrenia, including evidence of reduced grey matter volume and cortical thickness especially in the frontal and temporal regions, as well as atypical structural connectivity (e.g., DeRosse et al., 2015; Wang et al., 2014a).

In summary, numerous studies have found substantial evidence for an overlap of cognitive, functional, and structural abnormalities in schizotypy and schizophrenia, with results from psychopharmacological and molecular studies further adding to this evidence (Fanous et al., 2007; Schmechtig et al., 2013). When taken together, they strongly support the dimensionality of the schizotypy-schizophrenia relationship. An important question that follows is: what drives a nonclinical individual with high levels of schizotypy to transition into schizophrenia or other related disorders? Therefore, research into nonclinical populations with schizotypy (when combined with longitudinal data) provides an opportunity to investigate the possible aetiological factors, premorbid influences, and prepathological processes that interact with other external and environmental factors, which may eventually lead to either potential dysfunction (e.g., full-blown psychosis), or to adaptive characteristics (e.g., enhanced creativity). In the current thesis, schizotypy will be examined from four

different neuropsychological perspectives (early sensory processing, language, creative thinking, and neuroanatomical), with the goal of identifying possible endophenotype candidates (defined as internal phenotypes that can be quantifiably measured; Gottesman & Gould, 2003) that characterise dimensional schizotypy. These perspectives were chosen because early sensory processing deficits and neuroanatomical differences, in particular, have consistently been found in schizophrenia patients. Language dysfunction has also been frequently implicated in schizophrenia, whereby its clinical symptoms may be due to "language being at the end of its tether" (Crow, 1997, p. 137). Finally, the putative link between creativity and psychopathology will be examined to see whether certain schizotypal traits are conducive to thinking creatively, possibly stemming from an aberrant cognitive style. In the next section, a brief summary of schizotypy research within the context of these perspectives will be introduced, ending with the current thesis rationale.

1.5 Early processing deficits in schizotypy

One of the main differences between individuals with high schizotypy and those with low schizotypy is the ability to actively suppress irrelevant information. This was first observed in schizophrenia patients who showed reduced cognitive inhibition when performing tasks that required selective attention, leading to the hypothesis that this deficit may underlie some of the behavioural symptoms observed in schizophrenia (Bullen & Hemsley, 1987; Daskalakis & Fitzgerald, 2002; Lubow, Kaplan, Abramovich, Rudnick, & Laor, 2000). More specifically, Frith (1979) suggested that the positive symptoms of schizophrenia (hallucinations, delusions, and thought disorders) could be the result of a failure to adequately inhibit the flow of information from preconscious processes to conscious awareness.

Inhibitory processes in nonclinical schizotypal individuals have also been tested by using a variety of modified cognitive experiments. A possible marker for measuring schizotypy is the latent inhibition (LI) effect, where participants typically show reduced learning when an event is presented with a stimulus which has already been seen previously without requiring a response from the participant. This renders the stimulus to become familiar but ineffective, which leads to decreased associative learning (Lubow & Moore, 1959). It is thought that LI results in a learning bias by selecting the stimulus that may be important over the stimulus which has already been conditioned as irrelevant (Braunstein-Bercovitz et al., 2002). Research has shown a consistent finding of a reduced LI in individuals with high schizotypy when compared to those with low schizotypy, leading to the hypothesis that this decrease in LI is due to dysfunctional attention processing in high schizotypes, and a failure to divert attentional resources from irrelevant stimulus (e.g., De la Casa, Ruiz, & Lubow, 1993; Granger, Prados, & Young, 2012; Lipp & Vaitl, 1992).

Another method of assessing selective attention is to utilise a negative priming paradigm (NPP) to measure inhibition effects in those with high and low schizotypy (e.g., Moritz, Mass, & Junk, 1998). Negative priming refers to the delayed reaction participants show when, for example, they have to name the ink colour of a second Stroop word after being negatively primed with an earlier Stroop word of the same colour that they had to ignore (Beech, Powell, McWilliam, & Claridge, 1989). It has been found that low schizotypal participants show a substantial inhibition effect in contrast to high schizotypal participants who display a significant facilitation effect, suggesting that distracting information can actually aid cognitive processing in those with high schizotypy. Interestingly, by using three different stimuli presentation times (100, 250, and 500ms), Beech et al. (1989) found that the inhibition/facilitation differences in highly schizotypal individuals were observed only at the

100ms presentation time, leading them to posit that such effects only occur with preconscious selection.

Another method of investigating abnormal selective attention is by using psychophysiological measurements of sensory (or sensorimotor) gating. A commonly utilised method within schizophrenia research is the measurement of the prepulse inhibition (PPI) responses. A reduction in the startle response is observed after a startling stimulus (pulse) if it is preceded by a weak prestimulus (prepulse) that does not elicit a measurable startle response itself (Braff, Geyer, & Swerdlow, 2001). Aside from schizophrenia and SPD, deficits in PPI has also been found in healthy individuals scoring highly on psychometric psychosis proneness measures, albeit to a lesser extent (Kumari, Toone, & Gray, 1997; Takahashi et al., 2010). This is taken as evidence for an impairment of inhibitory processes, where the individual is unable to filter out irrelevant sensory information during early stages of processing in order to focus on and attend to more important stimuli (for a review, see Giakoumaki, 2012).

Similarly, the P50 amplitude has also been extensively used to examine sensory gating mechanisms in schizophrenia and schizotypy, where affected individuals fail to show a reduction in the event-related potential (ERP) 50ms after stimulus to the *second* of the two identical auditory stimuli presented in close succession (e.g., Cadenhead, Light, Geyer, & Braff, 2000; Croft, Lee, Bertolot, & Gruzelier, 2001). It is thought that the P50 wave is the result of a preattentive stage of processing in response to auditory stimuli, and healthy controls show a robust attenuation of the test (second) stimulus (S_2) when compared to the conditioning (first) stimulus (S_1), which indicates normal sensory gating. This ability to filter out irrelevant external stimuli is found to be deficient in schizotypal participants, which could lead to sensory overload and disorganised thinking, resulting in symptomatic behaviour assessed by psychometric measures discussed earlier. Wang and colleagues (2004) used the

SPQ to determine the level of schizotypy traits in their participants and found that the level of P50 suppression was negatively correlated with SPQ scores whereby those who scored high in schizotypy showed the smallest $S_1 - S_2$ P50 amplitude difference. In another study, Evans, Gray, and Snowden (2007) used the O-LIFE to assess schizotypy levels and found reduced P50 attenuation in participants who scored high in the cognitive disorganisation factor. Earlier research also showed a correlation between reduced 'gating' and positive symptoms of schizotypy, which include abnormal perceptual experiences and magical ideation (Croft et al., 2001).

In addition to early auditory processing, early visual processing deficits have also been found in those with high schizotypy, leading to impaired cognitive performance. Koychev et al. (2010) utilised a matching-to-sample working memory task, and compared the amplitudes of the P100 peak (a positive ERP component peaking at 100ms poststimulus) between high and low schizotypal individuals. The results showed a significant overall decrease in accuracy for the high schizotypy group when compared to the low schizotypy group, as well as a significantly reduced P100 component for both encoding and retrieval stages of the task. The authors also compared the N100 and P200 components between the two groups but found no differences, adding to the evidence that *early* sensory abnormalities are an important characteristic of the schizophrenia spectrum (Koychev et al., 2010).

It is thought that a major consequence of reduced inhibitory processes and abnormal sensory gating is sensory overload, which may lead to the complex set of clinical deficits associated with schizophrenia and other related disorders. More specifically, such overload may lead to higher-level cognitive difficulties including cognitive fragmentation, thought aberrations, and disjointed speech (Javitt & Freedman, 2015), which are clinical manifestations of some personality traits observed in highly schizotypal individuals (Fanous, Gardner, Walsh, & Kendler, 2001). Therefore, when the results from these studies are taken

together, there is substantial evidence to suggest that a measure of sensory processing deficit could be used as a reliable biomarker to distinguish those on the higher end of the schizotypy spectrum from those on the lower end.

1.6 Language laterality in schizotypy

Numerous studies have found an association between high schizotypy and odd speech, including idiosyncratic word usage and illogical associations (Coleman, Levy, Lenzenweger, & Holzman, 1996; Edell, 1987). Such unusual language production in schizotypy is assessed by neuropsychological measures such as free word-association tests, where the participants are asked to generate a word that comes first to mind that is related to the presented word. Miller and Chapman (1983) found that individuals who scored high on the Perceptual Aberration-Magical Ideation scale (analogous to measuring the positive dimension of schizotypy) produced fewer common words and more unusual responses during a word-association test, when compared to the participants who scored low on the scale. Kiang and Kutas (2006) used the Category Fluency Test (Spreen & Strauss, 1998), in which the participants had to generate as many examples as they could that fit into the given category within a time limit (e.g., fruits, animals, clothing, vehicles). By calculating the number and the typicality of the responses, the authors found that the high schizotypal participants produced more atypical examples in the fruit category compared to those with low levels of schizotypy. These studies support the hypothesis that individuals with high schizotypy show a broader semantic activation network, especially to weakly related items, than those without schizotypal traits (Spitzer, 1997). This view is also consistent with unusual associations of ideas observed in schizophrenia patients, which is also thought to be due to abnormalities in semantic memory activations (Niznikiewicz, Singh Mittal, Nestor, & McCarley, 2010).

Following from these observations, initial investigations into the pattern of language lateralisation in schizotypal individuals began with divided visual field and dichotic listening experiments (which involve presenting verbal information to one visual field at a time for visual studies, and both ears concurrently for auditory studies), and measuring the reaction time and accuracy to determine the corresponding hemisphere's performance. In typical individuals, researchers have found a significant right visual field/ear advantage effect in these tasks due to the left hemispheric specialisation for language, where information presented to the right side is processed more quickly by the left hemisphere as a result of the crossing of the visual/auditory pathways, compared to information coming from the left side (Kimura, 1961; for a review, see Hugdahl, 2011).

However, results from visual field and dichotic listening studies in those with schizotypy have shown that those with high levels of schizotypy traits show reduced lateral asymmetry compared to those who score low, by either showing an attenuated right field/left hemisphere advantage, or an increased left field/right hemisphere advantage (Broks, 1984; Rawlings & Borge, 1987; Rawlings & Claridge, 1984). Kravetz, Faust, and Edelman (1998) found significant two-way interactions between visual field (to which the stimulus was presented) and three of the four schizotypy dimensions measured by O-LIFE (unusual experiences, cognitive disorganisation, and impulsive nonconformity). These interactions showed that individuals with high schizotypy had a slower reaction time compared to those with low schizotypy when stimuli were presented to the left hemisphere for the unusual experiences and cognitive disorganisation dimensions, and a faster reaction time when stimuli were presented to the right hemisphere for the impulsive nonconformity dimension. This is consistent with the hypothesis that certain dimensions of schizotypy are related to superior right hemispheric performance, while others result in inferior left hemispheric functioning (Claridge & Broks, 1984; Kostova, de Loye, & Blanchet, 2011; Rawlings & Claridge, 1984).

Researchers have also examined hemispheric differences for specific linguistic processes, as the left hemisphere is specialised for phonological processing compared to the right hemisphere (Vigneau et al., 2011). By using a consonant-vowel-consonant (CVC) task, Suzuki and Usher (2009) investigated the relationship between laterality and schizotypy in healthy individuals. The CVC task consists of strings of nonsense three-letter 'words' (e.g., G-A-T), which are vertically presented to the left, right and both visual fields. Because the left hemisphere processes words phonologically in contrast to the right hemisphere, CVC can be used to determine the type of linguistic processing each hemisphere uses during the experiment (Lohr et al., 2006). The results showed a smaller difference in processing styles between the right and left hemisphere for those with high levels of schizotypy when compared to the low schizotypy group. This suggests that, for these schizotypal individuals, the right hemisphere is also capable of phonological processing potentially leading to overactivation of the right hemisphere (Suzuki & Usher, 2009).

These behavioural findings are further supported by recent neuroimaging evidence. A functional magnetic resonance imaging (fMRI) study by Mohanty and colleagues (2005) utilised an emotional Stroop task and found increased right and decreased left hemispheric activity in the dorsolateral prefrontal cortex (DLPFC) of highly schizotypal individuals in response to negative emotion word stimuli when compared to those with low schizotypy. Because the right prefrontal cortex has been implicated in threat response (e.g., Nitschke & Heller, 2002), the authors concluded that this increased right DLPFC activity may be an inflated response to negative stimuli even though the meaning of the words are task irrelevant. This is also consistent with studies (noted earlier) that have found dysfunctional attentional processing in schizotypy (Mohanty et al., 2008).

Hori et al. (2008) used near-infrared spectroscopy to investigate the brain activity in female schizotypal participants when performing a verbal fluency task, in which they have to

respond with as many words as they can to a given letter. Functional imaging studies have repeatedly found the typical L > R asymmetry in the prefrontal cortex (PFC) in healthy low schizotypy populations (e.g., Schlösser et al., 1998). In this study, the authors observed significantly greater PFC activation (especially in the right hemisphere) in the high schizotypy group when compared to a low schizotypy group. This adds to the previous findings of increased prefrontal activity in those with SPD when performing cognitive tasks (e.g., Buchsbaum et al., 1997; see for review, Dickey, McCartney, & Shenton, 2002), and contributes to the growing evidence that schizotypy is associated with reduced laterality for cognitive language tasks due to increased right hemispheric activity (Folley & Park, 2005).

However, despite these findings, which seem mostly congruous across multiple studies, there are also some inconsistencies within the literature. In a more recent dichotic listening task study, Castro and Pearson (2011) found no laterality differences between their high and low schizotypy groups when using a word and emotional prosody task, where four rhyming words were repeated in four emotional tones (happy, sad, angry and neutral), although they did find that the high schizotypy group showed a poorer emotional prosody detection compared to the low schizotypy group. The authors posited that the severity of schizotypal symptoms could be related to functional laterality with only those who show highest levels of schizotypy displaying atypical left lateralisation (Castro & Pearson, 2011). In line with this, Schofield and Mohr (2014) also found inconsistent results in their laterality study with highly schizotypal individuals. They employed two schizotypy measures and two laterality tasks and found discrepancies within their sample, where positive schizotypy did not show associations with either task, compared to negative schizotypy which was found to be correlated with an enhanced left hermisphere advantage for both tasks. These results are yet again inconsistent with the majority of the findings in the literature (which mostly show an association between positive schizotypy and atypical laterality but no relationship between

negative schizotypy and laterality differences), leading the authors to make three alternate conclusions: that the difference between hemispheres is so subtle and fluctuating that it is unable to be assessed accurately; that it is indirect and other mediating factors need to be examined; or that there are in fact no laterality differences between high and low schizotypal populations.

It is possible that these conflicting results stem from the different types of language tasks used to examine laterality in these experiments. More specifically, it is unclear whether the laterality differences observed are from pure lexical processing differences (such as recognising a word from a nonword), or other factors that are included in the experimental tasks which could be influencing laterality (such as the role of semantic processing in sentence comprehension language tasks; Kostova et al., 2011). Given the above evidence of behavioural and neural differences in schizotypal populations, employing a straightforward lexical decision task may be beneficial in clarifying the contribution of lexical processes on laterality in schizotypy. This task involves discriminating words from nonwords, and is associated with strong left hemispheric activations in typical individuals, indicating an intact language network (Binder et al., 2003). However, in schizophrenia patients, this pattern of lateralisation is significantly reduced when performing the same task, and it has been suggested that this atypical laterality may be due to a failure to inhibit nondominant language areas (Sommer, Ramsey, Kahn, Aleman, & Bouma, 2001).

In summary, there is some evidence of atypical lateralisation for language in individuals with high schizotypy, which can behaviourally manifest as unusual language production (as measured by tasks such as the Category Fluency Test). However, these findings are far from being definitive and warrant further investigation, especially when compared to those found in schizophrenia studies, which consistently report language deficits and reduced lateralisation in patients (e.g., Marini et al., 2008; Sommer et al., 2001).

Aside from reduced laterality for language, greater performance in verbal fluency tests is thought to be the result of divergent thinking, which is defined as the ability to produce multiple solutions to an open-ended problem (Plucker & Renzulli, 1999). This has been commonly associated with creativity, where those who are able to generate a large amount of unusual ideas are often considered to be 'creative'. Interestingly, studies have frequently indicated an association between elevated levels of creativity and psychopathology, which suggests that creative behaviour may be a result of atypical (and perhaps psychotic) cognition (Barrantes-Vidal, 2004; Nettle, 2001). The following sections will briefly introduce the concept of creativity and its putative link with psychopathology, before focusing on the relationship between creativity and schizotypy.

1.7 Psychosis and creativity

Creativity is considered to be one of the attributes that define humanity (along with language and consciousness), and is tied to the concepts of originality/novelty, flexibility, and variety (Moore et al., 2009; Mumford & Gustafson, 1988). This is congruent with Runco's (2004) definition which describes creativity as more of a syndrome or a complex rather than just original behaviour, which is also both reactive (e.g., problem solving) and proactive (e.g., development of useful ideas). Creative ideas also have to be useful and adaptive as novelty alone is insufficient (Lindell, 2011). One of the most well-established behavioural creativity measures are the Torrance Tests of Creative Thinking (TTCT; Torrance, 1966; 2008a), which rate four subsets of creativity: fluency (the number of answers given); originality (uncommonness of the answers); elaboration (the amount of detail given); and flexibility (diversity of answers).

It has been proposed that a greater spread of cortical activation through semantic networks is an important factor in creative thinking, and in particular, divergent thinking

(Pizzagalli, Lehmann, & Brugger, 2001). Divergent production requires the individual to call for a variety of responses to a target item and tests their associative processes and flexibility (Moore et al., 2009). Research has indicated that divergent thinking scores are predictive of creative activities and accomplishments (Cline, Richards, & Needham, 1963; Russ, Robins, & Christiano, 1999), although there have been questions about whether intelligence (IQ) tests may be a better predictor of creativity than divergent thinking, and whether they even measure significantly different traits to each other (Kim, 2008). In fact, research has indicated mild to significant positive correlations between intelligence and creativity in artists, scientists, mathematicians, and writers, which has led some researchers to believe that intelligence may be a prerequisite to creative performance, and to a further extent, divergent thinking (see for review, Barron & Harrington, 1981). On the other hand, other studies have found little to no relationship between cognitive ability and creativity, with extrovert personality being a better predictor of creative performance than intelligence (e.g., Furnham & Bachtiar, 2008; Sánchez-Ruiz, Hernández-Torrano, Pérez-González, Batey, & Petrides, 2011).

Aside from intelligence, another commonly mentioned association in the literature is the link between creativity and psychopathology (Nettle, 2001). There is substantial evidence to support this relationship, including: psychobiographical studies which have found an increased amount of aberrant and psychotic behaviours (as well as high levels of psychopathology) in eminent achievers, especially in the fields of literature and the arts (Horrobin, 2001; Ludwig, 1995; Reichsman, 1981); and family studies which have shown increased levels of creative aptitudes and interests in relatives of psychiatric patients (Kinney et al., 2001; Richards, Kinney, Lunde, Benet, & Merzel, 1988). Andreasen (1987), using a formal psychiatric diagnostic criteria, conducted structured interviews on writers, controls, and the first degree relatives of both groups, and found a much higher rate of mental illness

(including affective disorder, bipolar disorder, and major depressive disorder) in the writers and their first degree relatives groups compared to their control counterparts. Furthermore, in other studies, psychiatric patients (usually schizophrenic) have demonstrated superior performance compared to controls on divergent thinking tasks (Andreasen & Powers, 1975; Keefe & Magaro, 1980). Finally, numerous studies have also found a positive correlation between tests of creative performance and measures which assess psychosis liability, specifically schizotypy (Fisher et al., 2004; Schuldberg, 1990).

This last finding is especially important as it provides insight into both cognitive and behavioural correlates of creativity. An interesting aspect of psychosis is its resilience within populations over many generations. Huxley, Mayr, Osmond, and Hoffer (1964) first suggested the idea that the relatives of psychosis patients may be physiologically stronger than their ill counterparts, which effectively made up for the patients' lower survival rate. However, there is a lack of empirical evidence for this hypothesis and, in 1972, Jarvick and Chadwick posited that there may be a *psychological* advantage to these relatives, rather than a physiological one, where certain behavioural and personality traits may be advantageous in the social environment. This is in line with research which shows that although creative performance has been observed in psychosis patients, their non-affected relatives often show a higher level of creativity (Richards et al., 1988). Even though the family members share certain traits and predispositions, the non-affected members may have a lower loading of these characteristics, thus leading to the development of creativity without the debilitating effects of psychosis (Karlsson, 1970; Nettle, 2006). When taken together with the evidence that shows an increase in levels of schizotypy in relatives of schizophrenia patients, this suggests that creative behaviour may be a manifestation of schizotypal traits, indicating that there are adaptive characteristics related to schizotypy.

1.8 Creativity and schizotypy

The relationship between schizotypy and creativity has been described as an inverted U curve, where the levels of creativity rises with schizotypy up to a certain point when psychopathology becomes full-blown and therefore detrimental to any creative process (Nettle, 2006). Eysenck (1993) suggested that unusual thought processes observed in schizotypy may be due to a lack of cognitive inhibition; that is, those who are highly schizotypal may inhibit fewer ideas during early processing leading to the possibility of using an increased amount of information in an original manner. As mentioned previously, reduced latent inhibition is a characteristic of the schizophrenia spectrum, and this has also been found in studies with creative individuals (e.g., Carson, Peterson, & Higgins, 2003).

Research has consistently found an association between schizotypy and creativity (Eysenck & Furnham, 1993; Merten & Fischer, 1999; O'Reilly, Dunbar, & Bentall, 2001; Zanes, Hatfield, Houtler, & Whitman, 1998). Nettle (2006) recruited large groups of poets, visual artists, mathematicians, and psychiatric patients along with a control group, and assessed their levels of schizotypy by using the O-LIFE. He found that both the poets and artists displayed higher levels of schizotypal traits when compared to controls, especially in the unusual experiences factor (in which their scores were comparable to schizophrenia patients). They also showed lowest levels of introvertive anhedonia, even when compared to the control group. On the other hand, mathematicians showed the opposite trend scoring the highest in introvertive anhedonia, and the lowest in the other three schizotypy factors than controls. Overall, these results demonstrate that both the artistic and psychiatric groups share a tendency towards unusual thoughts and experiences; however, the former lacks anhedonic qualities, which distinguishes them from the latter.

Batey and Furnham (2008) further investigated the relationship between creativity and schizotypy measures and found positive correlations between creativity and two schizotypy

factors (unusual experiences and impulsive nonconformity), and a negative correlation between creativity and cognitive disorganisation, which suggests that chaotic, disordered thinking is detrimental to creative activity. They did not find evidence for a negative relationship between levels of creativity and introvertive anhedonia, which implies that enjoyment of social and physical pleasures is not a requisite for creative behaviour. In some cases, having elevated levels of anhedonia may even be necessary for creativity as found by Cox and Leon (1999), who discovered a strong association between social anhedonia and divergent thinking. In contrast, Claridge and McDonald (2009) found evidence for relationships between negative schizotypy, autistic traits, and *convergent* thinking when they tested for correlations between measures of cognitive style (divergent vs. convergent), schizotypy, and autistic traits. Although convergent thinking is traditionally viewed as a measure of intelligence rather than creativity (Riding & Cheema, 1991), other research has supported a link between intelligence and creativity (e.g. Barron & Harrington, 1981), which suggests that divergent and convergent thought patterns are positively related (Sternberg & O'Hara, 2000). Claridge and Beech (1995) further posited that higher intelligence (as measured by IQ tests) may even be a protective factor against psychopathology for those with schizotypal traits, by providing them with broader and more flexible cognitive and psychological resources to cope better with stress.

Although it is not yet clear whether certain factors of schizotypy are more highly correlated with creativity than others, when the results are taken together, they support the hypothesis of a link between creativity and schizotypy. This leads to the question of neuropsychological bases of creativity, and whether this quality is seen in schizotypal individuals in conjunction with other maladaptive qualities often associated with schizotypy, such as sensory gating deficits.

1.9 Structural differences in schizotypy

Although a large amount of research has examined schizotypy at a phenotypic level, only a few studies have thus far investigated the neurobiological basis of schizotypy. Findings of structural differences between high and low schizotypal populations could provide an anatomical basis for the behavioural expression of symptoms, and present an opportunity to elucidate the pathophysiology and neurodevelopmental processes of schizophrenia-spectrum disorders. Furthermore, the degree and the amount of neural structures affected may provide further insight into the continuous distribution of symptoms within the general population.

To date, the findings show similar brain abnormalities between schizotypal individuals and schizophrenia patients, including grey matter volume reductions in cortical regions such as the superior temporal gyrus and the inferior frontal gyrus, as well as areas in the parietal cortex (Zhou et al., 2007). There is also evidence of atypical connectivity (Wang et al., 2014a) and decreased white matter integrity in those with high levels of schizotypy (DeRosse et al., 2015). Some discrepancies do exist, however, with some schizotypy studies showing an *increase* in grey matter volume (Modinos et al., 2010). Interestingly, such increases in structural volumes have also been found in individuals with SPD (e.g., Hazlett et al., 2008), which has led to the hypothesis of a possible compensatory mechanism in those with high levels of schizotypy or a diagnosis of SPD. This may also explain why these individuals do not suffer from overt psychosis that is prevalent in schizophrenia patients (Kühn et al., 2012; Modinos et al., 2010). Although further research into the structural differences in schizotypy is needed before further speculations can be made, these highly schizotypal individuals may provide an unbiased and useful insight into the possible neuroanatomical anomalies that exist within the schizophrenia spectrum prior to any onset of psychopathology, as brain structures have been found to be particularly sensitive to the

effects of antipsychotic medication (Ho, Andreasen, Ziebell, Pierson, & Magnotta, 2011; Radua et al., 2012).

1.10 Thesis rationale

The proposed research aims to obtain a more thorough understanding of the effect of schizotypy on brain function and structure by using behavioural and neuroimaging methods. Schizotypy provides a valuable construct for examining the aetiological, phenomenological, and developmental variations across the schizophrenia-spectrum of psychopathology. The current research may also add the possibility of statistical power to investigations, as the dimensional nature of the construct allows for the inclusion of all members of the general population. Therefore, the four studies in the current thesis were intended to investigate schizotypy from four separate neuropsychological perspectives using the same core sample of 35 participants, with the aim of defining possible cognitive and structural markers which may lead to an improved and more comprehensive definition of the construct.

Study 1 uses EEG to examine whether there are preattentive sensory gating differences in individuals with high levels of schizotypy (as measured by the O-LIFE) compared to those with low schizotypy. By using the paired pulse paradigm, the P50 amplitude responses will be compared between groups. Finding a difference would indicate that the P50 amplitude may be used as a reliable psychophysiological correlate of schizotypal personality, as well as establishing gating differences within the current sample. Study 2 investigates possible language laterality differences between the high and low schizotypy groups using both behavioural and fMRI methods. In Study 3, the link between schizotypy and enhanced creativity is examined by firstly using a behavioural creative measure, and then with fMRI to determine neural regions pertinent to creative thinking. This will be then correlated with the scores from the O-LIFE to find associations between specific regions and

schizotypy dimensions. Finally, Study 4 extends the existing literature on structural differences associated with schizotypy by examining regional grey matter volumes using structural MRI.

Particular attention will be paid to the following hypotheses:

1) That the current sample of high schizotypal individuals will display reduced sensory gating compared to the low schizotypal individuals, suggesting that early sensory deficits are present in nonclinical schizotypy;

2) That there will be a reduced pattern of lateralisation for language in the high schizotypy group when compared to the low schizotypy group, in line with prior findings of an overall left hemisphere dysfunction in schizophrenia;

3) That creative thinking will result in a different pattern of neural activation compared to non-creative thinking, which is significantly correlated with the positive dimension of schizotypy (characterised by unusual experiences and thoughts);

4) That schizotypy is associated with regional grey matter volume reductions, in line with the majority of schizotypy and schizophrenia research.

Overall, the findings will provide a more comprehensive understanding of the neural bases of schizotypy, and contribute to the evidence that, although schizotypy may lead to atypical neural activity and a weaker control of preconscious processes, it may also positively affect the individual's creative processes and enhance their artistic performance.

Chapter 2: General methodology

2.1 Participants

Potential participants were recruited using an advertising flier which was posted around the city campus of the University of Auckland, as well as from an online research recruitment website. The initial sample included 64 volunteers who all met the strict exclusion criteria, which were: 1) being left-handed; 2) being bi-/multi-lingual with English not being their first language; 3) currently taking either anti-depressant or anti-psychotic medications; 4) having hearing deficits; 5) being outside the 18-40 years age bracket; 6) being a regular smoker; and 7) having a reading difficulty. As the main objective of this thesis was to investigate the role of schizotypy using different tasks and methods *within* the same group of individuals, 16 volunteers who could not complete all three experimental sessions (described below) were excluded from further testing.

In total, 48 adults participated in this study who completed all screening and experimental procedures (31 females and 17 males). All procedures for recruitment and testing were approved by the University of Auckland Human Participants Ethics Committee (Appendix A). Written informed consent to participate was obtained from all participants, who received NZ$20 (cash or a voucher equivalent) for each of the three experimental sessions as reimbursement for their time (Appendix B).

2.2 Screening procedures

2.2.1 Handedness assessment

The Edinburgh Handedness Inventory (EHI; Oldfield, 1971) was used to confirm that all participants were right-handed (Appendix C). There are ten items in this inventory, where the participant has to indicate their hand preference for different tasks including writing,

drawing, throwing, striking a match, opening a box, and using tools such as scissors, a toothbrush, a knife (without a fork), a spoon, and a broom. Additionally, there are two items related to the dominant foot and eye. Usual hand preference is indicated by placing a cross (+) in either the left hand or the right hand column. In addition, participants can indicate a strong preference by placing two crosses in one column, or an equal preference (for either hand) by placing a cross in each column for the same task.

Handedness is calculated as a Laterality Quotient (LQ) = (R – L / R + L) × 100, where R represents the number of right hand column responses, and L the number of left hand column responses. A positive LQ indicates right hand preference while a negative LQ indicates left hand preference. All 48 participants had a LQ between +60 and +100, indicating strong right handedness.

2.2.2 Hearing assessment

Hearing assessment was required due to the inclusion of an auditory EEG experiment in the study, and was administered on a Dell Latitude D620 laptop running on Windows Vista™ Enterprise. Auditory threshold for each participant was checked by using an Otovation Amplitude T3 series audiometer (Otovation LLC, King of Prussia, PA). The pure tones were delivered wirelessly using the Symphony NOAH Module software Build 1.2.1.0 (Otovation LLC, King of Prussia, PA), which presented tones between 125 and 8000Hz, ranging from -10 up to around 120dB HL (decibels Hearing Level, a measure of sound sensitivity). Each ear was tested separately while background white noise was presented concurrently to the other (non-tested) ear. Participants responded to the pure tones by pressing a button on the audiometer. All tones were presented in a semi-darkened, quiet room, and repeated at least twice to ensure there were no accidental or guess responses. All participants met our cut-off of a pure-tone average threshold of 15dB HL or less for each ear.

The average dB HL for the left and right ears across all 48 participants was 7.07 and 9.02dB HL, respectively.

2.2.3 Schizotypy assessment

The Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE; Mason et al., 1995) was used to assess the level of schizotypy in all participants (Appendix D). The O-LIFE consists of 104 self-reported 'yes/no' items that load onto four factors of schizotypy, some of which are related to the positive and negative symptoms found in schizophrenia (Dinn et al., 2002). These include: unusual experiences, which refer to items that describe perceptual and hallucinatory experiments including magical thinking; cognitive disorganisation, which measures the level of social anxiety as well as poor attention, concentration, and decision making; introvertive anhedonia which describes a lack of enjoyment from both physical and social sources; and lastly, impulsive nonconformity, which consists of items that refer to impulse-driven, anti-social, and disinhibited behaviour (Mason & Claridge, 2006). A total overall O-LIFE score is taken from the average of the four subscale scores. In addition, individual subscale scores can be taken separately if investigating a specific dimension of schizotypy, such as the positive factor (unusual experiences).

The O-LIFE was chosen to assess the level of schizotypy in the current thesis as it is based on a fully dimensional model of schizotypy where it takes a more personality-based approach, and considers schizotypal traits as part of normal personality differences (Claridge, 1997). This is in contrast to the Schizotypal Personality Questionnaire (SPQ; Raine, 1991; another well-used and validated measure in the literature), which is a questionnaire based on the DSM-III-R criteria for schizotypal personality disorder (a clinically diagnosed disorder). Therefore, the SPQ treats schizotypy as a possible precursor to schizophrenia, and follows the

three-factor structure of the disorder (positive, negative, and disorganised), compared to the O-LIFE which includes a fourth impulsive behaviour factor (Asai, Sugimori, Bando, & Tanno, 2011). This difference may be due to the design of the O-LIFE, which was derived using factor-analytic studies of nonclinical personality measures, and therefore the broader nature of this questionnaire is particularly suited to testing nonclinical populations, who may provide a more stable investigative opportunity (Mason et al., 1995).

Furthermore, it also has good psychometric properties, including good test-retest reliability, good validity, high internal consistency, and acceptable levels of skewness and kurtosis (Burch, Steel, & Hemsley, 1998; Mason et al., 1995).

In the current thesis, out of the 48 participants who completed all screening and experimental procedures, only those with a total O-LIFE score of half a standard deviation above or below the mean O-LIFE score were included in the data analyses. This was to ensure that those who scored in the middle were not arbitrarily included into either the high or the low schizotypy group. Furthermore, two factors of the O-LIFE (unusual experiences and impulsive nonconformity) were examined separately in Chapters 3 and 4, in addition to the total O-LIFE. Again, from the sample of 48 participants, those who scored half a standard deviation above or below the mean on the unusual experiences factor or the impulsive nonconformity factor were included in the separate analyses. These mean scores are presented in Table 2.1.

Table 2.1

Mean scores and standard deviations for the schizotypy measures (total O-LIFE, unusual experiences, and impulsive nonconformity) for the high and low scoring groups from an initial sample of 48 participants. The scores are listed for each gender, as well as for both.

Gender	Total O-LIFE			UnEx			ImpNon		
	n	HS Mean (SD)	LS Mean (SD)	n	HP Mean (SD)	LP Mean (SD)	n	HIN Mean (SD)	LIN Mean (SD)
Males	11	13.44 (0.63)	6.82 (1.17)	10	19.50 (4.95)	4.13 (2.30)	10	13.00 (1.16)	4.50 (1.52)
Females	24	15.64 (2.20)	6.40 (1.57)	17	21.18 (3.12)	5.50 (1.87)	23	14.31 (2.93)	5.20 (2.15)
Total	35	15.15 (2.16)	6.57 (1.40)	27	20.92 (3.25)	4.71 (2.16)	33	14.00 (2.65)	4.94 (1.91)

Note: O-LIFE = the Oxford-Liverpool Inventory of Feelings and Experiences; UnEx = unusual experiences; ImpNon = impulsive nonconformity; HS/LS = high overall schizotypy/low overall schizotypy; HP/LP = high positive (unusual experiences) factor/low positive factor; HIN/LIN = high impulsive nonconformity/low impulsive nonconformity; n = number of participants; SD = standard deviation.

2.3 Experimental methods and analyses

This section provides a broad overview of the techniques utilised in this thesis. Specific procedures and analyses relevant to each study can be found in the Methods section of the corresponding chapters.

2.3.1 Electroencephalography (EEG)

EEG is the measurement of electrical activity produced by the brain, which is detected by electrodes that are placed on the scalp and recorded continuously. This activity is caused by local current flows that result from synaptic excitations of cortical pyramidal neurons, which can only be detected when there are large populations of active neurons firing in synchrony in the right orientation (Teplan, 2002). By amplifying the electrical signals, the activity is recorded as EEG data from multiple scalp locations allowing for the measurement of potential changes over time, which then can be analysed. As well as being a non-invasive procedure, EEG also has a very high temporal resolution in the order of a few milliseconds,

making it well suited for investigations into temporal patterns of neural activity (Otten & Rugg, 2005).

The data can be analysed in several ways depending on the experimental tasks and research hypotheses. One approach is by looking into the oscillations of the brain waves, which differ by frequency and are categorised by their amplitude and phase. It is thought that these oscillations occur due to spatially distant neuronal assemblies synchronising their activities for effective communication (Fries, 2005). Each frequency band has been associated with different states and functions, and is categorised as delta (0-4Hz), theta (4-8Hz), alpha (8-12Hz), beta (12-30Hz), and gamma (30-80Hz) bands. Alpha rhythm, in particular, has been studied extensively due to its relationship with cortical excitability, with decreases in alpha power corresponding to task processing and sensory stimulation and increases corresponding to sensory input inhibition (Teplan, 2002). Although such divisions are traditionally used to describe the different characteristics of brain waves, overall they occur concurrently and are present most of the time.

Another approach of examining EEG data is to examine event-related potentials (ERPs), which represent small voltage changes in the electrical activity in response to certain external and internal stimuli or tasks (Coles & Rugg, 1995; Sun & Sinha, 2009). The EEG data are segmented into epochs, where the signal is time-locked to a specific stimulus. By averaging the epochs that are collected over multiple trials, an average ERP can be calculated for that stimulus. As ERPs are thought to be the physiological correlates of perceptual, sensory, and cognitive processes, it is widely used to investigate typical and atypical cognitive function. They are utilised across all domains, including at a functional level (e.g., distinguishing different emotions such as happy or sad faces; Balconi & Pozzoli, 2003), as well as at a lower level (e.g., differentiating the speed of interhemispheric transmission; Moes, Brown, & Minnema, 2007). Generally, they are presented in a waveform format

comprising of peaks and troughs (depending on the polarity of the deflections), commonly referred to as components (see Figure 2.1). Various studies have characterised individual components by linking them to specific functional processes, which are named in terms of their polarity (negative or positive) and latency (in milliseconds) after stimulus onset.

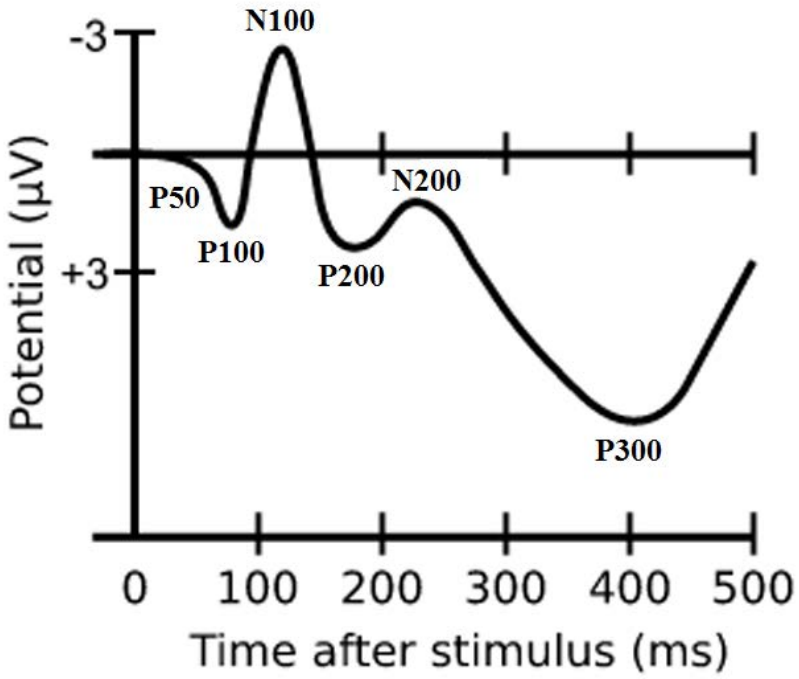

Figure 2.1 An averaged ERP waveform displaying major components, including early waves such as P50, P100, and N100, and late waves such as N200, and P300. Broadly, early components are responses to sensory/exogenous stimuli, whereas late components are elicited by cognitive/endogenous information processing (Sur & Sinha, 2009). By convention, negative peaks are plotted up and positive down. Image adapted from the Wikimedia Commons file "File:ComponentsofERP.svg" and retrieved from http://en.wikipedia.org/wiki/Event-related_potential.

One of the most studied components within auditory research is the N100, which is the first negative evoked potential (indicated by the N) that occurs at around 100ms after the presentation of a stimulus. It is thought to reflect preattentive auditory perception and is particularly sensitive to predictability of speech sounds and phonetic processing (Näätänen & Picton, 1987). Other important components include: the P100, a positive waveform elicited

by visual stimuli (Hillyard & Anllo-Vento, 1998); the N200, which is seen in response to deviant or mismatched visual and auditory stimuli (Folstein & Van Petten, 2008); the P300, which reflects subjective and evaluative aspects of the presented stimuli such as their relevance (Polich, 2007); and the N400, a negative component usually associated with language processing, including sign language (Kutas & Federmeier, 2011). Although the components are named according to when they approximately occur after stimulus presentation, the latencies are variable with some components having longer periods than others (e.g., P300 has a latency of approximately 250 to 500ms, seen in Figure 2.1).

Another component that has been frequently investigated within the context of psychopathology is the P50, which is a small positive peak elicited around 45-75ms after a stimulus presentation (Korzyukov et al., 2007). It is the first major response observed in an ERP, reflecting preattentive sensory information processing, and has been extensively used to especially examine sensory gating mechanisms in schizophrenia patients (Edgar et al., 2003). Such mechanisms are usually tested by administering two identical auditory clicks close in succession and assessing the individual's P50 response to both the first and second clicks. In typical populations, the P50 wave response to the second click is diminished compared to the first click, which is taken as a sign of intact sensory gating. However, a large number of studies have shown this reduction to be often absent in schizophrenia patients, suggesting that such gating deficits indicated by abnormal P50 suppression may be an endophenotype of the disorder (Freedman, Adler, & Leonard, 1999). Whether this is also observed in individuals with nonclinical schizotypal personality will be directly examined in Chapter 3.

Although EEG is widely utilised due to its excellent temporal properties, its main disadvantage is the low spatial resolution that mostly depend on neural activity occurring within the superficial layers of the cortex. However, other neuroimaging techniques which offer high spatial functional maps, such as positron emission tomography (PET) and

functional magnetic resonance imaging (fMRI), can be utilised in conjunction to provide a more complete picture of the neural bases of corresponding cognitive behaviours. In the current thesis, fMRI was used as the imaging technique in Chapters 4 and 5.

2.3.2 Functional Magnetic Resonance Imaging (fMRI)

fMRI is a non-invasive neuroimaging technique that measures changes in blood flow in the brain. It relies on the assumption that cortical blood flow and oxygenation changes depend on neural activity, with increased blood perfusion being correlated with greater cognitive effort. The technique is most commonly based on the measurement of BOLD (blood-oxygenation-level-dependant) signal changes that occur due to the magnetic properties of haemoglobin, where deoxyhaemoglobin (haemoglobin without bound oxygen molecules) has a magnetic susceptibility of about 20% greater than oxyhaemoglobin. This paramagnetic effect of deoxyhaemoglobin molecules induces inhomogeneities into the magnetic field resulting in an endogenous contrast between the blood vessels and the surrounding tissue (Ogawa, Lee, Kay, & Tank, 1990).

More specifically, increases in synaptic metabolism results in a drop in the oxyhaemoglobin concentration in the blood vessels, as neural activity requires more oxygen. From this, vasodilation occurs as a compensatory mechanism, allowing the concentration of oxyhaemoglobin levels to rise which reach a peak approximately 5-8 seconds after stimulus onset (Aguirre, Zarahn, and D'Esposito, 1998). This results in increased MRI signal intensity, which can be used as an indirect indicator of neural activity. Such haemodynamic response to a neural event is named the haemodynamic response function (HRF), which is used in conjunction with the stimulus function to model a typical BOLD response. By using appropriate magnetic resonance (MR) pulse sequences with parameters that are sensitive to

changes in magnetic susceptibility, hypotheses can be made regarding the neural bases of cognitive mechanisms (Huettel, Song, & McCarthy, 2009).

In general, two main fMRI designs are employed in empirical research: task and rest. A task-based fMRI experiment consists of acquiring a series of brain images while the participant is performing a functional task, usually involving an experimental condition and a control condition. The changes in the BOLD signal between individual images are used to investigate task-related activations in the brain. Furthermore, these conditions may be designed in a way that they require similar types of responses but with a targeted distinction, allowing researchers to make inferences about specific functional roles of differentially activated cortical regions. fMRI can also be used to examine resting state activity, where regional interactions that occur in the absence of an explicit task, can be used to explore functional connectivity in typical and atypical populations (Damoiseaux et al., 2006).

All fMRI data require extensive preprocessing and statistical analyses before any interpretations can be made regarding the activations. Numerous sophisticated software exist for full and partial analyses of data, with some containing tools for a full analysis process while others specialise only in certain aspects. Standard preprocessing protocol includes: 1) slice timing correction, which is required due to the fact that the scanner is unable to acquire all slices within a volume simultaneously; 2) realignment and unwarping (by using fieldmaps) of images to correct for any participant movement and inhomogeneities in the magnetic field; 3) spatial normalisation to a standardised co-ordinate space (either Talairach or Montreal Neurological Institute; MNI); and 4) spatial smoothing, which improves the signal-to-noise ratio usually by applying a Gaussian spatial filter (Ashburner et al., 2013).

Statistical analysis of fMRI images requires a design matrix specifying experimental parameters including all conditions and their onsets and durations. This is derived from the BOLD signal for each condition acquired from the experiment, which in turn is modelled by

the convolution of the stimulus function with the HRF, as mentioned earlier in this section (Figure 2.2). The main analysis approach is then chosen on the basis of the research question, with many empirical studies using a univariate general linear model (GLM) approach, most commonly used with Statistical Parametric Mapping software (SPM; Friston et al., 1994). This examines specific brain areas that are significantly activated for different conditions within an experiment, which is obtained by specifying linear contrasts. A typical subtractive approach may specify a contrast of 1 -1, where 1 is the condition of interest (e.g., an experimental condition) and -1 is the condition that needs to be subtracted (e.g., a control condition) from the condition of interest. This results in a parametric map (usually overlaid onto an anatomical image) which presents the results of the statistical analysis, where colour-coded brain voxels (those that exceed a certain statistical significant threshold) imply cortical activation in response to the experimental task (Lindquist, 2008).

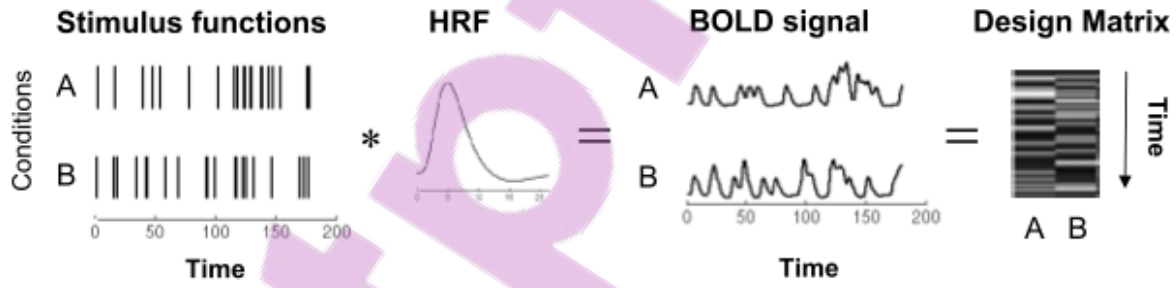

Figure 2.2 An experiment design with two different conditions (A and B), where the stimulus function is convolved with an HRF resulting in BOLD responses for each condition. By transposing the signals into two columns within a design matrix, statistical methods can be used to find significant correlations between the signal and the two conditions (Lindquist, 2008).

Although SPM is a powerful tool to investigate voxel signal changes and examine spatial patterns of neural activity, there are a few limitations to using this method. As the GLM approach is based on univariate statistics, each voxel is analysed separately which increases the number of false positives (type I error). Because the brain is a multivariate

structure where each individual voxel is heavily correlated with its neighbouring voxels, a correction for multiple comparisons is necessary. This is usually achieved by using a family-wise error (FWE) or a false discovery rate (FDR) correction; however, this in turn increases the number of false negatives (type II error). Furthermore, as it involves parametric statistics, violations of distributional assumptions (such as outliers in the dataset) can affect the results negatively rendering them invalid (Raz, Zheng, Ombao, & Turetsky, 2003). Due to these inherent weaknesses, a nonparametric multivariate approach may be preferred (especially if the task design is exploratory rather then hypothesis-driven) as it identifies a network across all regions of the brain that is correlated to the experimental conditions, rather than focusing on a specific cortical region that has been defined by a set of voxels. Such approaches include Principal Component Analysis, Multivariate Pattern Classification Analyses, and Partial Least Squares (PLS), which are not subject to the limitations that affect univariate analyses. Therefore in the current thesis, PLS was chosen as the method of analysis to investigate functional MRI data in Chapters 4 and 5, and structural MRI data in Chapter 6. Further explanation of this approach will be discussed below in Section 2.3.4.

2.3.3 Structural Magnetic Resonance Imaging (sMRI)

In contrast to fMRI, structural MRI provides information on neuroanatomical features allowing detailed insight into the structural relationships between different parts of the brain. Brain structure volumes are measured by using volumetric scan sequences, and can be used to examine specific regions of interest (e.g., insula) or an overall tissue type (e.g., grey matter). An important advantage of MR imaging is the high quality of contrast between the tissue classifications, which is possible due to the variation in amounts of water and water proton relaxation times between the tissues. The main types of contrasts used in neuroscience research are T_1- and T_2- weighted contrasts, which are specified in the scanning parameters

prior to image acquisition. T_1 is usually used in neuroanatomical studies as it is particularly suited to identifying cortical tissue from other brain matter, such as skull (bone) and cerebrospinal fluid. T_2 is often utilised in lesion/pathophysiology studies as certain types of pathology are more readily observed using this contrast (Symms, Jäger, Schmierer, & Yousry, 2004). Unlike functional imaging, essentially only one volumetric measurement of each voxel needs to be made in sMRI, allowing for the acquisition of high-resolution voxels in a shorter scanning time.

Analysis of structural data is similar to the steps taken for functional data, where image preprocessing is needed for further statistical analyses, which in turn allow for inferences to be made from the data. Again, both univariate and multivariate approaches exist with one of the most common methods being voxel-based morphometry (VBM), which is based on voxel-wise parametrical statistical tests (Ashburner & Friston, 2000). However, same weaknesses found in univariate functional analyses are also present in parametric analyses of structural data. Therefore, a multivariate structural PLS method was used in Chapter 6 to investigate grey matter structure differences in schizotypy, which to date has never been examined using PLS.

2.3.4 Partial Least Squares (PLS) analysis method

Both functional and structural data were analysed using a multivariate statistical technique called Partial Least Squares (PLS) by using a PLS graphical user interface (PLSgui; Rotman Research Institute of Baycrest Centre, Toronto, Canada; http://www.rotman-baycrest.on.ca), which was implemented in MATLAB R2012b (MathWorks, Inc.). This method is useful when looking at the overall distributed patterns in the data (rather than focusing the analysis on an individual element, such as voxels), and focuses on the covariance between the images and the experimental design or the behavioural

measure. Therefore, a major advantage of this technique is its simultaneous assessment of activation/structural changes rather than using a voxel-by-voxel method, eliminating the need for multiple comparisons corrections. Although there are two different types of PLS techniques (correlation and regression), PLS correlation is the more widely utilised technique in neuroscience research, and therefore will be discussed more in detail next.

There are four subtypes of functional PLS correlations: task PLS; behaviour PLS; seed PLS; and multi-block PLS. The basic premise of all four types is the cross-correlation of brain activity (data matrix) with a design matrix. However, the definition of the design matrix is dependent on the PLS subtype, with task PLS using experimental conditions as the variable in the matrix, behaviour PLS using behavioural measures, seed PLS using voxel values from specific regions of interest, and multi-block PLS using multiple design blocks consisting of a combination of experimental/behavioural/voxel activation variables. The principle is similar for structural PLS correlation, with the data matrix containing columns of brain volumes (rather than brain activity) for each voxel, which is cross-correlated with a behavioural variable.

This cross-correlation results in a set of vectors, which are then entered into a single cross-product matrix, where latent variables (LV) are derived using singular value decomposition (SVD; McIntosh, Bookstein, Haxby, & Grady, 1996). LVs identify the patterns of cortical activity which represent the optimal covariance between functional/structural data and experimental conditions, and consist of three components: voxel saliences; design saliences; and singular values (*d*). The voxel saliences indicate the distributed spatiotemporal activity/structural pattern of brain voxels that corresponds the most to the LV identified, and can be displayed as a singular image which shows the strength and direction (positive or negative) of the voxel pattern that are weighted in proportion to the data-design correlation. The design saliences indicate the amount to which the experimental

conditions correlate with the voxel saliences, and singular values (*d*) denote the proportion of the covariance between the task and the functional/structural data for the specified LV, indicating the strength of the relationship (indexed by the % crossblock). The number of LVs depends on the number of experimental conditions/behavioural measures, with the first LV accounting for the largest amount of the cross-covariance matrix, and subsequent LVs contributing progressively decreasing amounts. Finally, brain and design scores are calculated for each individual as the dot product of the individual's data matrix and voxel/design saliences. Brain scores indicate the strength of the individual's contribution to the pattern expressed in the LV, whereas design scores reflect the relationship between brain activity/structure and the experimental design/behaviour (for a more detailed description of the method, see Krishnan, Williams, McIntosh, & Abdi, 2011).

Assessment of significance is achieved by the nonparametric method of permutation testing, which determines whether the observed effect in each LV is statistically strong enough to be different from random noise. This is accomplished by sampling without replacement to reorder the rows in the data matrix while leaving the experimental design matrix unchanged, and the LVs resulting from this new cross-correlated matrix are recomputed using the same SVD algorithm. This permutation process is repeated multiple times, with the probability of significance resulting from the number of times the permuted singular value exceeds the observed singular value. Such *p*-values are calculated for all LVs, which are then used to determine which LVs to retain (McIntosh et al., 1996).

Finally, the reliability of the voxel saliences contributing to each LV is determined by estimating the standard error of saliences using bootstrap sampling (Efron & Tibshirani, 1985). The samples are generated using sampling with replacement, which keeps the assignment of experimental conditions/behaviour fixed for all observations in both the data and design matrices. From this, a ratio of voxel saliences over estimated error is calculated

for each voxel. This bootstrap ratio (BSR) is analogous to a *z*-score, with voxels that have a BSR of larger than 3 are considered to be significantly stable and contributing reliably to the pattern expressed by the LV. Moreover, the bootstrap estimate can also be used to derive confidence intervals for the LV correlations in behaviour PLS analyses, and also for brain scores in task PLS analyses (McIntosh & Lobaugh, 2004).

PLS has been utilised widely in neuroimaging studies across different imaging modalities (e.g., fMRI, sMRI, PET, MEG, ERP) and study designs (e.g., block, event-related, structural). In particular, task and behaviour PLS have been used in a large number of studies including (but not limited to) examining cognitive control in bilinguals (Bialystok et al., 2005) and in the Stroop task (Floden, Vallesi, & Stuss, 2010), memory retrieval networks (Addis, McIntosh, Moscovitch, Crawley, & McAndrews, 2004), effects of aging on large-scale brain networks (Grady et al., 2010), emotional processing (Keightley et al., 2003), as well as investigating network patterns in clinical disorders such as Alzheimer's disease (Grady et al., 2003), obsessive-compulsive disorder (Menzies et al., 2007), and schizophrenia (Kim et al., 2010). On the other hand, investigations into neuroanatomical structures using structural PLS are comparatively rare, with only a handful of studies using this method mainly for neuropsychological research. These include looking at the relationships between: brain volume changes and traumatic brain injury (Levine et al., 2008); cortical structure and neuropsychological test performance in schizophrenia patients (Nestor et al., 2002); retrograde amnesia and structural atrophy in Alzheimer's disease (Gilboa et al., 2005); and structural changes in obsessive-compulsive disorder that is associated with behavioural performance on a response inhibition task (Menzies et al., 2007).

In the context of the current research, we decided to employ both task and structural PLS techniques to investigate the concept of schizotypy from a neuroimaging perspective. Specific details of the PLS analyses are reported in the relevant study chapters.

2.4 Experimental tasks

2.4.1 Behavioural measures

2.4.1.1 Torrance Tests of Creative Thinking (TTCT)

The TTCT (Torrance, 1966; 2008a) consists of figural (TTCT-F) and verbal (TTCT-V) versions, which are designed to test creative behaviour by measuring four cognitive components of creativity through divergent thinking. Participants completed Form A of both figural and verbal TTCT. The TTCT-F consisted of three tasks: picture construction; picture completion; and repeated lines; which all had a set time limit of 10 minutes per task. The TTCT-V consisted of six tasks: forming unusual questions; guessing causes; guessing consequences; product improvement; unusual uses; and a just-suppose task. Four of these tasks had a time limit of 5 minutes each, while the other two had a longer limit of 10 minutes. In total, the TTCT-F took 30 minutes and the TTCT-V 40 minutes to complete. Before each task, explicit instructions were read out loud from the Directions Manual and any questions were answered before starting the timer. The participants were not aware of what each task involved prior to receiving instructions for that task.

The answers for both versions are marked on fluency, flexibility, originality, and elaboration of ideas, with the TTCT-F having additional creativity indicators called “creative strengths”, which include emotional expressiveness, storytelling articulateness, internal visualisation, humour, fantasy, and richness of imagery. To ensure objective scoring, the answer booklets for both TTCT-F and -V were submitted to the Scholastic Testing Service Scoring Centre in St.Louis, Missouri, where trained professional raters evaluated the answers using the streamlined scoring guide established by Torrance, Ball, and Safter (2008) and Torrance (2008b), respectively. The TTCT has shown strong predictive validity (Cramond, Matthews-Morgan, Bandalos, & Zuo, 2005), acceptable concurrent validity and reliability (Kim, 2006a), and is the most widely used measure to assess creativity (Wechsler, 2006).

Similar to tests that measure intelligence quotients, the scores are standardised with a mean of 100 and a standard deviation of 20. The average scores for both TTCT-V and TTCT-F are listed in Table 2.2.

2.4.1.2 Wechsler Abbreviated Scale of Intelligence (WASI)

The WASI is a short behavioural measure of intelligence (IQ), which has been well-used in both clinical and research settings (The Psychological Corporation, 1999). It consists of four subtests: Vocabulary; Block Design; Similarities; and Matrix Reasoning; and takes approximately half an hour to complete. Verbal IQ is calculated from scores of the Vocabulary and Similarities sections, which test word knowledge and abstract verbal reasoning. Performance IQ consists of Block Design and Matrix Reasoning, which test spatial perception and nonverbal abstract problem solving. The total IQ score is taken from the sum of all four subscales (Table 2.2), and accounts for 85% of the Wechsler Adult Intelligence Scale (third edition) full-scale IQ scores (Wechsler, 1999). It has excellent reliability and content validity, as well as high concurrent validity with other intelligence tests (The Psychological Corporation, 1999; Stanos, 2004).

Table 2.2

Mean scores and standard deviations for the behavioural measures (including the schizotypy scale, both versions of the TTCT, WASI, and the handedness inventory) for the total overall O-LIFE group, as well as the high and low overall schizotypy (measured by the O-LIFE) groups.

Measure/ Task	Total (n=35)		HS (n=18)		LS (n=17)	
	Mean	SD	Mean	SD	Mean	SD
O-LIFE	10.99	4.71	15.64	2.20	6.57	1.40
TTCT - V	115.09	15.53	116.39	17.57	113.71	13.42
TTCT - F	115.57	11.25	120.17	9.63	110.71	11.03
WASI	119.97	8.94	120.17	9.71	119.76	8.33
EHI	80.83	11.17	81.01	10.23	80.64	12.41

Note: O-LIFE = the Oxford-Liverpool Inventory of Feelings and Experiences; TTCT – V = verbal version of the Torrance Tests for Creative Thinking; TTCT – F = figural version of the Torrance Tests for Creative Thinking; WASI = Wechsler Abbreviated Scale of Intelligence; EHI = Edinburgh Handedness Inventory; HS = high overall schizotypy group; LS = low overall schizotypy group; n = number of participants; SD = standard deviation.

2.4.2 Dual-task paradigm

The dual-task was used as a behavioural measure of language laterality in the participants. This task has been successfully used previously to determine language lateralisation in both typical and bilingual adults (Badzakova-Trajkov, Kirk, & Waldie, 2008; Waldie & Mosley, 2000), and is based on the idea that when individuals perform two unrelated tasks at the same time, they should show increased interference if the tasks are lateralised to the same hemisphere of the brain compared to if they are controlled by separate hemispheres (Kinsbourne & Cook, 1971).

The task consisted of speeded right and left index finger tapping, either alone or with a language task, which was to read short narrative passages on a computer screen either silently or aloud. In total, there were six different conditions, with two single task baseline conditions (right and left index finger tapping only) and four tapping and reading conditions

(right and left finger tapping with reading out loud or silently). There were 12 narrative passages which were presented one at a time in its entirety, and displayed on a 24inch Dell computer screen for 14 seconds. E-Prime 2.0 was used to programme the task (Psychological Software Tools, Pittsburgh, PA). Responses were recorded by using the spacebar on the keyboard as the tapping apparatus. Tapping rate data were collected across all conditions, which were presented in a randomised order by E-Prime. At the end of the task, all participants were required to complete List 13 of the Boder Test of Reading-Spelling Patterns to ensure normal adult reading proficiency (Boder & Jarrico, 1982).

2.4.3 Neuroimaging tasks

A paired pulse auditory EEG task and two functional MRI tasks (a language task and a drawing task) were used in this research project, which are described briefly below. An anatomical image was also taken using structural MRI for each participant; however, there was no task associated with this scan. A full and detailed description for each task is included in the relevant chapters.

2.4.3.1 P50 paired pulse EEG paradigm

In this task, participants were asked to passively listen to auditory clicks through ER2 insert earphones (Etymotic Research Inc., Elk Grove Village, IL). No responses were required; instead, a black fixation cross was presented on a computer monitor to ensure they did not fall asleep. Three blocks were presented in a randomised order**,** consisting of two experimental paired pulse blocks and one control single pulse block. In the paired pulse condition, forty pairs of identical clicks were presented binaurally through the earphones. In the single pulse condition, forty single clicks were presented. Depending on the length of the breaks between each block, the experiment took approximately half an hour to complete.

EEG was recorded continuously at a 1000Hz sampling rate with a 0.1-400Hz analogue bandpass, and was acquired using a common vertex (Cz) reference, which was later re-referenced to the average reference offline (Bertrand, Perrin, & Pernier, 1985).

2.4.3.2 Lexical decision fMRI paradigm

This blocked-design 'go/no-go' experiment consisted of three conditions: nonverbal; lettercase judgement; and lexical decision. Participants were instructed to respond ('go') for pointy shapes, uppercase letters, and real English words, respectively. Each round consisted of three blocks (one block per condition), which were always presented in the above order. There were 18 stimuli per block in each round, and four rounds in total. Before the start of the experiment, all participants were reminded by the researcher the order of the stimuli (nonverbal, lettercase judgement, lexical decision) and which stimuli needed responses (pointy shapes, uppercase, real words). In total, the experiment running time was 12 minutes.

All stimuli were presented in the fMRI scanner through a projector. The response box was placed under the participant's right hand, with their right index finger on the response button. Both accuracy and reaction time data were recorded.

2.4.3.3 Drawing task fMRI paradigm

The drawing task was also a blocked experimental design with two conditions: Create and Trace. There were ten experimental (Create) and ten control (Trace) blocks, in which the participant had to either draw a picture or trace a line on paper. For the experimental blocks, participants were given ten incomplete lines on paper (one line per block) and were asked to draw a picture with the line forming a part of their drawing. For the control blocks, participants traced ten dotted lines (one dotted line per block). Each block lasted for 30 seconds each, with a 10 second fixation/baseline block in between the experimental and

control blocks. A custom-built MRI-compatible table was placed over the participant's stomach, and adjusted so that they could clearly see the paper which was laid on the table via a mirror which was attached to the head coil. An assistant was present in the scanning room for the duration of the experiment to remove the completed stimuli at the end of each time period. The total experiment running time was 13.3 minutes.

2.5 Experimental procedures

All potential participants contacted the researcher initially through email, in which they expressed their interest in participating in the study. After checking that all exclusion criteria were met, those who were still interested were invited to come into the university for three separate testing sessions. The sessions were randomised across participants, with some starting with the behavioural session, while others started with the imaging sessions. Before commencing the first session, all participants were provided with a participant information sheet (Appendix A) and a consent form was signed (Appendix B). Each individual testing session is described more in detail below.

2.5.1 Behavioural session

The behavioural session took place in a testing room on Level 3 of the Human Sciences Building, School of Psychology. The participants filled out a demographic questionnaire detailing their background, which included information on their age, education, interests, family history of mental disorders, as well as self-rated creativity scales (Appendix E). They also completed the O-LIFE and the EHI, prior to the commencement of the behavioural experiment tasks. Both the WASI and the TTCT (verbal and figural) were administered by the researcher, following strict guidelines and instructions. The dual-task

was also completed during this session. The order of the tasks was counterbalanced across all participants.

2.5.2 EEG session

This session took place in the School of Psychology EEG laboratory. After being set up with the EEG cap and equipment, participants completed three tasks in a randomised order (the paired pulse task and two others which are not discussed in this thesis). After the session, the auditory threshold for each participant was measured as described in Section 2.2.2. This also took place in the Faraday cage within the EEG laboratory where the EEG was recorded.

2.5.3 MRI session

All scans were acquired at the Centre for Advanced MRI (CAMRI) at the Faculty of Medical and Health Sciences. Prior to the actual experiment, all participants completed a practice session in a mock scanner in the Human Sciences Building, to familiarise themselves with the setting and the tasks. At CAMRI, participants were required to sign an MRI consent form, after which a structural image was acquired first, followed by functional images for three tasks (the lexical decision task, the drawing task, and one other not discussed in this thesis). Again, the order of the tasks was counterbalanced.

Chapter 3: P50 sensory gating deficits in schizotypy[1]

Abstract:

Sensory gating is the ability to filter out, or 'gate', irrelevant stimuli from the environment. Individuals with schizophrenia consistently demonstrate deficits in this ability leading to sensory overload and cognitive fragmentation. This dysfunction has also been found in schizotypy, which is defined as a manifestation of nonclinical symptoms and personality traits qualitatively similar to those found in schizophrenia. Sensory gating may be assessed by testing the attenuation of the P50 event-related potential using an auditory paired stimulus paradigm, where two identical clicks are presented in quick succession. In the present study, auditory P50 suppression was assessed in non-smoking individuals, and the degree of suppression correlated with assessment of schizotypy using the O-LIFE questionnaire. Relative to the low-scoring individuals, P50 suppression was significantly reduced in those with high levels of schizotypy. Furthermore, the degree of deficit in P50 gating correlated with both cognitive disorganisation and impulsive nonconformity dimensions of schizotypy. These results suggest that schizotypal individuals may have early sensory gating deficits similar to schizophrenia patients, especially if they display a disorganised or impulsive profile. As they do not exhibit overt psychotic symptoms, it is likely that such deficits represent an underlying core cognitive dysfunction within the schizophrenia spectrum.

Keywords: Schizotypy; P50; Sensory gating; Disorganisation; Impulsivity; ERPs

[1] Material from this chapter can be found in the following publication:
Park, H.R.P., Lim, V.K., Kirk, I.J., & Waldie, K.E. (2015). P50 sensory gating deficits in schizotypy. *Personality and Individual Differences, 82,* 142-147. doi:10.1016/j.paid.2015.03.025

3.1 Introduction

Sensory gating is defined as the preattentional habituation of responses to repeated sensory input, which is used to distinguish important stimuli from those that may be irrelevant and redundant (Hall, Taylor, Salisbury, & Levy, 2011). Research has shown that this ability to actively suppress and/or ignore unimportant information is greatly affected in schizophrenia patients, who often show reduced cognitive inhibition when performing tasks which require selective attention. This has led to the hypothesis that such deficits in sensory gating may be the cause of some of the behavioural symptoms observed in schizophrenia, such as psychotic hallucinations and sensory overload (e.g., Bullen & Hemsley, 1987; Daskalakis & Fitzgerald, 2002; Lubow et al., 2000; Waters, Badcock, Meybery, & Michie, 2003).

A method to measure this dysfunction is the P50 paired pulse paradigm, which has been well-used to examine sensory gating dysfunction in schizophrenia patients (Boutros, Belger, Campbell, D'Souza, & Krystal, 1999) and their first degree relatives (Clementz et al., 1998), as well as those with schizotypal personality disorder (Cadenhead et al., 2000), Huntington's disease (Uc, Skinner, Rodnitzky, & Garcia-Rill, 2003), Alzheimer's disease (Jessen et al., 2001), autism (Lv et al., 2014), and bipolar disorder (Olincy & Martin, 2005). By using electroencephalography (EEG), the P50 can be measured as the largest positive deflection at vertex approximately 50ms post-stimulus. The paradigm consists of two identical auditory clicks which are presented in close succession. In neurotypical subjects, the P50 wave elicited by the second stimulus (S_2) is reduced when compared to the wave elicited by the first stimulus (S_1). This relative decrease is taken to be evidence of an intact sensory gating mechanism (Boutros et al., 1999; Croft et al., 2001). In contrast, those with schizophrenia show reduced P50 suppression, which suggests that such deficits in inhibiting excess and trivial information could lead to the development of disorder-related symptoms

and cognitive behaviours (Braff, 1993; Clementz et al., 1997; for a review, see Bramon, Rabe-Hesketh, Sham, Murray, & Frangou, 2004).

As this evoked potential is thought to reflect early preattentive sensory information processing, it can be taken as a functional correlate of neuropathology rather than be a result of the disease process (Nagamoto, Adler, Waldo, & Freedman, 1989; Brockhaus-Dumke, Mueller, Faigle, & Klosterkoetter, 2008; for a review, see Potter et al., 2006). Furthermore, because of the high heritability of schizophrenia, this method can be used to detect possible gating dysfunction in individuals with a genetic predisposition to the disorder, as well as those who display schizotypal traits (Cadenhead, Light, Geyer, McDowell, & Braff, 2002). Therefore, abnormalities of the P50 response may be an intermediate phenotype of the disorder that could potentially be utilised as a biological marker for individuals who may be at risk of developing schizophrenia at a later date, such as those with high levels of schizotypy (Hall et al., 2006).

Schizotypy is a construct used to describe a cluster of nonclinical symptoms and personality traits within a healthy population, which may lead to a predisposition to schizophrenia and other related disorders (Claridge, 1997; Jahshan & Sergi, 2007; Raine et al., 1995). Individuals who score high in self-report measures of schizotypal characteristics exhibit specific psychological and biological abnormalities, which are qualitatively similar to those observed in schizophrenia patients but less severe (Mohanty et al., 2005). It has been proposed that early environmental and genetic influences work throughout development to modify brain function and structure which, in turn, give rise to alterations in cognitive processes resulting in a schizotypal personality (Raine, 2006). As there is consistent and substantial evidence of a genetic liability which links schizotypy and schizophrenia, symptoms of schizotypy may be especially effective in identifying those at risk of developing the disorder at a later date (Seeber & Cadenhead, 2005).

Although there is considerable evidence for impaired sensory gating in those with schizophrenia-spectrum disorders, there has been less focus on those who display high levels of schizotypy. Only a few studies have directly looked at the relationship between schizotypy and P50 sensory gating in nonclinical populations, which have all found a correlation between high levels of schizotypy and reduced P50 suppression (Croft et al., 2001; Evans et al., 2007; Wan, Crawford, & Boutros, 2006).

There are two important covariates to consider when evaluating earlier research: smoking status of participants; and the dimensions of schizotypy. Smoking tobacco is thought to facilitate early sensory gating by stimulating nicotinic cholinergic receptors, which results in enhanced central nervous system functioning (Heishman, Taylor, & Henningfield, 1994). Animal studies have shown that nicotinic agonists increase auditory gating in rats (Radek et al., 2006). This normalisation is also present in individuals with schizophrenia where patients who smoke show temporary improvements in P50 sensory gating compared to non-smokers (Adler et al., 1998). Wan, Crawford, and Boutros (2006) found a similar result in schizotypy, where the high-scoring schizotypy group displayed poorer P50 gating compared to the low-scoring schizotypy group among the non-smokers. Importantly, among smokers, the high schizotypy group showed better P50 suppression than the low schizotypy group. Croft et al. (2004) also found gating differences in schizotypy depending on the participants' smoking status, but this was only related to the 'unreality' dimension of schizotypy. These results indicate that smoking may be a major confound if not assessed and controlled for prior to testing.

The concept of dimensionality in schizotypy is another important consideration. Similar to those of schizophrenia, schizotypy symptoms can also be divided into positive, negative, and disorganisation factors; all of which seem to have different effects on cognitive function and performance (Barrantes-Vidal, Ros-Morente, & Kwapil, 2009; Fanous et al.,

2001). Therefore, it is necessary to assess not only global schizotypy, but also each of the separate contributing dimensions as some may be better predictors of attenuated P50 suppression than others. In this regard the data are inconsistent. Some studies found a relationship between a positive dimension ('unreality') with atypical gating (e.g., Croft et al., 2001, 2004), whereas others found this deficit to be related to either the negative 'withdrawn' dimension (Wang et al., 2004), or the 'cognitive disorganisation' dimension of schizotypy (Evans et al., 2007). Furthermore, these studies used different schizotypy scales, which could add to the variability of the results. These include the Schizotypal Personality Questionnaire (SPQ; Raine, 1991), the Personality Syndrome Questionnaire (PSQ; Gruzelier, Croft, Kaiser, & Burgess, 2000) and the Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE; Mason et al., 1995).

Overall, the converging evidence suggests a link between reduced P50 suppression and schizotypy in nonclinical populations, but the exact nature of this relationship is not yet clear. In the present study, we investigated the role of schizotypy on P50 suppression in healthy non-smoking individuals. We expected that individuals with high global schizotypy scores would display reduced P50 sensory gating compared to participants with low schizotypy. We also examined the relations between the different dimensions of schizotypy and P50 gating to investigate the link between schizotypy subgroups and sensory gating deficits using the O-LIFE, thereby replicating the only other study that has used the O-LIFE questionnaire to assess schizotypy (Evans et al., 2007).

3.2 Methods

3.2.1 Participants

A total of 48 participants (mean age = 23.42 years; SD = 4.50; 17 males) were recruited from the University of Auckland, New Zealand, and through advertising online on

research recruitment websites. Exclusion criteria were: 1) being left-handed; 2) being bi-/multi-lingual with English not being their first language; 3) currently taking either anti-depressant or anti-psychotic medications; 4) having hearing deficits (hearing was assessed using an Otovation Amplitude T3 series audiometer; Otovation LLC, King of Prussia, PA); 5) being outside the 18-40 years age bracket; 6) being a regular smoker. Participants gave their written informed consent to participate in the study and were free to withdraw from the study at any time without penalty. All experimental procedures were approved by the University of Auckland Human Participants Ethics Committee.

3.2.2 Schizotypy assessment

The Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE; Mason et al., 1995) was used to assess the level of schizotypy in all participants. The O-LIFE consists of 104 self-reported 'yes/no' items that load onto four factors of schizotypy: unusual experiences; cognitive disorganisation; introvertive anhedonia; and impulsive nonconformity. An overall O-LIFE score is taken from the average of the four subscale scores. A full description of this questionnaire can be found in Section 2.2.3 of Chapter 2.

3.2.3 EEG procedure and analyses

Electroencephalogram (EEG) was conducted with Electrical Geodesics Inc. amplifiers (300mV input impedance) using 128-channel Ag/AgCl electrode nets (Tucker, 1993). Participants were seated comfortably in a reclining chair in an electromagnetic shielded and sound-attenuating room. They were asked to focus on a black fixation cross, which was presented on a grey background on a SVGA computer monitor (1024 x 768 pixel resolution; 60Hz refresh rate) at a distance of 57cm. This was done to ensure that they did not fall asleep. EEG was recorded continuously at a 1000Hz sampling rate with a 0.1 – 400Hz analogue

bandpass, and was acquired using a common vertex (Cz) reference, which was later re-referenced to the average reference offline (Bertrand et al., 1985). All electrode resistances were less than 40kΩ. The participants wore ER2 insert earphones (Etymotic Research Inc., Elk Grove Village, IL) for auditory stimulus presentation and were instructed to listen to the clicks through the earphones. Audio clicks were 4ms in duration with a frequency of 1000 Hz (stereo recording at 44100Hz sampling rate) and were presented to both ears at 77dB. Forty identical pairs of these clicks were presented binaurally through the earphones, with a 500ms interstimulus interval and a randomised 9-12s intertrial interval. This block was repeated twice. A control block consisting of 40 single auditory clicks was also presented using the same intertrial interval; however, this block was not used in further analyses. The order of the three blocks was randomised for each subject to counterbalance any order effects. The participants were also instructed to take a short break between each block to reduce the risk of the subject falling asleep and/or displaying delta waves.

The EEG data were segmented into epochs lasting 1300ms, starting 100ms before the onset of the stimulus and ending at 1200ms post-stimulus onset. Eye movement correction was made according to the methods of Jervis and colleagues (1985). The channels were screened for artifacts, and any trials over the eye blink threshold of 70μV and eye movement threshold of 100μV were not included in the waveform averaging. Due to artifact rejection, the number of epochs per participant differed; in total, 85% to 100% of the epochs (68 to 80 trials) were included in the final analyses. A bi-directional three pole Butterworth filter was applied to the averaged evoked potentials, with a band-pass filter of 0.1-30Hz.

The P50 component was taken from the Cz electrode as this has been shown to be the best site for discriminating those with schizophrenia from control subjects (Clementz et al., 1998). However, the component also had to be present in at least one additional channel to increase the reliability of the P50 measurement. The P50 was identified as the most positive

deflection between 30ms and 80ms after stimulus presentation. P50 amplitude was calculated by using the peak-to-peak method, where the absolute difference in amplitude was taken between the P50 component and the preceding negativity (Nb). If Nb was absent, the preceding baseline value was used. This was done for both the conditioning (first) stimulus (S_1) and the test (second) stimulus (S_2). P50 suppression was then calculated by using the P50 amplitude of S_2 divided by the P50 amplitude of S_1. S_2/S_1 ratio which approached 1 indicated weak suppression of the test stimulus, whereas ratios above 1 indicated facilitation. Ratios greater than 2 were assigned the value 2 to prevent outliers which may have a disproportionate effect on the group means (as used by Nagamoto et al., 1991), leading to the use of truncated S_2/S_1 ratio measures in the following analyses. $S_2 – S_1$ differences were also calculated by subtracting the S_2 P50 amplitude from the S_1 P50 amplitude.

3.2.4 Data analyses

Statistical analyses were conducted using the Statistical Package for the Social Sciences (SPSS) software (Standard Version 22.0, IBM, Armonk, NY). Mann-Whitney U tests were performed to calculate the differences in attenuation of the P50 between the high and low schizotypy groups (based on both the total O-LIFE score and the impulsive nonconformity dimension score). For the group analysis, a participant was categorised to be in the high global schizotypy (HS) group if their O-LIFE score, averaged across the four dimensions, was higher than half a standard deviation above the mean score of the total participant sample. Similarly, a participant was included in the low schizotypy (LS) group if their overall O-LIFE score was half a standard deviation below the mean score. In the final sample using the overall O-LIFE scores, there were 18 participants in the HS group (O-LIFE mean = 15.15; SD = 2.16), and 17 LS participants (O-LIFE mean = 5.97; SD = 1.74).

As well as looking at the overall O-LIFE score, a separate analysis was performed using the impulsive nonconformity dimension scores as research has shown a link between disinhibited, impulsive behaviour and reduced sensory gating (Houston & Stanford, 2001; Lijffijt et al., 2012). Again, a participant was categorised to be in the high/low impulsive nonconformity (HIN/LIN) group if their ImpNon score was higher/lower than half a standard deviation above/below the mean score of the total participant sample for this dimension. In this analysis, there were 17 participants in the HIN group (ImpNon mean = 14.00; SD = 2.65), and 16 in the LIN group (ImpNon mean = 4.94; SD = 1.91).

In addition, Spearman's correlation coefficients were calculated for each of the four dimensions in the O-LIFE (unusual experiences, cognitive disorganisation, introvertive anhedonia, and impulsive nonconformity) to assess the relationship between P50 sensory gating and each schizotypy dimension. Both the truncated P50 suppression ratio and the amplitude difference were used as a measure of sensory gating. Two-tailed tests were conducted to determine the significance of the correlations. For this analysis, the overall global O-LIFE score was used to determine the HS and LS groups. The same participants from the overall O-LIFE group analysis (n = 35) were used.

3.3 Results

3.3.1 Group comparisons

For both the low and high schizotypy groups, there was an attenuation of their ERP responses for S_2 compared to S_1 (seen in Figure 3.1).

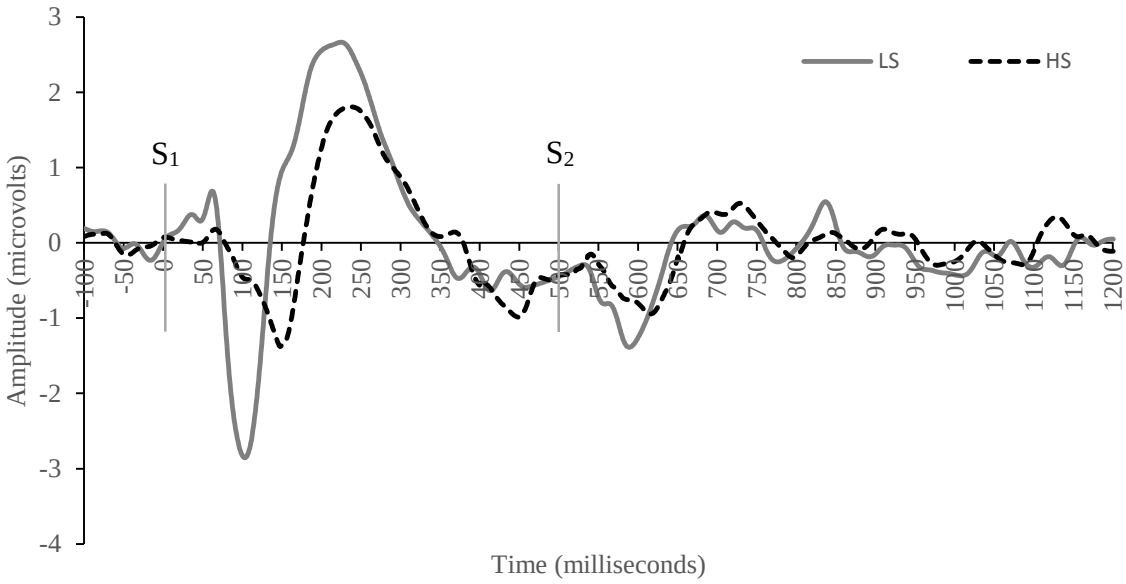

Figure 3.1 The grand average event-related potential waveforms of the low schizotypy (LS) and high schizotypy (HS) groups at Cz. Stimulus-onsets are denoted by the short vertical lines; the P50 responses can be seen as the most positive deflection at approximately 60ms for S_1, and 40ms for S_2.

When using the global O-LIFE score as the measure of schizotypy, the P50 ratio in the HS group (O-LIFE median = 14.75) differed significantly from the LS group (O-LIFE median = 7). Those who scored high on the O-LIFE overall showed reduced P50 suppression for the second stimulus compared to those who scored low on schizotypy (U = 74.00, z = -2.61, p = .008, r = -.441).

When the ImpNon dimension of schizotypy was used as the behavioural measure, rather than the overall O-LIFE score, attenuated P50 suppression was again seen in the group with high ImpNon scores (ImpNon median = 14) when compared to the LIN group (ImpNon median = 5). This reduction in P50 ratio was significant (U = 48.00, z = -3.17, p = .001, r = -.552).

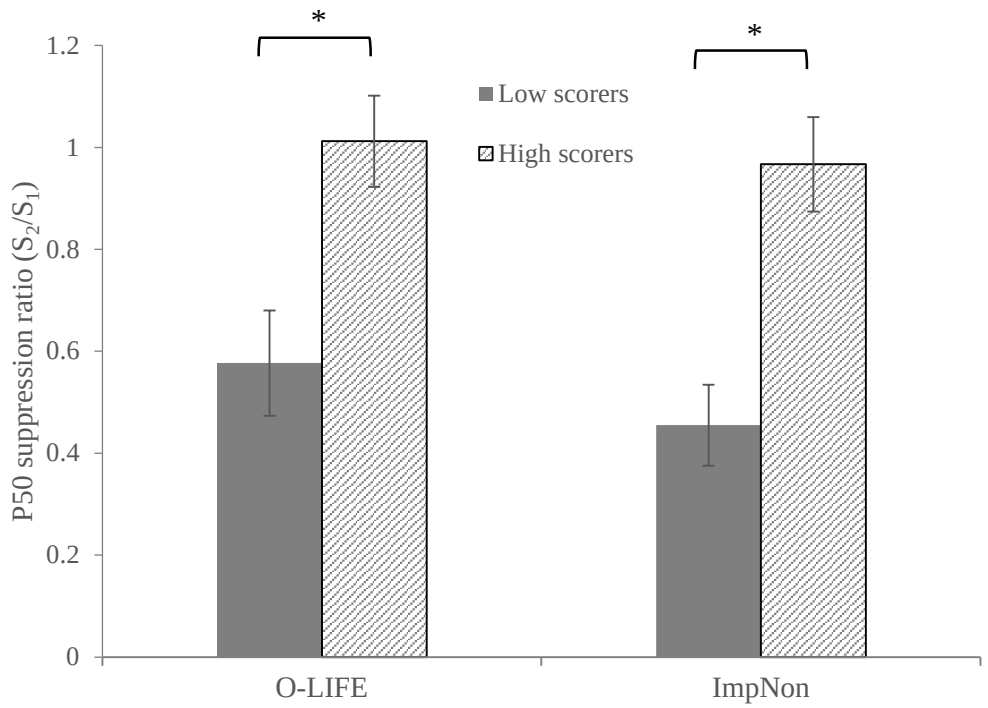

Figure 3.2 The truncated ratio of P50 suppression for the high and low schizotypy groups based on the overall O-LIFE score, and on the impulsive nonconformity (ImpNon) dimension score. A higher S_2/S_1 ratio reflects a decrease in sensory inhibition, where there is a larger response to the S_2 than observed in intact sensory gating. Significant differences between groups are marked by asterisks ($p < .05$). The error bars represent ±1 standard error of the mean.

3.3.2 Correlational analyses

Spearman's correlations between P50 measurements and the four schizotypy dimensions of O-LIFE are shown in Table 3.1. The P50 amplitudes for both S_1 and S_2 showed no significant correlations for any of the dimensions. A significant correlation was found with the P50 ratio and CogDis ($p = .030$), and also with ImpNon ($p = .019$). These correlations were positive indicating that when the suppression ratio increased (indicating a large response for S_2), the CogDis and ImpNon scores also increased.

Table 3.1

Spearman's correlation coefficients and p-values between P50 sensory gating measures and O-LIFE dimensions.

Measure	UnEx		CogDis		IntAn		ImpNon	
	r	*p*	*r*	*p*	*r*	*p*	*r*	*p*
S_1 amplitude	-.111	.526	-.108	.538	-.300	.080[a]	-.027	.879
S_2 amplitude	.089	.611	.209	.228	-.114	.513	.285	.096[a]
S_2/S_1 trunc. ratio	.283	.099[a]	.367	.030*	.157	.367	.395	.019*
S_2 - S_1 difference	.155	.373	.283	.099[a]	.239	.166	.313	.067[a]

Note: trunc. = truncated; UnEx = unusual experiences; CogDis = cognitive disorganisation; IntAn = introvertive anhedonia; and ImpNon = impulsive nonconformity. [a] = $p < .1$, * = $p < .05$.

The S_2 - S_1 difference did not show significant linear correlations with any of the dimensions. The directionality of these correlations can be seen in Figure 3.3.

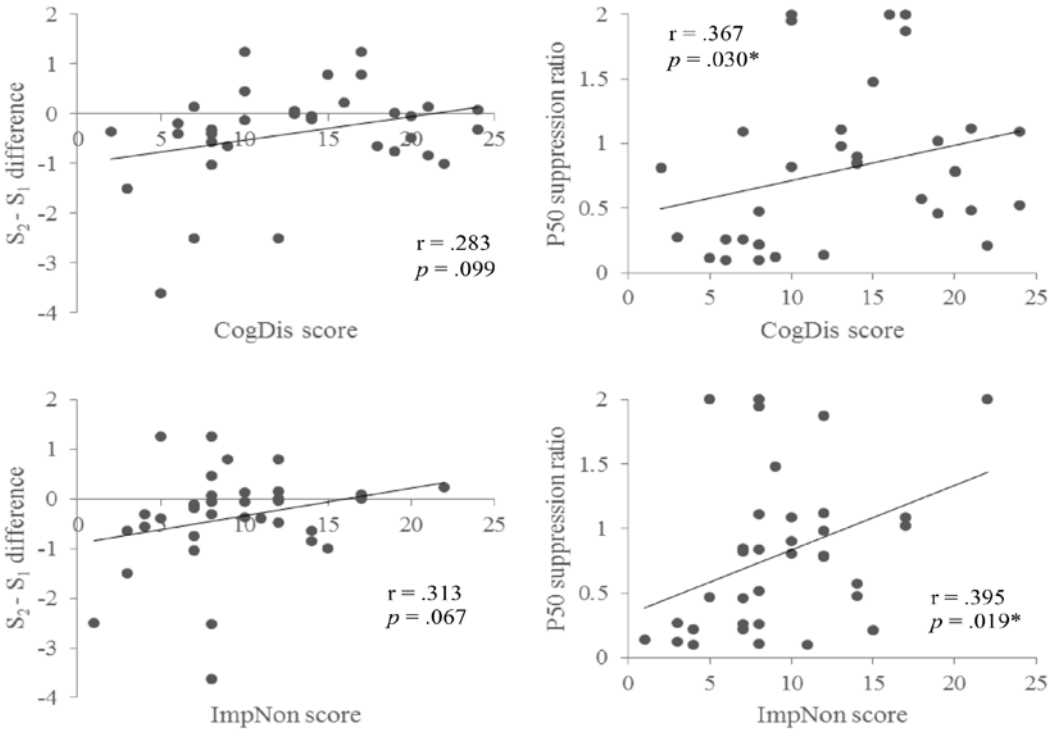

Figure 3.3 The linear correlations of P50 difference (S_2 - S_1) and truncated P50 suppression ratio (S_2/S_1) with the dimensions of the O-LIFE: cognitive disorganisation (CogDis); and impulsive nonconformity (ImpNon). Significant correlations are marked by asterisks ($p < .05$).

3.4 Discussion

The aims of the present study were to further investigate the relationship between schizotypy and P50 sensory gating. In sum, our results indicate that highly schizotypal individuals show early sensory gating deficits when compared to those with lower schizotypy scores. This was particularly true for those scoring above the norm for both cognitive disorganisation and impulsive nonconformity. Both the S_2/S_1 truncated ratio and the $S_2 - S_1$ difference showed weak to moderate associations with schizotypy, although this relationship was only significant with the ratio measure.

The P50 paired click paradigm is used to test the involuntary attention regulation of participants by presenting repetitive stimuli which are neither useful nor interesting. The long intertrial interval allows for the first stimulus of the pair to be relatively novel, capturing the attention of the individual and thus inducing a large event-related potential. However, the second stimulus is presented only after a short interstimulus interval, and it is expected that the participant will show a much reduced or diminished response. This is then taken as evidence for regulation or sensory gating of irrelevant stimuli in healthy individuals. However, in some populations, this effect is attenuated where individuals show a smaller difference between the evoked responses for S_1 and S_2. In particular, researchers have consistently shown this in schizophrenia patients (for a review, see Bramon et al., 2004), and similar findings in schizotypy provide support for the premise that nonclinical individuals with high levels of schizotypy are genotypically related to clinical patients with schizophrenia-spectrum disorders. Therefore, the results of this study are consistent with suggestions that atypical P50 attenuation is related to the core symptoms of the disorder, rather than being the result of the disease process.

There were two strengths of the present study. First, only non-smoking participants were recruited, and other medications were screened in order to establish P50 sensory gating

effects in individuals without any potential confounding effects of medication or nicotine. Second, the overall O-LIFE score was used as a global measure of higher and lower schizotypal personality. This initial analysis was done as although looking at separate dimensions of schizotypy is valuable, research into the overall concept of schizotypy is also beneficial and of importance. As expected, there were significant differences in P50 suppression in the two groups, where the lower schizotypy group showed the expected 'gating' or the suppression of the conditioning stimulus when compared to the test stimulus. In contrast, the higher schizotypy group showed a significant P50 attenuation effect, where the testing stimulus elicited a response similar to the conditioning stimulus leading to an almost null suppression effect (seen by the S_2/S_1 truncated ratio of just over 1 in Figure 3.2).

Such robust effects have consistently been observed in schizophrenia, where patients show considerable reductions in P50 suppression, as well as in other waveforms such as the P300 (Bramon et al., 2004; Shan et al., 2013). These effects may manifest behaviourally in cognitive tasks, such as the Stroop task, where facilitation effects have been observed in schizophrenia rather than interference (Barch et al., 1999; Carter, Robertson, & Nordahl, 1992; Taylor, Kornblum, & Tandon, 1996). Therefore, our result might be interpreted as being indicative of impairments in early selective attention for individuals on the schizophrenia spectrum (including schizotypy) when assessed by measures of inhibitory processes such as prepulse inhibition and negative priming (Cadenhead, Geyer, & Braff, 1993; Park, Lenzenweger, Püschel, & Holzman, 1996; Vink, Ramsey, Raemaekers, & Kahn, 2005). Thus, this increase in S_2 response may be a reflection of decreased ability to selectively discriminate previously-presented stimuli leading to diminished inhibition.

It is noteworthy that we also observed a reduced S_1 response in our HS group compared to the LS group. This has also frequently been observed in schizophrenia research, where patients exhibit a decreased response to S_1 compared to healthy controls (e.g.,

Patterson et al., 2008), and has led to a debate over whether the reduction in the S_1 amplitude is contributing more to the P50 gating abnormality than the increased S_2 amplitude. Therefore, although the S_2/S_1 ratio method has been well-used to index sensory gating, the exact mechanism underlying the gating difference remains unknown. It has been suggested by Adler et al. (1982) that such decrease in S_1 may be due to neuronal populations being more hyperactive in schizophrenia, making it less likely that they will respond synchronously to any stimulus. Furthermore, patients have shown to display greater temporal variability in S_1 latency, which may result in a reduced mean signal amplitude (Jin et al., 1997).

However, a meta-analysis by Chang, Arfken, Sangal, and Boutros (2011) examined the means of S_1 amplitude, S_2 amplitude, and the S_2/S_1 ratio from 35 studies investigating P50 in schizophrenia patients, and found that the S_1 amplitude showed the smallest effect size (0.19) compared to the S_2 amplitude (0.65) and the S_2/S_1 ratio (0.93). From this, the authors posited that, despite findings of S_1 amplitude attenuation, it alone is not sufficient to predict sensory gating differences, and that the S_2 amplitude and the ratio are more informative when assessing gating deficits. Due to the current data displaying a similar S_1 amplitude reduction, effect sizes were calculated for both the S_1 and S_2 amplitudes (r = -.167 and r = -.218, respectively) for the global O-LIFE group. When taken together with the effect size of the S_2/S_1 ratio (r = -.441), our data are in line with Chang et al. (2011)'s meta-analysis.

Therefore, it seems that the truncated ratio is a reliable and valid measurement of possible gating deficits despite the variability often found in other measurements across studies. Even though this reduction has not been previously discussed within the context of schizotypy and P50 gating, on reflection our results seem similar to what is observed in schizophrenia research, further lending support for an overlap between the two in regards to sensory gating.

We also found that the impulsive nonconformity dimension of schizotypy moderated P50 attenuation. Impulsive nonconformity (ImpNon) is considered to be a standalone dimension (neither a positive nor negative factor of schizotypy), and is not included in the SPQ (Raine, 1991) or the PSQ (Gruzelier et al, 2000). Therefore, we performed a separate group analysis based on the participants' ImpNon score, as literature has shown a link between poor impulse control and deficits in sensory gating (e.g., Houston & Stanford, 2001). Our high ImpNon group showed a significant reduction of P50 suppression when compared to the low ImpNon group, suggesting that impulsive behaviour may also be a manifestation of inadequate stimulus gating. This is not surprising as impulsivity has been associated with other disorders such as bipolar disorder (Najt et al., 2007), antisocial personality disorder (Swann et al., 2009), and schizophrenia (Hoptman et al., 2004). This finding has implications for schizotypal individuals, as high impulsivity has been linked with maladaptive behaviours such as substance abuse, which may precipitate the onset of a psychotic episode (Gut-Fayand, Dervaux, Olié, Poirier, & Krebs, 2001).

Positive relationships between the P50 ratio and both cognitive disorganisation and impulsive nonconformity dimensions were further observed, where individuals (from the overall O-LIFE group) who scored highly in these particular dimensions of schizotypy displayed robust reductions of P50 suppression. This finding partly replicates the results from Evans et al. (2007)'s study where they also found a significant relationship between cognitive disorganisation and P50 suppression deficits. However, these results are inconsistent with other studies where P50 deficits has been linked with either a negative dimension ('withdrawn', Wang et al., 2004), or a positive dimension ('unreality', Croft et al., 2001, 2004) of schizotypy. These differences may be due to the type of measures used to assess the level of schizotypy in participants. As Evans and colleagues (2007) have already posited, the 'unreality' dimension of the PSQ (Gruzelier et al., 2000) may actually tap into the

disorganisation dimension of schizotypy, leading to an overlap between the dimensions across different schizotypy measures.

Different experimental parameters may also have contributed to the discrepant findings between studies. Wang et al. (2004) used an interstimulus interval of 250ms, rather than 500ms which is the standard interval used by the majority of P50 gating studies. Nagamoto et al. (1991), who refined the paired pulse paradigm, found that schizophrenia patients displayed atypical P50 responses at 500ms, but not at the 100ms interval. This lends support to the idea that P50 suppression is sensitive to the length of interstimulus intervals, which may explain why at 250ms, Wang et al. (2004)'s results are inconsistent with other studies.

Another reason why results differ between studies may come from looking into more detail what the 'withdrawn' factor is. This is classified as a negative dimension in the SPQ (Raine, 1991), and includes subfactors such as 'social anxiety', which has been found to have an effect on negative priming tasks in schizotypy (Moritz et al., 1998). However, Claridge and Beech (1995) classify social anxiety and introversion as part of cognitive disorganisation, and as O-LIFE was co-authored by Claridge (Mason & Claridge, 2006), it could be that having a disorganised profile may be the underlying factor in sensory gating deficits, rather than any specified dimension of schizotypy.

Finally, the correlational analyses showed significant relationships only when the S_2/S_1 truncated ratio was used as a measure of P50 gating deficits, and not when the $S_2 - S_1$ difference was used. There is a lack of consensus in the literature as to which measurement is more suited to determining P50 suppression with some research showing $S_2 - S_1$ difference as the superior measure in healthy subjects (Fuerst, Gallinat, & Boutros, 2007; Rentzsch, Jockers-Scherübl, Boutros, & Gallinat, 2008). In studies that specifically examine sensory gating in clinical populations, the S_2/S_1 truncated ratio seems to be a reliable measurement

(for a review, see Patterson et al., 2008), although again there seems to be variability in ratios *within* the clinical sample, and overlap *between* the clinical and control samples. In the present study, no significant correlations were found between schizotypy and the S_2 - S_1 difference, although a trend was observed with cognitive disorganisation (p = .099) and impulsive nonconformity (p = .067). This trend is in line with the results of the S_2/S_1 ratio correlational analysis, and therefore suggests that both the ratio and the difference may be utilised as potential endophenotypes, albeit larger sample sizes may be necessary to establish significance when the difference measurement is used.

Our small sample size was the main limitation of the present study. Though we could have split the sample by the mean or median O-LIFE score, we felt that it was important to differentiate schizotypal individuals who are at the more extreme ends of the spectrum. It could be, however, that the variability of results may be due to the subjective grouping of participants, which may further differ depending on the schizotypy scale used. Therefore, further research is needed to determine whether gating deficits are differentially affected by the severity of the schizotypy score, when measured globally and also dimensionally.

In conclusion, the present study found P50 gating differences between individuals who display high schizotypy and those with low schizotypy. This difference was evident when high schizotypy was defined by taking the global O-LIFE score, and also when the dimensions were treated independently. This suggests that there are associations between deficient sensory gating and certain personality traits, including impulsivity and disorganised thinking. In particular, having a cognitively disorganised profile seems to be one of the main determinants of atypical P50 suppression when other literature is taken into account, and therefore may be the most suitable attribute within the schizotypy construct for examining gating deficits. We were also able to partially confirm the findings by Evans et al. (2007)

using the same O-LIFE schizotypy scale, which appears to be a particularly reliable measure for studying the construct in nonclinical populations.

Chapter 4: Language laterality in schizotypy[2]

Abstract:

Atypical lateralisation for language has consistently been found in schizophrenia, suggesting that language and thought disorders within the schizophrenia spectrum may be due to left hemispheric dysfunction. However, research into the association between schizotypy and functional laterality has reported inconsistent results, with some studies finding reduced or reversed language laterality, and others finding typical left hemsipheric specialisation. Furthermore, when each factor of schizotypy is examined separately in relation to functional laterality, there is evidence of a link between positive schizotypal traits and reduced lateralisation. The aim of the current study was to use a behavioural dual reading-finger tapping task and an fMRI lexical decision task to investigate language laterality in a nonclinical sample of high and low schizotypal individuals. Findings revealed no evidence for atypical lateralisation in our sample for both overall schizotypy (measured by the O-LIFE) and positive schizotypy (measured by the UnEx subscale of the O-LIFE) groups. As such, any differences may be too weak and fluctuating to be measured reliably in nonclinical schizotypal populations. Alternatively, high levels of schizotypy are not associated with atypical language laterality.

Keywords: Schizotypy; Language; Laterality; Dual-task; fMRI; Left hemisphere

[2] Material from this chapter has been submitted for publication:
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4.1 Introduction

It is well established that each hemisphere of the brain is characterised by a variety of specialised motor, perceptual, and cognitive functions that are processed predominantly by either the right or the left hemisphere. The need for lateralisation is thought to have risen in order to maximise the use of cerebral space and expand cognitive capacity, with facial and space processing being mainly lateralised to the right hemisphere, and language to the left (Levy, 1977; Corballis, Funnell, & Gazzaniga, 2000). However, a large number of studies have observed laterality abnormalities in atypical populations such as individuals with autism (Kleinhans, Müller, Cohen, & Courchesne, 2008), epilepsy (Yuan et al., 2006), ADHD (Hale, Zaidel, McGough, Phillips, & McCracken, 2006; Rolfe, Kirk, & Waldie, 2007), and schizophrenia (Gur & Chin, 1999; Weiss et al., 2006), suggesting a possible link between reduced functional lateralisation and clinical symptoms of these disorders.

In particular, abnormal language pathways in schizophrenia patients have been hypothesised to be one of the key deficits leading to thought disorders and auditory hallucinations, where misconnections within the pathway may cause internal thoughts being perceived as external speech, and vice versa (Crow, 2008). Although the majority of healthy, right-handed individuals show a leftward pattern of lateralisation for language and other related tasks (e.g., Knecht et al., 2000; Toga & Thompson, 2003), research into schizophrenia has consistently found abnormalities in left hemispheric activity in patients across multiple domains using behavioural (e.g., Løberg, Hugdahl, & Green, 1999), electrophysiological (e.g., Thoma et al., 2003), and neuroimaging (e.g., Sommer et al., 2001) methods. More specifically, decreased left lateralisation for language has been found in prefrontal and temporal lobes when performing verbal fluency and lexical decision tasks in both clinical patients and individuals at a high risk of developing schizophrenia, indicating that abnormal

language processing may be a basis rather than the result of the pathological process (Li et al., 2007; Natsubori et al., 2014).

It has been suggested that reduced lateralisation for language may be symptom-specific in schizophrenia, where positive symptoms (such as hallucinations and delusions) are frequently linked to left hemisphere dysfunction. This association has been found in a large number of behavioural studies, including observations of a smaller right ear (left hemisphere) advantage in schizophrenia patients compared to healthy controls when using dichotic listening methods (e.g., Bruder et al., 1995; Hugdahl et al., 2012). This has further been corroborated by imaging studies including structural MRI, which found reduced left temporal lobe volumes in patients (e.g., Levitan, Ward, & Catts, 1999; Neckelmann, Specht, Lund, & Ersland, 2006), as well as increased right hemisphere regional cerebral blood flow (e.g., Malaspina et al., 2000), and activations in the superior temporal regions (e.g., Shergill et al., 2004). A large amount of research has focused particularly on auditory hallucinations as an index of atypical lateralisation, as it has been suggested that abnormalities in the left temporal lobe (which typically processes external speech) may result in the language deficits observed in schizophrenia patients (Crow, 1990; Woodruff et al., 1997).

Stemming from these findings, recent research has also examined possible laterality differences in individuals with high levels of schizotypy, who display nonclinical personality traits that are qualitatively similar to schizophrenia symptoms but less severe. This construct is based on the assumption that such traits and symptoms exist on a continuum, with psychosis and psychopathology at one extreme end (such as schizophrenia) and mild behavioural manifestations of nonclinical traits at the other end (such as schizotypal personality; Claridge, 1997; Meehl, 1962; for a review, see Nelson et al., 2013). Similar to schizophrenia, schizotypy also has a three- or four-factor structure (positive, negative, disorganised, and impulsive), which can be measured by using psychometric scales such as

the Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE; Mason et al., 1995) or the Schizotypal Personality Questionnaire (SPQ; Raine, 1991). These measures are comprised of questions from the different factors, from which a global schizotypy score can be calculated from taking the sum of the answers. In addition, each factor can be examined individually by taking a subscale score, which may be useful when focusing on specific symptoms such as perceptual delusions. Overall, investigations into hemispheric asymmetries in schizotypy have also shown some evidence of reduced laterality in healthy schizotypal individuals, although the findings are much less consistent compared to schizophrenia, which has consistently been linked atypical hemispheric asymmetry (Oertel-Knöchel & Linden, 2011).

In brief, numerous studies that utilise language tasks have shown a pattern of greater right-than-left asymmetry in those with high overall levels of schizotypy compared to low. A near-infrared spectroscopy study by Hori, Ozeki, Terada, and Kunugi (2008) used a letter verbal fluency task in which the participant had to generate as many words as possible starting with a given letter within a set time period, to examine the relationship between psychometric schizotypy and language. They found that their high overall schizotypy group displayed a greater right prefrontal preference when completing the task, compared to their low schizotypy group. In addition, a behavioural lexical decision 'go/no-go' task study by Asai, Sugimori, and Tanno (2009) also found that those with high global schizotypal personality scores performed equally with their right and left hands when responding to an auditory stimulus that was presented to both ears at the same time. This is in contrast to those with low schizotypy scores, who typically react faster with their right hand in response to a linguistic stimulus coming from the right ear/left hemisphere (rather than left ear/right hemisphere, even when the stimulus is presented binaurally), suggesting that schizotypy is associated with bilateral language representation (Asai et al., 2009). Similarly, deficits in left

hemispheric functioning have been found in a language comprehension study, where participants were aurally presented sentences ending with either a semantically expected or noncongruent word. When compared to the low schizotypy group, the high schizotypy group showed no right ear/left hemisphere semantic compatibility effect, where the participants took longer to respond to the expected words when they were presented to the right ear/left hemisphere (Kostova et al., 2011).

Reduced left hemispheric dominance for language is also found when the positive dimension of schizotypy is studied separately. This is of particular interest as this dimension parallels the positive symptoms seen in schizophrenia including auditory hallucinations, which are thought to be a possible indicator of atypical laterality, as mentioned previously (Youn, Park, Kim, Kim, & Kwon, 2003). In line with clinical findings, a study by Mohr and colleagues (2005) examined the effect of dopamine on schizotypy by recruiting forty healthy men and dividing them into levodopa and placebo groups. They used a divided visual field, lexical decision task to examine the effect of dopamine on the relationship between positive schizotypy and hemispheric laterality. The results showed a more efficient left visual field/right hemisphere performance (as measured by reaction times of correct lexical decision trials) in the placebo group only, indicating an increased right hemispheric language contribution in relation to their Magical Ideation scale score (a positive factor). This suggests that while decreased laterality is modulated by positive schizotypy, the administration of dopamine may restore typical interhemispheric asymmetry in men with high positive schizotypy scores (Mohr et al., 2005).

In summary, individuals with high scores on psychometric positive schizotypy (such as magical ideation) have shown equal lexical decision proficiency in both visual fields, rather than the typical right visual field/left hemisphere advantage (Kravetz, Faust, & Edelman, 1998; Leonhard & Brugger, 1998). In particular, Leonhard and Brugger (1998)

suggested this relationship to be the product of an overreliance on the right hemisphere, which is typically responsible for coarse (rather than focused) semantic activations, leading to remote associations and ultimately resulting in paranormal beliefs and delusions.

In addition to the results showing both reduced and reversed lateralised language, there are also reports of *reduced* right hemisphere involvement in schizotypal populations. By using hemisphere-specific language tasks, Nunn and Peters (2001) reported reduced right hemisphere functioning in positive schizotypy, where low scores on right hemisphere language tasks (which included proverb and humour interpretations) significantly predicted high scores in the Unusual Experiences (UnEx; a positive factor in the O-LIFE) dimension. The authors posited that perhaps positive symptoms are a product of impaired right hemispheric function, rather than being due to an overreliance as suggested by Leonhard and Brugger (1998). They also found left and right hemisphere dysfunction in those scoring highly on the Cognitive Disorganisation (CogDis; a disorganised factor in the O-LIFE) dimension, suggesting that performance on language tasks is dependant on the different factors of schizotypy. Similar left-over-right dominance has been found in spatial laterality tasks, where a rightward bias was found in a line bisection task as well as a whole-body movement task for participants with high UnEx scores (Liouta, Smith, & Mohr, 2008).

Finally, null findings have also been reported for both overall and positive schizotypy, where no language laterality differences were seen in either those with high overall schizotypy (Castro & Pearson, 2011), or with high UnEx scores (Herzig, Tracy, Munafò, & Mohr, 2010) compared to low scoring individuals. Despite previous findings of an association between high levels of schizotypy and superior right hemispheric engagement in language tasks, Humphrey, Bryson, and Grimshaw (2010) did not find any differences in metaphor processing (typically processed by the right hemisphere; Brownell, Simpson, Bihrie, Potter, & Gardner, 1990) between high positive and low positive schizotypy groups.

This led the authors to suggest that there does not seem to be a relationship between positive schizotypy and increased right hemispheric involvement (when measured by a metaphor processing task), at least within nonclinical populations.

Further discrepancies are found within the literature when other dimensions of schizotypy are taken into account such as Introvertive Anhedonia (IntAn; a negative factor in the O-LIFE), which may be primarily due to the very limited number of studies which have examined these factors directly (e.g., Gooding & Braun, 2004; Najt, Bayer, & Hausmann, 2012). Overall, these disparate findings are likely to be due to the inconsistent methodology used across laterality studies, including different psychometric measures and task designs. A recent study by Schofield and Mohr (2014) aimed to address this problem by utilising two different psychometric schizotypy measures and two laterality tasks (lexical decision and face processing). They found positive schizotypy (measured by both O-LIFE and SPQ) to be unrelated to either of the laterality tasks, whereas increasing negative schizotypy (measured by both scales) was associated with an enhanced left hemisphere advantage for both tasks. This again is in contrast to studies finding a lack of association between laterality and negative schizotypy across different experimental domains, including language (Nunn & Peters, 2001), mixed-handedness (Chapman, Grimshaw, & Nicholls, 2011), and hemispatial inattention (Gooding & Braun, 2004).

Overall, a large number of behavioural studies have examined the potential relationship between language laterality and schizotypy, which have resulted in mixed findings. However, apart from the Hori et al. (2008) study mentioned earlier, there is a lack of neuroimaging evidence for reduced left hemispheric activity in nonclinical schizotypal individuals. Therefore, the aim of the current study was to help clarify the relationship between schizotypy and cerebral laterality by using both behavioural and fMRI experimental designs in the same sample of high and low schizotypy groups (overall schizotypy as well as

positive schizotypy measured by the UnEx dimension of the O-LIFE). We included a dual-task paradigm to observe any behavioural language asymmetries within our participant sample, and then employed a 'go/no-go' lexical decision task to determine functional laterality differences using MRI.

The dual-task is thought to be a reliable measure of language laterality in the brain, and involves reading short passages on a computer screen either silently or out aloud while tapping the space bar of the keyboard with either the left or the right index finger (Kinsbourne & Cook, 1971). Laterality differences are deduced by calculating the interference rates from the recorded finger tapping rates. Because of the crossing of motor pathways, the hemisphere contralateral to the hand showing a higher interference (i.e., a greater decrease in tapping rate) is said to be the primary hemisphere for language processing (Clark, Guitar, & Hoffman, 1985). As language is lateralised to the left hemisphere for the majority of the population, interference rates in the general population are greater for the right hand than for the left (Waldie & Mosley, 2000). Thus, we hypothesised that those with low overall O-LIFE scores would show a high interference rate for their right hand compared to the left, whereas those with high overall O-LIFE scores would display similar interference rates for both hands, reflecting a more symmetrical hemispheric structure for language.

We also utilised fMRI to determine possible cortical activation differences between high and low schizotypy groups when performing a lexical decision task. In order to maximise the possible laterality differences, we utilised a multivariate partial least squares method. As this is particularly useful when detecting patterns of activation that are most correlated with each group, it allowed us to compare possible differences in lateralisation by comparing activations specific to our high and low schizotypy groups. Based on previous work, we investigated possible functional differences for overall schizotypy, as well as positive schizotypy only (measured by the UnEx dimension of the O-LIFE). We expected a

reduced pattern of lateralisation in the high schizotypy group when compared to the low schizotypy group, in line with findings of an overall left hemisphere dysfunction in schizophrenia research (see for a review, Li, Branch, & DeLisi, 2009). With our positive schizotypy sample, we further hypothesised that this group would display a significantly reduced left hemisphere pattern of activation when compared to a low positive schizotypy group, consistent with the idea that auditory hallucinations (a positive schizophrenia symptom) may be a product of reduced left temporal lobe functioning.

4.2 Methods

4.2.1 Participants

A total of 48 participants (mean age = 23.42 years; SD = 4.50; 17 males) were recruited from the University of Auckland, New Zealand, and through advertising online on research recruitment websites. Exclusion criteria were: 1) being left-handed as assessed with the Edinburgh Handedness Inventory (Oldfield, 1971); 2) being bi-/multi-lingual with English not being their first language; 3) currently taking either anti-depressant or anti-psychotic medications; 4) having hearing deficits; 5) being outside the 18-40 years age bracket; 6) being a regular smoker; and 7) having a reading difficulty.

To assess reading proficiency, all participants needed to complete the highest reading age (List 13) of the Boder Test of Reading-Spelling Patterns (Boder & Jarrico, 1982) and receive an adult reading age score. Left-handed and bi-/multi-lingual participants were excluded to minimise variance in data, as both subpopulations have shown to display greater right hemispheric dominance for language, compared to right-handed, native English speakers (Knecht et al., 2000; Hull & Vaid, 2007; Badzakova-Trajkov, Kirk, & Waldie, 2008).

Participants gave their written informed consent to participate in the study, which consisted of a behavioural session, an electroencephalography session (not discussed here), and a functional magnetic resonance imaging (fMRI) session. They were reimbursed NZ$20 for each session and were free to withdraw from the study at any time without penalty. All experimental procedures were approved by the University of Auckland Human Participants Ethics Committee.

4.2.2 Procedure and stimuli

4.2.2.1 Schizotypy assessment

The O-LIFE (Mason et al., 1995) was used to assess the level of schizotypy in all 48 participants. The O-LIFE consists of 104 self-reported 'yes/no' items that load onto four factors of schizotypy, some of which are related to the positive and negative symptoms found in schizophrenia (Dinn et al., 2002). The items are scored as +1 for a 'yes' response and a 0 for a 'no' response, except for the negative items (which are scored +1 for a 'no' response and a 0 for a 'yes' response) that are included to reduce the response rate bias. The overall O-LIFE score is taken from the average of the scores across the four factors which include: unusual experiences (UnEx), which refer to items that describe perceptual and hallucinatory experiments including magical thinking; cognitive disorganisation (CogDis), which measures the level of social anxiety as well as poor attention, concentration, and decision making; introvertive anhedonia (IntAn), which describes a lack of enjoyment from both physical and social sources; and lastly, impulsive nonconformity (ImpNon), which consists of items that refer to impulse-driven, anti-social, and disinhibited behaviour (Mason & Claridge, 2006).

The O-LIFE is based on a fully dimensional model of schizotypy where it takes a more personality-based approach, and considers schizotypal traits as part of normal personality differences (Claridge, 1997). Therefore, it is particularly suited to testing

nonclinical populations, who may provide a more stable investigative opportunity. It also has robust psychometric properties, including good test-retest reliability, good validity, high internal consistency, and acceptable levels of skewness and kurtosis (Burch et al., 1998; Mason et al., 1995).

4.2.2.2 Dual-task paradigm

The right and left speeded finger tapping task consisted of three separate conditions: 1) finger tapping alone which was used as the baseline tapping rate; 2) simultaneous finger tapping and silent (covert) reading of a short passage; and 3) simultaneous finger tapping and reading out loud (overt) a short passage. Interference rate for the tapping rates were calculated as Interference = 100 × (ST – DT) / ST, where ST is the single baseline tapping condition and DT is the dual-task condition. The calculated interference value represents the percentage by which tapping rate is either decreased or increased, indicated by either a positive or a negative interference rate, respectively.

The task was programmed using E-Prime 2.0 (Psychological Software Tools, Pittsburgh, PA), and each passage was presented in Courier New Bold, font size 15, on a light grey background. The narrative passages were taken from the Classroom Reading Inventory Sixth Edition (Silvaroli, 1982). Participants sat approximately 57cm away from the screen and were instructed to tap the spacebar on the keyboard with either their right or left index finger at a fast and constant rate. The experiment started with a practice block in which they were presented with one example of each condition (baseline tapping, covert reading, overt reading). The experimental blocks consisted of 20 blocks in total, which included four baseline blocks for each hand, and three reading blocks for each hand for both the overt and covert reading conditions. The different conditions were randomised between participants to ensure that block order did not systematically influence the results. After each block,

participants were asked short questions about the passage to ensure they had read the paragraph. At the end of the experiment, all participants completed List 13 of the Boder Test of Reading-Spelling Patterns (Boder & Jarrico, 1982), which was used to assess reading proficiency or reading age to exclude dyslexia/atypical reading. Scores of 10 and above were considered normal adult reading age. All participants fulfilled this criterion.

4.2.2.3 Lexical decision task paradigm

The paradigm consisted of three experimental and three fixation/baseline blocks, which was repeated four times in total (Figure 4.1). The experimental blocks were a 'go/no-go' design where the participants were instructed to press a button with their right index finger for a response ('go'), or hold still if no response was required ('no-go'). Each experimental block lasted for 45 seconds and was followed by a 15 second fixation block. Stimuli were presented in Courier New Bold, font size 35, using E-Prime 2.0 (Psychological Software Tools, Pittsburgh, PA). Eighteen stimuli were randomly presented in black on a grey background for each experimental block. Each stimulus was presented for 2000ms preceeded by a 500ms interstimulus interval, which was a blank grey screen. The fixation blocks consisted of a black cross in the centre of the screen.

The three experimental blocks consisted of a nonverbal task, a lettercase judgement task, and a lexical decision task. The nonverbal stimuli consisted of various shapes which had either pointed or smooth edges. Stimuli in the lettercase judgement condition consisted of letter strings which were presented either in lower or uppercase (e.g., LKGHT or mlckt). The lexical decision stimuli were regular English words and pronounceable nonwords (e.g., CHAIR or ANTIG). All English words used in the lexical decision condition were chosen from the Oxford 3000^{TM}, which is a list of 3000 most frequent English words compiled by the Oxford University Press (available online at http://www.oxfordlearnersdictionaries.com/

about/oxford3000). The nonwords were both letter frequency- and length-matched to the English words. The participants had to respond by pressing the button if the shape on the screen was pointy for the nonverbal condition, if the letter string presented was in uppercase for the lettercase judgement condition, and if the word presented was a real English word for the lexical decision condition.

Both reaction times (in milliseconds) and accuracy data were recorded. Each experimental task consisted of 36 ‘go’ and 36 ‘no-go’ stimuli (72 in total per condition) which were divided into four blocks, resulting in eighteen randomised ‘go’ and ‘no-go’ stimuli per block for each condition.

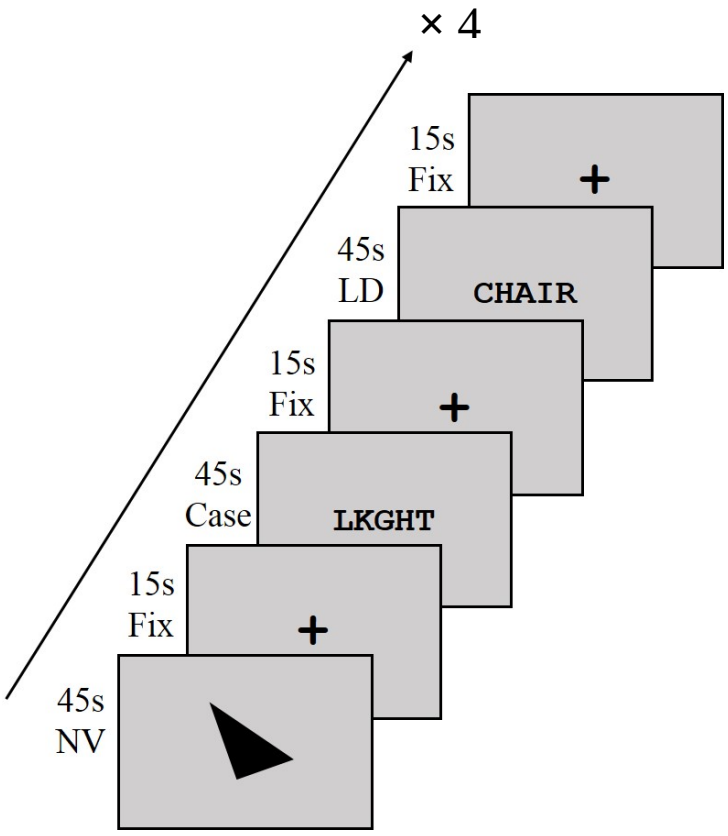

Figure 4.1 Schematic of the block design. The participants completed three experimental blocks (NV: nonverbal; Case: lettercase judgement; LD: lexical decision), which were interspersed with the fixation blocks (Fix). This cycle was repeated four times in the same order. Total experiment running time was 12 minutes.

4.2.2.4 Image acquisition

Images were acquired using a 3T Siemens Magnetom Skyra scanner (Erlangen, Germany) at the Centre for Advanced MRI (CAMRI), Faculty of Medical and Health Sciences, Grafton, Auckland. T1-weighted structural volumes were acquired from each participant using a 3D magnetisation-prepared rapidly acquired gradient echo (MP-RAGE) sequence with the following parameters: repetition time (TR) = 1900ms; echo time (TE) = 2.07ms; field of view (FOV) = 256mm^2; flip angle = 9 degrees; 176 sagittal slices; matrix size = 256 × 256mm; voxel size = 1 × 1 × 1mm; scanning time = 4.26min.

The functional scanning session began with the acquisition of 314 T2*-weighted echo-planar imaging (EPI) images with the following parameters: TR = 2300ms; TE = 27ms; FOV = 225mm^2; flip angle = 90 degrees; 45 transverse slices approximately oblique to the superior temporal gyrus, using an interleaved sequence beginning at the back; matrix size = 256 × 256mm; voxel size = 3.5 × 3.5 × 3.5mm; scanning time = 13.3min. Total scanning time, which included a localiser scan, a field map, and three functional MRI sequences (two of which are not reported here), amounted to 44.25 minutes.

4.2.2.5 Image preprocessing

The data were processed using SPM8 software (Wellcome Trust Centre for Neuroimaging, London, UK; http://www.fil.ion.ucl.ac.uk/spm) following the standard preprocessing protocol (realignment, coregistration, normalisation, and smoothing). The first volume of the session was used as a reference to realign the rest of the volumes. A mean of all functional volumes across the conditions was created and used for coregistration of the T1-weighted structural scan. By using the unified segmentation procedure, normalisation parameters were estimated (Ashburner & Friston, 2005). This was then used to normalise both the functional and structural images to the stereotactic coordinate system defined by the

Montreal Neurological Institute (MNI). Lastly, the functional volumes were then spatially smoothed using an isotropic Gaussian filter of 8 × 8 × 8mm at full-width half maximum (FWHM).

4.2.2.6 Partial Least Squares analyses

Functional data were analysed using a multivariate statistical technique called Partial Least Squares (PLS) by using a PLS graphical user interface (PLSgui; Rotman Research Institute of Baycrest Centre, Toronto, Canada; http://www.rotman-baycrest.on.ca), which was implemented in MATLAB R2012b (MathWorks, Inc.). This method is useful when examining the overall distributed patterns in the data (rather than focusing the analysis on individual elements, such as voxels), and focuses on the covariance between the images and the experimental design. A detailed summary of this method can be found in Chapter 2.

In the current chapter, a non-rotated PLS method was utilised to examine the patterns of laterality between high and low schizotypy groups. This method allows *a priori* contrasts to be entered prior to the analysis, which are then used to restrict the patterns found using PLS. This results in a set of latent variables (LV) that are derived from singular value decomposition, and optimally account for the maximum covariance between the functional data and the experimental conditions (McIntosh & Lobaugh, 2004).

Two separate sets of analyses were performed with an overall high/low schizotypy sample and a high/low UnEx sample. The first analysis of each set examined laterality patterns in both the overall O-LIFE and UnEx samples to establish lateralisation for language in the current participants. Following this, a second analysis was conducted to investigate potential group by task interaction effects, in order to distinguish any laterality differences across groups for the lexical decision condition.

The significance and the reliability of the LV were determined by permutation testing and bootstrap resampling (McIntosh et al., 1996; Efron & Tibshirani, 1985). Clusters with bootstrap ratios (BSR) of ±3 were determined as reliable.

4.3 Results

4.3.1 O-LIFE results

All 48 participants completed the O-LIFE questionnaire. From here, a participant was categorised to be in the high overall schizotypy (HS) group if their O-LIFE score, averaged across the four dimensions, was higher than half a standard deviation above the mean score of the total participant sample. Similarly, a participant was included in the low schizotypy (LS) group if their overall O-LIFE score was half a standard deviation below the mean score. In the final overall schizotypy sample, there were 18 participants in the HS group (O-LIFE mean = 15.15; SD = 2.16), and 17 LS participants (O-LIFE mean = 5.97; SD = 1.74).

For the positive schizotypy analyses, a participant was categorised to be in the high positive schizotypy (HP) group if their UnEx score was higher than half a standard deviation above the mean score of the total participant sample of 48 for this dimension. The low positive schizotypy (LP) group consisted of participants with UnEx scores of half a standard deviation below the mean score. In this analysis, there were 13 participants in the HP group (UnEx mean = 20.92; SD = 3.25), and 14 in the LP group (UnEx mean = 4.71; SD = 2.16).

4.3.2 Dual-task paradigm

4.3.2.1 O-LIFE

A preliminary mixed-design ANOVA was conducted to examine any possible gender effects within our sample, with Gender (male, female) as the between-group variable and Hand (right, left) as the within-group variable. The right and left hand values for each

participant were taken from the average of the four baseline blocks for each hand. Overall, the participants responded significantly faster with their right hand (tapping mean = 77.86; SE = 2.18) compared to their left hand (tapping mean = 72.96; SE = 1.75; $F_{(1,33)} = 28.46$; $p < .001$; $r = .68$). This right hand preference was also in line with the results from the Edinburgh Handedness Inventory, where the participants scored between 60-100% (with an average of 80%) indicating strong right-handedness as seen in Table 4.1 (Oldfield, 1971; Bishop, Ross, Daniels, & Bright, 1996). No significant gender differences or interaction effects were found.

A Group (HS, LS) × Hand (right, left) × Condition (overt, covert) mixed-design ANOVA on interference rates was conducted with Hand and Condition as the within-group variables, and Group as the between-group variable. A significant main effect of Condition was found ($F_{(1,33)} = 23.23$, $p < .001$, $r = .64$) with the overt condition showing significantly more interference (mean = 5.75; SE = .79) compared to the covert condition (mean = 2.41; SE = .81). No other effects were significant.

Table 4.1

Mean interference rates and standard deviations for each condition in the dual-task experiment for the total O-LIFE sample, high overall schizotypy, and low overall schizotypy groups, as well as the laterality quotients from the EHI.

Dual-task Condition	Total (n=35)		HS (n=18)		LS (n=17)	
	Mean	SD	Mean	SD	Mean	SD
RH Overt	6.41	5.57	6.43	5.86	6.38	5.43
LH Overt	5.08	4.90	4.54	5.74	5.65	3.91
RH Covert	2.74	6.67	2.68	4.19	2.81	8.71
LH Covert	2.07	6.12	2.42	6.45	1.69	5.93
EHI	80.83	11.17	81.01	10.23	80.64	12.41

Note: RH Overt = tapping with the right hand while reading out aloud; LH Overt = tapping with the left hand while reading out aloud; RH Covert = tapping with the right hand while reading silently; LH Covert = tapping with the left hand while reading silently; EHI = Edinburgh Handedness Inventory laterality quotient; HS = high overall schizotypy group; LS = low overall schizotypy group; n = number of participants; SD = standard deviation.

4.3.2.2 UnEx

A Gender (male, female) × Hand (right, left) mixed-design ANOVA was conducted to test for potential gender effects in this sample. Again, the right and left hand values were taken from the average of the four baseline blocks for each hand. There was a significant main effect of hand with participants responding faster with their right hand (tapping mean = 76.34; SE = 2.35) than their left (tapping mean = 71.07; SE = 1.92; $F_{(1,25)} = 21.40$; $p < .001$; $r = .68$). There were no gender or interaction effects.

The interference data were subjected to a Group (HP, LP) × Hand (right, left) × Condition (overt, covert) mixed-design ANOVA with Hand and Condition as the within-group variables, and Group as the between-group variable. A significant main effect of Condition was found ($F_{(1,25)} = 17.76$, $p < .001$, $r = .64$) with the overt condition showing significantly more interference (mean = 5.36; SE = .91) compared to the covert condition (mean = 2.44; SE = .97). No other effects were significant.

Table 4.2

Mean interference rates and standard deviations for each condition in the dual-task experiment for the total UnEx sample, high positive factor, and low positive factor groups, as well as the laterality quotients from the EHI.

Dual-task Condition	Total (n=27)		HP (n=13)		LP (n=14)	
	Mean	SD	Mean	SD	Mean	SD
RH Overt	6.06	5.08	5.38	5.14	6.70	5.14
LH Overt	4.66	5.22	4.30	6.45	4.98	4.00
RH Covert	2.33	6.15	1.95	3.97	2.69	7.80
LH Covert	2.55	5.73	3.58	5.62	1.59	5.87
EHI	80.40	12.92	81.72	10.70	79.17	14.99

Note: RH Overt = tapping with the right hand while reading out aloud; LH Overt = tapping with the left hand while reading out aloud; RH Covert = tapping with the right hand while reading silently; LH Covert = tapping with the left hand while reading silently; EHI = Edinburgh Handedness Inventory laterality quotient; HP = high unusual experiences group; LP = low unusual experiences group; n = number of participants; SD = standard deviation.

4.3.3 Lexical decision paradigm – behavioural results

4.3.3.1 O-LIFE

The accuracy and reaction time (RT) data were subjected to independent samples overall O-LIFE Group (HS, LS) *t*-tests. No significant differences were found with either the accuracy data (HS mean = .99, LS mean = .98; $t_{(33)}$ = -1.04, p = .309, d = .372) or the RT data (HS mean = 564.65ms, LS mean = 570.00ms; $t_{(33)}$ = .163, p = .872, d = .057).

4.3.3.2 UnEx

Independent samples *t*-tests were performed for the UnEx Group (HP, LP) on the accuracy and RT data. Again, no significant differences were found with either the accuracy (HP mean = .99, LP mean = .98; $t_{(25)}$ = -.669, p = .501, d = .268) or the RT data (HP mean = 555.19ms, LP mean = 598.73ms; $t_{(25)}$ = 1.27, p = .217, d = .507).

4.3.4 Lexical decision paradigm – non-rotated PLS analyses

4.3.4.1 Main effect of task

Non-rotated PLS analyses were conducted for both the overall O-LIFE and UnEx samples with a specified contrast, where the lexical decision task was weighted against the sum of the two baseline (nonverbal and lettercase judgment) conditions across the high- and low-scoring groups (i.e., 1 -0.5 -0.5; 1 -0.5 -0.5).

For the overall O-LIFE sample, a significant LV was produced showing that the HS and LS groups most strongly activated the typical language network (see Table 4.3) when completing the lexical decision task compared to the baseline tasks (using 1500 permutations and 1000 bootstraps; d = 53.84, which denotes the proportion of the covariance between the task and the functional data for the specified LV, p = .021). This significant main effect of task was also observed in the UnEx sample where the lexical decision task elicited the

strongest pattern of left lateralisation for both the HP and LP groups when compared to the other two baseline tasks (d = 61.98, p = .013; Figure 4.2).

Table 4.3

Brain regions associated with the experimental conditions in the latent variables identified by the non-rotated PLS analyses, for both the overall O-LIFE and UnEx groups.

	Brain region	*x*	*y*	*z*	BSR	Cluster size (*k*)
Overall O-LIFE						
Lexical decision > Baseline conditions						
L	Inferior occipital gyrus	-20	-92	-10	14.66	3129
R	Lingual gyrus	24	-92	-8	12.69	1465
L	IFG (p. Opercularis)	-56	16	32	5.57	728
R	Superior medial gyrus	6	36	40	3.93	319
R	IFG (p. Triangularis)	62	24	24	4.53	305
L	Middle temporal gyrus	-58	-32	2	5.02	204
L	IFG (p. Triangularis)	-38	36	-2	4.90	121
L	Temporal pole	-52	8	-16	4.43	39
R	IFG (p. Triangularis)	50	32	12	3.42	20
L	Cerebellum (VII)	-22	-76	-50	3.95	18
Baseline conditions > Lexical decision						
R	Middle occipital gyrus	20	-72	-8	-4.93	798
L	Parahippocampal gyrus	-44	-86	16	-4.09	37
R	Fusiform gyrus	30	-42	-6	-3.67	33
Unusual Experiences						
Lexical decision > Baseline conditions						
L	Inferior occipital gyrus	-18	-94	-10	12.41	2588
R	Inferior occipital gyrus	26	-92	-6	12.85	1488
R	Superior medial gyrus	2	30	52	4.28	863
L	Fusiform gyrus	-42	-38	-24	5.19	222
L	Temporal pole	-30	26	-28	5.19	194
L	IFG (p. Triangularis)	-56	16	30	4.57	181
L	Middle temporal gyrus	-58	-32	2	4.70	147
L	IFG (p. Triangularis)	-38	36	-2	4.83	120
R	IFG (p. Triangularis)	56	36	18	3.94	63
R	Superior medial gyrus	6	70	10	3.85	62
L	Cerebellum (Crus 2)	-28	-72	-44	3.94	47
R	Fusiform gyrus	42	-46	-26	4.16	31
L	Cerebellum (Crus 2)	-22	-80	-50	3.59	19
L	IFG (p. Opercularis)	-44	8	24	3.49	19
L	IFG (p. Triangularis)	-46	22	22	3.40	15
R	Paracentral lobule	4	-40	66	3.24	12
Baseline conditions > Lexical decision						
R	Calcarine gyrus	10	-88	10	-4.84	658
R	Precuneus	16	-48	16	-4.05	35
L	Calcarine gyrus	-6	-92	6	-4.24	31
R	Anterior cingulate cortex	12	40	6	-3.81	31
L	Fusiform gyrus	-22	-44	-12	-3.58	10

Note: Clusters evident with a bootstrap ratio of greater than 3 and a minimum cluster size of 10 voxels are reported. Cluster size indicates the number of voxels in the cluster. Co-ordinates are in MNI space and were anatomically labelled using the SPM Anatomy toolbox (Eickhoff et al., 2005; http://www.fz-juelich.de/inb/inb-3//spm_anatomy_toolbox). BSR = bootstrap ratio; L = left; R = right; IFG = inferior frontal gyrus.

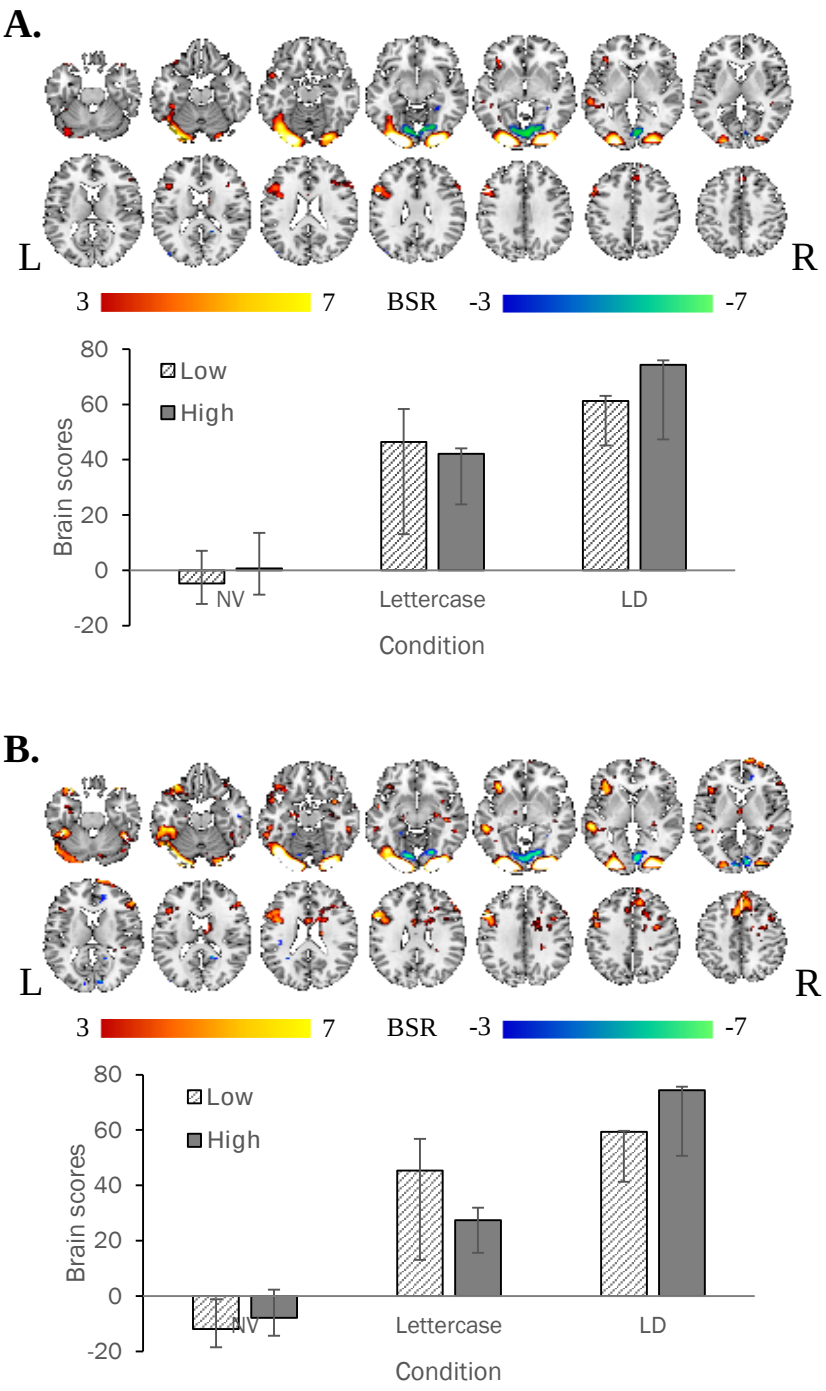

Figure 4.2 Singular images showing the areas of neural activations identified in the non-rotated task PLS where: A) is the high and low overall O-LIFE group analysis; and B) is the high and low UnEx group analysis. Warm regions (corresponding to positive BSR scores) indicate stable activations that are greater for the lexical decision (LD) condition than the average of the nonverbal (NV) and lettercase conditions. Cool regions (corresponding to negative BSR scores) indicate stable activations that are greater for the average of the two baseline conditions than the LD condition. Colour bars indicate the strength of correlation between the condition and the neural activation for each voxel with a threshold bootstrap

ratio (BSR) of ±3. The bar graphs show the brain scores for each condition per group, which indicate the strength of each condition's contribution to the pattern expressed in the LV. L = left; R = right.

4.3.4.2 Task by group interaction effect

Two further non-rotated PLS analyses were conducted to examine possible group differences in the lexical decision condition (i.e., 1 -0.5 -0.5; -1 0.5 0.5). A non-significant LV was produced for the overall O-LIFE sample suggesting that the HS and LS groups do not display different patterns of laterality for language (using 1500 permutations and 1000 bootstraps; d = 34.94, p = .338). The PLS analysis for the UnEx dimension also revealed non-significant differences in laterality between the HP and LP groups (d = 38.89, p = .461).

4.4 Discussion

Contrary to our hypothesis, we did not find any behavioural or functional differences in language laterality between our sample of high and low schizotypal individuals. This was regardless of whether we divided the initial sample according to their overall O-LIFE scores or their UnEx scores. These are in contrast with earlier findings of atypical lateralisaty in both overall schizotypy (Hori et al., 2008; Kostova et al., 2011) and positive schizotypy (Kravetz et al., 1998; Mohr et al., 2005).

Our findings do support others that have reported null findings (Castro & Pearson, 2011; Herzig et al., 2010) and, as such, add to the evidence that both low and high nonclinical schizotypal individuals experience the typical left hemisphere lateralisation for language. Castro and Pearson (2011), for example, found left hemisphere specialisation for word detection in both low and high schizotypy groups and suggested that schizotypy traits at a nonclinical level may not be severe enough to induce laterality changes. A recent study by Carlin and Lindell (2015) similarly failed to find differences in lateralised lexical decision

task performance as a function of self-reported schizotypal personality traits. The authors suggested that further neuroimaging evidence is needed to confirm hemispheric lateralisation in schizotypal individuals. When taken together with the behavioural and fMRI results of the current study, it may be that reduced laterality is only observed in clinical schizophrenia patients, and not in healthy individuals despite their high levels of schizotypy.

Given the inconsistencies which exist in the literature, it could be that the association between laterality and schizotypy is influenced by external factors other than (or in addition to) the effect of schizotypy. This is further complicated by the measurement of the dimensions (and ultimately the overall level of schizotypy), with psychometric measures often utilising similar questions for examining different dimensions. In general, although there is a large amount of research examining the relationship between schizotypy and laterality, there is a lack of consistency in both the laterality tasks and schizotypy scales used to study the possible link between the two constructs. This makes it particularly hard to compare and replicate results, and to establish any concrete associations. Such problems are directly observed in Schofield and Mohr's (2014) study, which found inconsistent results using two different types of measures and tasks, leading the authors to posit that there may be no relationship between schizotypy and laterality due to "the lack of any significant, discernible consistent result pattern" (p. 16).

Despite these concerns, a consistent finding in the literature that is partly in agreement with our results is lack of a link between magical ideation (MI – a subset of positive schizotypy and schizophrenia) and *performance* measures of handedness, which is in contrast to the findings of an association between MI and *self-reported* measures of handedness. More specifically, even though those with high levels of MI may indicate reduced hand preference, this is not translated into behavioural performance where typically no differences are found between low and high scoring MI individuals (e.g., Badzakova-Trajkov, Häberling, &

Corballis, 2011; Grimshaw, Yelle, Schoger, & Bright, 2008; Herzig et al., 2015; Nicholls, Orr, & Lindell, 2005). This is in line with our finding of no differences between high and low positive schizotypy groups (UnEx), who performed similarly in the behavioural dual-task. This suggests that even though handedness is strongly related to language laterality (e.g., Khedr, Hamed, Said, & Basahi, 2002; Knecht et al., 2000), it is not related to any positive aspects of schizotypy, where having a positive schizotypal personality does not influence cerebral asymmetry, at least when measured by linguistic performance tasks. However, this speculation must be presented with caution, as this is in conflict with other studies which have found a direct association between decreased laterality and positive schizotypy (e.g., Leonhard & Brugger, 1998).

Similarly, our result of a lack of a difference between overall schizotypy and laterality further contradicts some of the findings in the literature, which show a pattern of laterality differences between high and low schizotypal individuals. However, as mentioned earlier, this pattern of difference does not seem to correlate across studies which have found significant yet dissimilar results, including some showing differences in laterality in highly schizotypal males only (Najt et al., 2012) versus both males and females displaying atypical laterality (Mason & Claridge, 1999), and a right-over-left hemispheric dominance (Suzuki & Usher, 2009) versus a left-over-right hemispheric dominance (Nunn & Peters, 2001). This suggests that any relationship between overall schizotypy and laterality may be weak and unstable, which may be caused by small disparities in the sample recruitment and testing procedures.

In addition, it could be that our choice of tasks may not have been sensitive enough to measure any subtle asymmetry differences. Because language is strongly lateralised to the left hemisphere in majority of the right handers, using a lexical decision paradigm has been successful in uncovering laterality differences between subpopulations who may show

atypical language networks. Such differences have been found studies examining dyslexia (Milne, Syngeniotis, Jackson, & Corballis, 2002; Waldie, Haigh, Badzakova-Trajkov, Buckley, & Kirk, 2013), autistic personality traits (Lindell, Notice, & Withers, 2009), bilingualism (Park, Badzakova-Trajkov, & Waldie, 2012), ADHD (Sigi Hale et al., 2005), and schizophrenia (Angrilli et al., 2009). However, it could be that within a healthy population with no overt symptoms (e.g., psychosis) or behavioural characteristics (e.g., bilingualism), there are no measurable language laterality differences in nonclinical schizotypy, which may be more exaggerated in clinical populations. This is further supported by our finding of no differences in both the behavioural dual-task and the fMRI lexical decision task, suggesting that language is processed in the same manner for our sample of high and low schizotypal participants (also indicated by the near ceiling performance of both the high/low groups and overall O-LIFE/UnEx analyses). Moreover, even if there are subtle differences, it could be that hemispheric laterality may be unstable and fluctuate in individuals with high levels of schizotypy as suggested by Schofield and Mohr (2014), and therefore cannot accurately be determined with conventional methodologies.

Another reason for the discrepancies in the literature may be due to the choice of tasks utilised to test laterality. A large amount of empirical studies have used linguistic paradigms which involve other cognitive processes as well as language, such as priming (Kravetz et al., 1998), verbal fluency (Hori et al., 2008), and irony comprehension (Rapp et al., 2010). As the lexical decision task involves word recognition only, it may be the case that laterality differences become apparent when task complexity is increased.

Following from this, an important consideration is the characteristics of the current sample of participants, which consisted of young, healthy adults studying (or have studied in the past) at a tertiary level. The idea of ‘healthy’ schizotypy has previously been suggested, where those with high levels of nonclinical schizotypy (particularly positive schizotypy) are

able to function comparably to those with low schizotypy levels (e.g., Goulding, 2004; Hori et al., 2014; Tabak & Weisman de Mamani, 2013), and may even have an advantage for certain types of tasks which require loose cognitive associations and creative thinking (e.g., Burch, Pavelis, Hemsley, & Corr, 2006; Tsakanikos & Claridge, 2005). These benefits have been suggested to be the consequence of a more widespread network of cortical activations, allowing for the linkage of indirect associations (Pizzagalli et al., 2001). Therefore it could be further speculated that reduced functional hemispheric asymmetry does exist in highly schizotypal individuals but perhaps only when performing cognitive tasks that are not purely language-based. This putative link between schizotypy and creativity will be directly examined in the next chapter.

Additionally, the current sample consisted of strongly right-handed individuals as evidenced by both the self-reported (EHI) and performance (dual-task) measures of handedness. This was to allow us to attribute any laterality differences to the effect of schizotypy; however, the null results indicate that perhaps within nonclinical populations, those who are strongly right-handed express typical lateralisation of language *regardless of their level of schizotypy.* As there is a large amount of research which have found an association between schizotypy and mixed handedness (Asai et al., 2009; Chapman, Grimshaw, & Nicholls, 2011; Somers, Sommer, Boks, & Kahn, 2009), it may be that this trait is a necessary prerequisite for atypical laterality, or at least is a consequence of reduced cerebral asymmetry along with schizotypal beliefs.

In summary, we did not see any evidence of reduced hemispheric laterality in our sample of high scoring schizotypal individuals compared to those with low levels of schizotypy. Although a surprising finding, this suggests that nonclinical individuals with high levels of schizotypy have no discernible laterality differences when tested using both a pure language comprehension fMRI paradigm and a behavioural dual-task. Furthermore, it may be

that these differences only become apparent when other cognitive processes (such as emotional processing; Van Strien & Kampen, 2009) are involved, which add to the complexity of the language task.

When the contradictory pattern of findings in previous research is taken into account, it also seems that current empirical studies are either not utilising a paradigm that ideally measures the possible association between laterality and schizotypy, or that this association is unable to be reliably quantified with conventional methodologies. Furthermore, there may be a third factor influencing this relationship which has not yet been clearly elucidated by research examining the effect of schizotypy on laterality, including other personality factors, family history of disorders such as schizophrenia, substance usage, environmental factors (such as trauma, attachment, and stress), and mixed handedness, that may be important when it comes to investigating a cognitive function that is usually heavily lateralised such as language. Therefore, the present study highlights the need for systematic assessment of testing methods and psychological factors, which may need to be streamlined in order for future studies to further investigate and clarify any valid associations between language lateralisation and schizotypy.

Chapter 5: Neural correlates of creative thinking and schizotypy[3]

Abstract:

Empirical studies indicate a link between creativity and schizotypal personality traits, where individuals who score highly on schizotypy measures also display greater levels of creative behaviour. However, the exact nature of this relationship is not yet clear, with only a few studies examining this association using neuroimaging methods. In the present study, the neural substrates of creative thinking were assessed in healthy individuals using fMRI. These regions were then statistically correlated with the participants' level of schizotypy as measured by the Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE), which is a questionnaire consisting of four dimensions. Neural activations associated with creativity were observed in bilateral inferior temporal gyri, left insula, left parietal lobule, right angular gyrus, as well as regions in the prefrontal cortex. This widespread pattern of activation suggests that creative thinking utilises multiple neurocognitive networks, with creative production being the result of collaboration between these regions. Furthermore, the correlational analyses found the Unusual Experiences factor of the O-LIFE to be the most common dimension associated with these areas, followed by the Impulsive Nonconformity dimension. These correlations were negative, indicating that individuals who scored the highest in these factors displayed the least amount of activation when performing the creative task. This is in line with the idea that 'less is more' for creativity, where the deactivation of specific cortical areas may facilitate creativity. Thus, these findings contribute to the evidence of a common neural basis between creativity and schizotypy.

Keywords: Schizotypy; Creativity; fMRI; Divergent thinking; Personality; O-LIFE

[3] Material from this chapter can be found in the following publication:
Park, H.R.P., Kirk, I.J., & Waldie, K.E. (2015). Neural correlates of creative thinking and schizotypy. *Neuropsychologia, 73,* 94-107. doi:10.1016/j.neuropsychologia.2015.05.007

5.1 Introduction

Although the exact relationship between creativity and psychopathology is still a contentious issue, there seems to be some consensus regarding a putative link between creative behaviour and mental illness. Anecdotal evidence of artists who suffered from depressive episodes, hallucinations, or drug abuse has led way to empirical studies which indicate a quantitative link between atypical cognition and elevated levels of creativity (e.g., Andreasen, 1987; Becker, 2001; Nettle, 2001; Post, 1994; Richards et al., 1988). This includes evidence of increased creativity in psychiatric patients with bipolar disorder (Santosa et al., 2007), depression (Akinola & Mendes, 2008), affective disorder (Andreasen, 1987), and schizophrenia (Keefe & Magaro, 1980).

However, full-blown psychosis is detrimental to any creative process, leading to the suggestion that this relationship between creative thinking and psychosis lies on an inverted U curve, where the level of creativity rises with certain traits of mental illness but then decreases with the onset of clinical psychopathology (Nettle, 2006). This is in line with the finding of creative achievement in non-affected relatives of patients (Nettle, 2006; O'Reilly et al., 2001). They often share certain traits and predispositions with the affected relative, but have a lower loading of these characteristics which may contribute to the development of creativity without the debilitating effects of psychosis. Large familial studies conducted by Kyaga and colleagues (2011) indicate increased representation of creative professions in those with a family history of schizophrenia, bipolar disorder, anorexia nervosa, and possibly autism, and adoption studies have also shown increased levels of creativity in adopted healthy children of schizophrenic parents (Heston, 1966; Kinney et al., 2001). Thus far, research has shown that these psychologically healthy relatives often show higher levels of schizotypal personality traits compared to the general population, as well as increased creative performance (Fisher et al., 2004; Kinney et al., 2001; Schuldberg, 1990). Therefore,

investigating the role of schizotypal personality (or schizotypy) on creative behaviour may provide insight into both behavioural and cognitive correlates of creativity.

Schizotypy is defined as a cluster of nonclinical symptoms and personality traits within a healthy population, which are qualitatively similar to schizophrenia symptoms but less severe (Claridge, 1997). The development of this construct derives from observations of individuals who display schizophrenic-like thought patterns and symptoms without the presence of psychosis (Lenzenweger, 2006). Similar to schizophrenia, schizotypy is a heterogeneous construct which can be divided into three factors: positive schizotypy, which describes unusual perceptual experiences, delusional thoughts and hallucinations; negative schizotypy, which encompasses physical and social anhedonia as well as high introversion; and disorganised schizotypy, which includes traits such as disorganised cognition and thoughts (Arndt, Alliger, & Andreasen, 1991; Holt, Simmonds-Moore, & Moore, 2008). Furthermore, a fourth impulsive factor is often included. The level of schizotypy can be measured using psychometric questionnaires such as the Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE; Mason et al., 1995), which loads schizotypy onto four factors: unusual experiences; cognitive disorganisation; introvertive anhedonia; and impulsive nonconformity.

A possible overlapping aspect of psychosis and creativity is overinclusive thinking, where the individual is unable to establish conceptual boundaries (Barrantes-Vidal, 2004; Ottemiller, Elliott, & Giovannetti, 2014). This is also observed in schizotypy research, where divergent thinking (DT) is often used as a proxy measure of creativity. DT is considered to be the useful equivalent of overinclusive thinking, and refers to the capacity of an individual to generate multiple alternative solutions to an open-ended problem (Plucker & Renzulli, 1999). It requires the individual to be flexible, associative, and open-minded, which are all requirements for creative thought generation (Thys, Sabbe, & De Hert, 2014). It is thought

that there is a greater spread of cortical activation through semantic networks in DT, leading to the activation of indirectly related associations and resulting in enhanced creative thinking (Pizzagalli et al., 2001). Although it is not a direct measurement of creativity and can only provide a useful estimate (for a review, see Runco & Acar, 2012), DT has been widely and consistently employed in the literature as the best method to predict creative potential (Runco, 1991).

Besides DT, another important indicator of creative performance is individual personality traits. There is consensus amongst researchers that extracognitive factors are crucial for creativity research, and studies have shown that personality makes a significant contribution to creativity (for a review, see Batey & Furnham, 2006). Both Eysenck's P factor (psychoticism; Eysenck, Eysenck, & Barrett, 1985) and O and E factors (openness to experience; extroversion; Costa & McCrae, 1992) from the Big Five have been implicated in enhanced DT, suggesting that individuals who think unusual thoughts, make uncommon associations, tolerate ambiguity, seek out uncertainty, and are impulsive may be particularly suited to creative endeavours (John, Donahue, & Kentle, 1991; Sánchez-Ruiz et al., 2011; Upmanyu, Bhardwaj, & Singh, 1996). Many of these personality traits are often observed in individuals who score highly on psychometric schizotypy measures, supporting the idea that common mental processes are involved in both creative thinking and psychosis proneness.

A considerable amount of research has shown a positive correlation between creativity and positive schizotypy (e.g., Folley & Park, 2005; Jones, Caulfield, Wilkinson, & Weller, 2011; Weinstein & Graves, 2001). This link is reflected in a study by Burch, Pavelis, Hemsley, and Corr (2006), who compared the level of schizotypy between visual artists and non-artists and found a significantly higher level of unusual experiences in the artists. Paranormal experiences were also found to be linked to artistic creativity (Kennedy & Kanthamani, 1995b), and Nettle (2006) also found that poets and artists displayed higher

levels of schizotypal traits compared to controls, especially in the unusual experiences factor of the O-LIFE.

Similarly, Eysenck (1993) suggested that unusual thought processes observed in schizotypy may be due to a lack of cognitive inhibition where highly schizotypal individuals inhibit fewer thoughts during early processing, allowing them to use an increased amount of information in a creative manner. However, the evidence for a link between impaired cognitive control and creativity is less clear, with disorganised thinking being linked both positively (O'Reilly et al., 2001) and negatively (Batey & Furnham, 2008) with creativity. The delivery of the unusual or novel associations in psychometrically measured creative tests may be further aided by an increased inclination to give socially undesirable responses, which may be driven by the impulsive nonconformity dimension of schizotypy (Burch et al., 2006). However, research into these factors are limited, possibly due to the fact that there is less of a consensus between psychometric schizotypal measures when examining factors which are neither strictly positive nor negative.

Literature regarding the relationship between creativity and negative schizotypy is also mixed. Most studies show decreased levels of creativity in individuals who score highly on negative schizotypy subscales (Batey & Furnham, 2009; Tsakanikos & Claridge, 2005), indicating that the avoidance of social interaction and engagement is detrimental to creative thought, possibly by being disengaged with the task. Nettle (2006) also found the lowest scores in introvertive anhedonia within his sample of professional poets and visual artists compared to both psychiatric patients and controls, indicating that the lack of anhedonia and avolition may contribute to artistic creativity. On the other hand, he also observed that mathematical ability (a subset of scientific creativity) was correlated with this negative dimension (Nettle, 2006), and Cox and Leon (1999) also found a positive association between DT and social anhedonia.

In summary, a large amount of behavioural research indicates a link between schizotypal personality and enhanced creative ability. Although there are numerous studies reporting that schizotypal individuals show atypical performance on behavioural tasks such as the Stroop (Mohanty et al., 2005), irony comprehension (Rapp et al., 2010), verbal fluency (Hori et al., 2008), and self-reflection (Modinos, Renken, Ormel, & Aleman, 2011), studies investigating this relationship from a neuroscience perspective are comparatively limited. Results from these few studies also support the evidence of atypical cortical activation in creative individuals with high schizotypy: a study using near-infrared optical imaging found that, in addition to enhanced DT ability, schizotypal individuals showed hyperactivation of the right prefrontal cortex during the DT task when compared to both control and schizophrenia groups (Folley & Park, 2005). The authors suggested that this result could be due to the schizotypal participants being able to use their unusual thoughts in a creative rather than dysfunctional manner, and that the right PFC may have a role in this difference of cognitive output.

A functional magnetic resonance imaging (fMRI) study has also shown reduced deactivation in the right precuneus in individuals scoring high on a schizotypy scale when performing a creativity task, compared to low-scoring individuals who, in turn, displayed a strong deactivation of the same region (Fink et al., 2014). Furthermore, Fink and colleagues (2014) found that the pattern of brain activity during creative thinking was similar for both the high schizotypy and high creativity groups, suggesting that common cognitive processes may be involved. Structural studies have also shown a possible link between brain structure, creativity, and psychopathology, where reduced white matter integrity (measured by fractional anisotropy) was found in similar cortical areas for schizophrenia and bipolar patients, and also with healthy participants scoring high in DT (Jung, Grazioplene, Caprihan, Chavez, & Haier, 2010; Sussman et al., 2009).

Nonetheless, apart from the two functional studies mentioned above, there is a lack of direct neuroimaging evidence for the brain mechanisms underlying creative thinking in schizotypal individuals. Therefore, the main objective of this study was to address this gap by using fMRI to examine whether the neural processes stemming from creative thought can be directly correlated to specific dimensions of schizotypy.

In brief, we assessed the level of schizotypy by using the O-LIFE questionnaire on young healthy adults, and selected the participants whose global O-LIFE scores (averaged across all dimensions) were on either end of the schizotypy spectrum. Creativity was measured by administering the Torrance Tests of Creative Thinking (TTCT; Torrance, 1966, 2008a), which is the most commonly used creativity/DT test in both experimental and clinical psychology (de Souza et al., 2010; Wechsler, 2006). This was to establish potential behavioural differences in our sample, with the hypothesis that the high global schizotypy group would perform better than the low global schizotypy group. From here, we used a continuous design, rather than a dichotomised sample, and included both high- and low-scoring participants in the fMRI analysis to determine the neural correlates of creative thinking. We expected to find differences in patterns of cortical activation for the creativity condition compared to the control condition. Finally, we used correlational statistical methods to examine the relationship between cortical regions implicated in creativity and the four dimensions of schizotypy (as measured by the O-LIFE). We hypothesised that unusual experiences (a positive schizotypy factor) would be the most common dimension associated with the cortical regions of interest. In contrast, we expected introvertive anhedonia (a negative schizotypy factor) to be unrelated to our measurement of artistic creativity, based on previous studies which show a lack of anhedonia in creative individuals (e.g., Nettle, 2006).

5.2 Materials and methods

This chapter reports analysis of some of the data collected in the same behavioural and scanning sessions as those discussed in Chapters 3 and 4. Therefore participant information and MRI data collection procedures are summarised in brief here.

5.2.1 Participants

A total of 35 participants (mean age = 23.26 years; SD = 4.88; 11 males) from the language laterality study (Chapter 4) were included in the current study. They all met the exclusion criteria detailed in Chapter 2. Subjects gave their written informed consent to participate in the study and all experimental procedures were approved by the University of Auckland Human Participants Ethics Committee.

5.2.2 Behavioural procedure and stimuli

5.2.2.1 Schizotypy assessment

The participants' level of schizotypy was measured using the O-LIFE (Mason et al., 1995), and the dimension scores from the four factors (UnEx, CogDis, IntAn, and ImpNon) were taken as behavioural measures. A full description of the psychometric schizotypy measure used (O-LIFE; Mason et al., 1995) can be found in Section 2.2.3 of Chapter 2.

5.2.2.2 Intelligence

The participants all completed the Wechsler Abbreviated Scale of Intelligence (WASI; The Psychological Corporation, 1999), as there may be a relationship between creativity and intelligence (Silvia, 2008; for a review, see Batey & Furnham, 2006). This four-subtest measure of cognitive ability consists of two verbal-based (Vocabulary and Similarities) and two performance-based (Matrix Reasoning and Block Design) tests. It has

excellent reliability and content validity, as well as high concurrent validity with other intelligence tests (The Psychological Corporation, 1999; Stanos, 2004).

5.2.2.3 Creativity assessment

Both the figural and verbal (Form A) versions of the TTCT (Torrance, 1966, 2008a) were administered to evaluate each participants' creative behaviour. Overall, the TTCT measures four cognitive components of creativity through DT including fluency, flexibility, originality, and elaboration. The verbal form (TTCT-V) consists of six tasks which include asking questions to make sense of a situation, coming up with ways to improve a product, and imagining the consequences of an unlikely event.

The figural form (TTCT-F) consists of three tasks which require the participant to produce unusual and interesting drawings within the time limit. As well as the four cognitive components, the TTCT-F also measures other creativity indicators, or "creative strengths", which include emotional expressiveness, storytelling articulateness, internal visualisation, humour, fantasy, and richness of imagery. These indicators are included to assess creative behaviour outside of traditional DT and therefore can add to the overall measured creativity (Kim, 2006b; LaFrance, 1995).

The TTCT has shown strong predictive validity (Cramond et al., 2005), acceptable concurrent validity and reliability (Kim, 2006a), and is the most widely used measure to assess creativity (Wechsler, 2006). In the current study, the order of the tests (including the WASI) was counterbalanced across all participants. Both the TTCT-F and the TTCT-V were scored by trained raters at the Scholastic Testing Service, Inc. to reduce inter-rater variability, using the streamlined scoring guide established by Torrance, Ball, and Safter (2008) and Torrance (2008b), respectively.

5.2.3 fMRI procedure and stimuli

5.2.3.1 Drawing task paradigm

The task consisted of ten experimental and ten control blocks with shorter baseline blocks in between. Each experimental and control block lasted for 30 seconds and was preceded by a 10 second baseline block. For the experimental blocks, participants completed a subset (Incomplete Figures) of the TTCT-F (Form B; Form A was used in the behavioural session) where they were given ten incomplete figures on paper (one figure per block) and were asked to draw a picture with the incomplete figure forming a part of their drawing. For the control blocks, participants traced ten dotted figures (one dotted figure per block). The baseline blocks consisted of the participant fixating on a blank piece of paper for ten seconds.

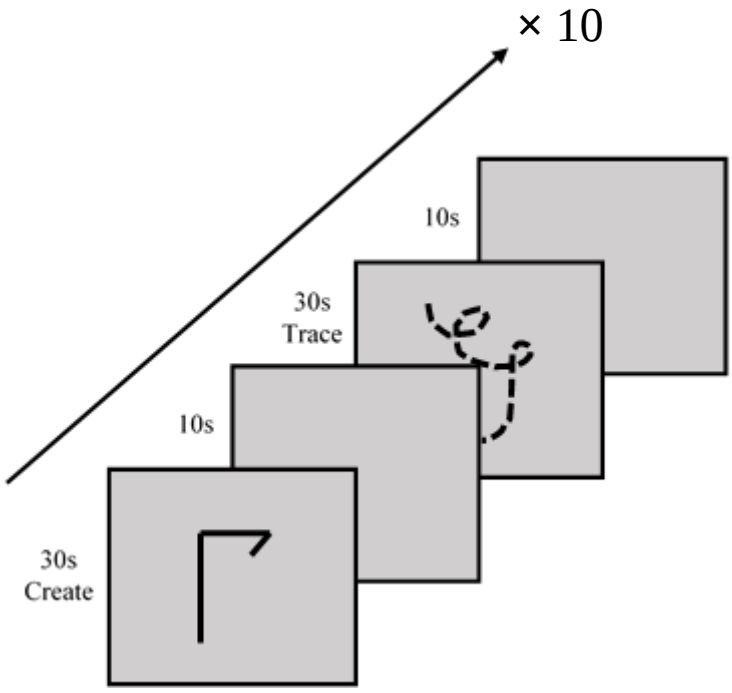

Figure 5.1 Schematic of the block design. The participants completed ten 'Create' blocks, which were denoted by the solid stimulus line, and ten 'Trace' blocks, which were denoted by the dotted stimulus line. Between each drawing block, there was a ten second baseline break. Total experiment running time was 13.3 minutes.

The stimuli were laid on a custom-built MRI-compatible table, which was placed over the participant's stomach. Prior to starting the experiment, checks were made to ensure that the participant had a clear view of the paper on the table (using a mirror mounted on the head coil), and their right upper arm was supported to make it easier for them to draw using a pencil. An assistant was present in the scanning room for the duration of the experiment to remove the stimuli at the end of each time period. They also signalled to the participant five seconds before the end of each block by placing the tip of their index finger on the top left hand corner of each page.

All participants completed a shortened version of the task in a mock scanner prior to the real experiment to ensure they were familiar with the stimuli and the procedure. The practice stimuli used were similar but not identical to the experimental stimuli.

Prior to both the practice and the real scan, all participants were instructed to: draw/trace for the full 30 second period; limit upper arm movements; and be aware of the observer's signal near the end of the time limit.

5.2.3.2 Image acquisition

Images were acquired using a 3T Siemens Magnetom Skyra scanner (Erlangen, Germany) at the Centre for Advanced MRI (CAMRI), Faculty of Medical and Health Sciences, Grafton, Auckland. Functional scanning sessions began with the acquisition of 348 T2*-weighted echo-planar imaging (EPI) images with the following parameters: TR = 2300ms; TE = 27ms; FOV = 225mm^2; flip angle = 90 degrees; 45 transverse slices approximately oblique to the superior temporal gyrus, using an interleaved sequence beginning at the back; matrix size = 256 × 256mm; voxel size = 3.5 × 3.5 × 3.5mm; scanning time = 13.3min. Total scanning time, which included a localiser scan, a field map, and three functional MRI sequences (two of which are not reported here), amounted to 44.25 minutes.

5.2.3.3 Image preprocessing

The data were processed using SPM8 software (Wellcome Trust Centre for Neuroimaging, London, UK; http://www.fil.ion.ucl.ac.uk/spm) following the standard preprocessing protocol (realignment, coregistration, normalisation, and smoothing). Same parameters and protocol as Chapter 4 were used here.

5.2.3.4 Partial Least Squares analyses

Functional data were analysed using a multivariate statistical technique called Partial Least Squares (PLS) by using a PLS graphical user interface (PLSgui; Rotman Research Institute of Baycrest Centre, Toronto, Canada; http://www.rotman-baycrest.on.ca), which was implemented in MATLAB R2012b (MathWorks, Inc.). This method is useful when looking at the overall distributed patterns in the data, and focuses on the covariance between the images and the experimental design. A brief summary of the method can be found in Section 2.3.4 of Chapter 2.

In the present study, a mean-centering PLS method was used to make inferences about the relationship between the brain activity and creative thinking. This is a data-driven form of PLS, which results in a set of latent variables (LV) that account for the maximum covariance between the functional data and the experimental conditions (McIntosh & Lobaugh, 2004). Both high- and low-scoring participants were included in one group, with two specified conditions: Create and Trace. The significance and the reliability of the LV were determined by permutation testing and bootstrap resampling (McIntosh et al., 1996; Efron & Tibshirani, 1985). Clusters with bootstrap ratios (BSR) of ±3 were determined as reliable.

From here, the activation clusters for both Create and Trace were extracted using the multiple voxel extraction tool in PLSgui, which gave signal change values for each condition.

The values for Trace were subtracted from the Create values to get the activation difference between the conditions. Finally, Spearman's correlation coefficients were calculated for the four dimensions of schizotypy (UnEx, CogDis, IntAn, and ImpNon) to investigate the relationship between the Create - Trace activation difference and each schizotypy dimension.

5.3 Results

5.3.1 Behavioural measures

From the total sample of 35, there were 18 participants in the HS group (O-LIFE mean = 15.15; SD = 2.16), and 17 participants in the LS group (O-LIFE mean = 5.97; SD = 1.74). Three Mann-Whitney U tests were performed to calculate the differences in IQ, TTCT-V, and TTCT-F between the HS and LS groups. There was no significant difference in IQ between the HS group (median = 117.00) and the LS group (median = 122.50). There also was no significant difference in verbal creativity (measured by TTCT-V) between the groups (HS median = 117.00; LS median = 113.00). In the TTCT-F however, the HS group (median = 121.00) scored significantly higher in figural creativity compared to the LS group (median = 114.00; U = 73.00, z = -2.65, p = .007, r = -.45).

5.3.2 Mean-centered task PLS analysis

We ran a mean-centered task PLS analysis to identify the pattern of activation which optimally distinguished the Create and Trace conditions. A significant LV was produced (using 1500 permutations and 1000 bootstraps; d = 58.00, p = .001) indicating a main effect of task in the group. A pattern highlighting the brain regions distinguishing the two conditions across the group was identified, with a positive salience associated with activations greater in the Create condition compared to Trace, and a negative salience with activations greater in the Trace condition compared to Create (Figure 5.2).

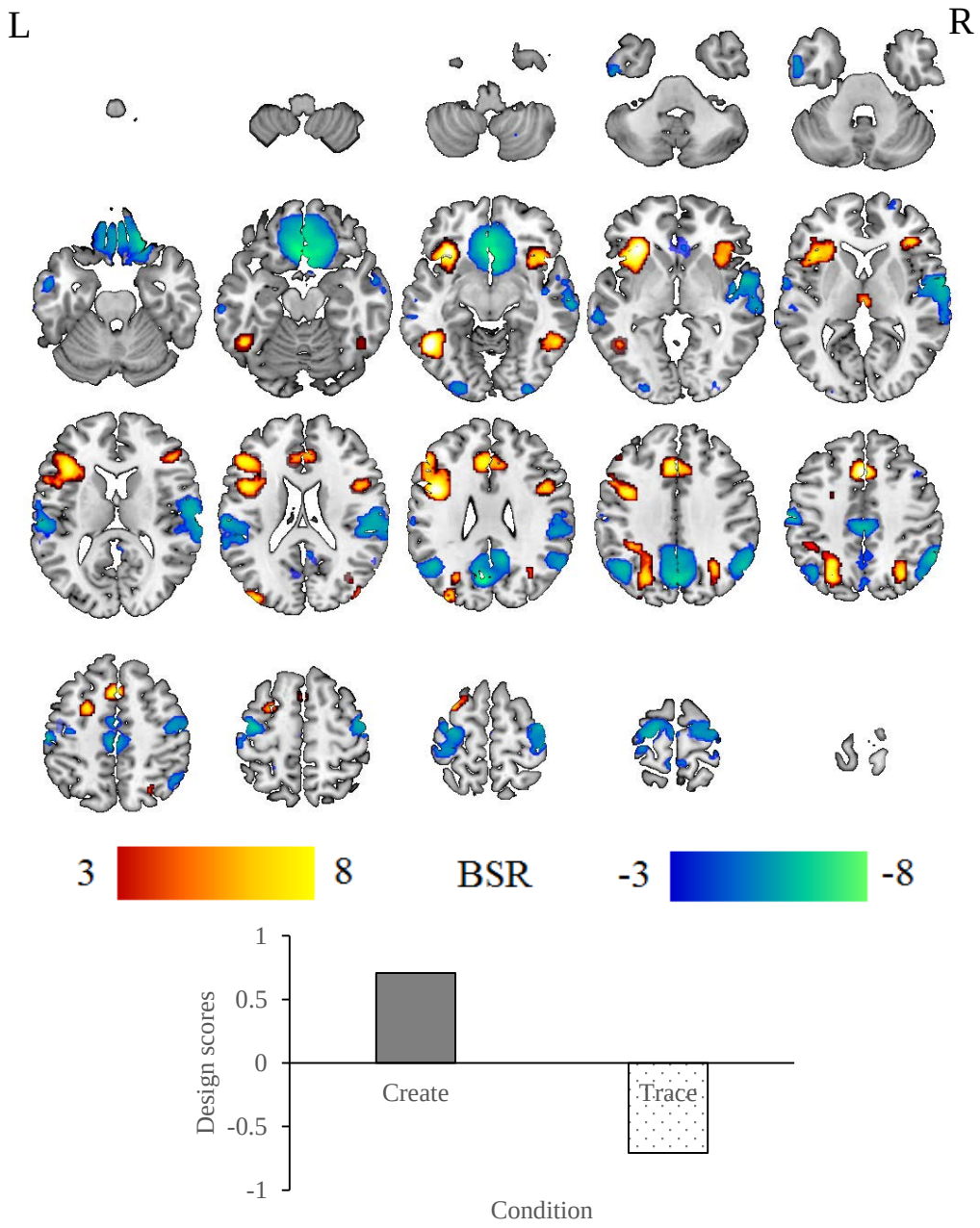

Figure 5.2 Singular image showing the areas of neural activation identified in the mean-centered PLS. Warm regions (corresponding to positive BSR scores) indicate stable activations that are greater for the Create condition than the Trace condition (Create > Trace). Cool regions (corresponding to negative BSR scores) indicate stable activations associated with the Trace > Create contrast. Colour bars indicate the strength of correlation between the condition and neural activation for each voxel (threshold of BSR = ±3). BSR; bootstrap ratio. The bar graph shows the design scores for each condition, which highlights the difference between the conditions (where design scores reflect the relationship between brain activity and the experimental design).

The Create condition elicited greater activations in the bilateral inferior temporal gyri, left insula, right angular gyrus, as well as areas in the prefrontal cortex when compared to the Trace condition, which are regions commonly linked to creative thinking (e.g., de Souza et al., 2010; Ellamil, Dobson, Beeman, & Christoff; 2012; Fink et al., 2009). The control task more strongly activated the orbitofrontal and posterior areas of the cortex, including bilateral activations of the inferior occipital gyri, left cuneus, left calcarine gyrus, and left lingual gyrus, as well as parts of the frontal, parietal, and temporal cortices compared to the Create condition. As we were particularly interested in the regions of activations related to creative thinking, only the saliences (i.e., the clusters of brain regions identified by the significant LV) associated with the Create > Trace difference will be discussed here. Co-ordinates of these regions are reported in Table 5.1.

Table 5.1

Brain regions associated with the positive salience (Create > Trace activations) in the latent variable identified by the mean-centered task PLS analysis.

	Brain region	*x*	*y*	*z*	BSR	Cluster size (*k*)
L	Insula lobe	-32	24	-6	6.89	3326
L	Superior medial frontal gyrus	-2	22	42	6.24	1217
R	IFG (p. Triangularis)	40	32	6	4.85	853
L	Inferior parietal lobule	-26	-56	40	5.53	778
L	Inferior temporal gyrus	-48	-56	-10	7.18	571
L	Middle frontal gyrus	-30	4	62	4.57	372
R	Angular gyrus	30	-66	44	5.13	367
R	IFG (p. Opercularis)	44	6	26	4.79	281
R	Inferior temporal gyrus	52	-52	-10	4.88	267
L	Thalamus	0	-18	6	4.10	156
R	Middle occipital gyrus	46	-80	18	3.55	17
R	Parahippocampal gyrus	36	-42	-8	3.22	7

Note: Clusters evident with a bootstrap ratio of greater than 3 and a minimum cluster size of 5 voxels are reported. Cluster size indicates the number of voxels in the cluster. Co-ordinates are in MNI space and were anatomically labelled using the SPM Anatomy toolbox (Eickhoff et al., 2005; http://www.fz-juelich.de/inb/inb-3//spm_anatomy_toolbox). BSR = bootstrap ratio; L = left; R = right; IFG = inferior frontal gyrus.

The voxel intensity response of each of these regions was examined for activation differences between the two conditions using intensity plots (Figure 5.3). This revealed an

overall pattern of greater recruitment of regions for the task condition (Create) compared to the control condition (Trace). However, there was a directionality difference, where some areas showed a greater task-induced activation (such as in the left middle frontal gyrus, Figure 5.3.1.A), while others displayed a reduced task-induced deactivation (e.g., left inferior parietal lobule, Figure 5.3.2.G).

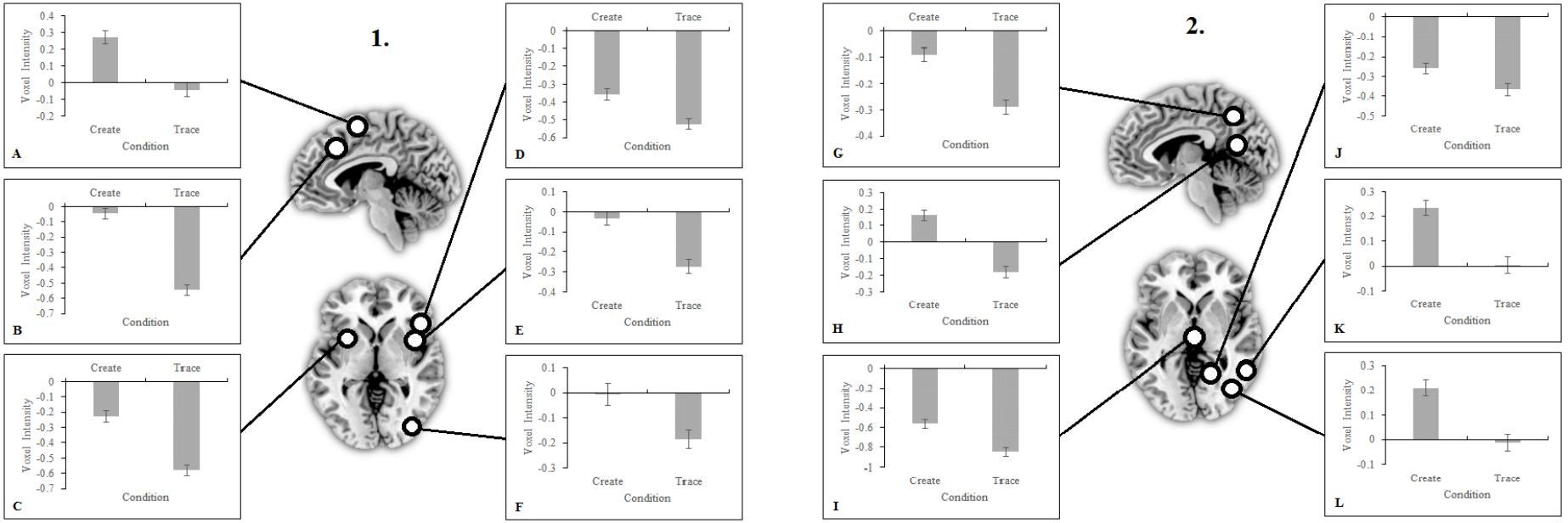

Figure 5.3 Bar graphs showing the voxel intensities of the Create and Trace conditions in regions associated with the positive salience (Create > Trace) identified by the LV. **1.** Within the frontal and occipital regions, voxel intensity differences were seen in: A) left middle frontal gyrus; B) left superior medial gyrus; C) left insula lobe; D) and E) right inferior frontal gyrus (p. Triangularis and p. Opercularis); and F) right middle occipital gyrus. **2.** Within the parietal and temporal regions, the differences were observed in: G) left inferior parietal lobule; H) left inferior temporal gyrus; I) left thalamus; J) right parahippocampal gyrus; K) right inferior temporal gyrus; and L) right angular gyrus. A positive voxel intensity value reflects task-induced activation in the region, whereas a negative value indicates task-induced deactivation. Overall, the Trace condition elicited greater deactivation of the regions compared to the Create condition. In the regions where the Trace condition displayed a level of (de)activation close to the baseline, the Create condition showed task-induced activation and engagement of these areas.

5.3.3 Correlational analyses

We performed multiple voxel extraction of the regions found to be associated with the Create condition to determine the mean signal intensity values for each condition. Peak voxels with a BSR of 3 were considered to be reliable, and the minimum cluster size was set at 5 voxels, with a minimum distance of 10mm between the cluster peaks. The difference in signal was calculated by subtracting the signal intensity for the Trace condition from the signal intensity for the Create condition in the regions of interest (ROI) for each participant. These differences were then correlated with the four dimensional scores of O-LIFE.

Significant correlations were found between three of the four dimensions (UnEx, IntAn, and ImpNon) and five ROIs. Overall, there was a consistent pattern across the dimensions and the regions. UnEx was found to be negatively correlated with the Create - Trace activation differences; that is, as the scores in UnEx increased, the difference in activations between tasks decreased. This was seen in the left superior medial frontal gyrus (r = -.399, p = .017), left middle frontal gyrus (r = -.414, p = .013), left inferior parietal lobule (r = -.373, p = .027), and the right inferior temporal gyrus (r = -.568, p < .001). These correlations are illustrated in Figure 5.4.

A similar trend was also found with ImpNon, with both the left middle frontal gyrus (r = -.372, p = .028) and the right inferior temporal gyrus (r = -.487, p = .003) being negatively correlated with this dimension (seen in Figures 5.5.B and 5.5.C). However, there was a positive association with the IntAn score and the signal difference in the right middle occipital gyrus, where there was a larger difference in signal change between Create and Trace in individuals scoring high on this dimension (r = .347, p = .041, Figure 5.5.A).

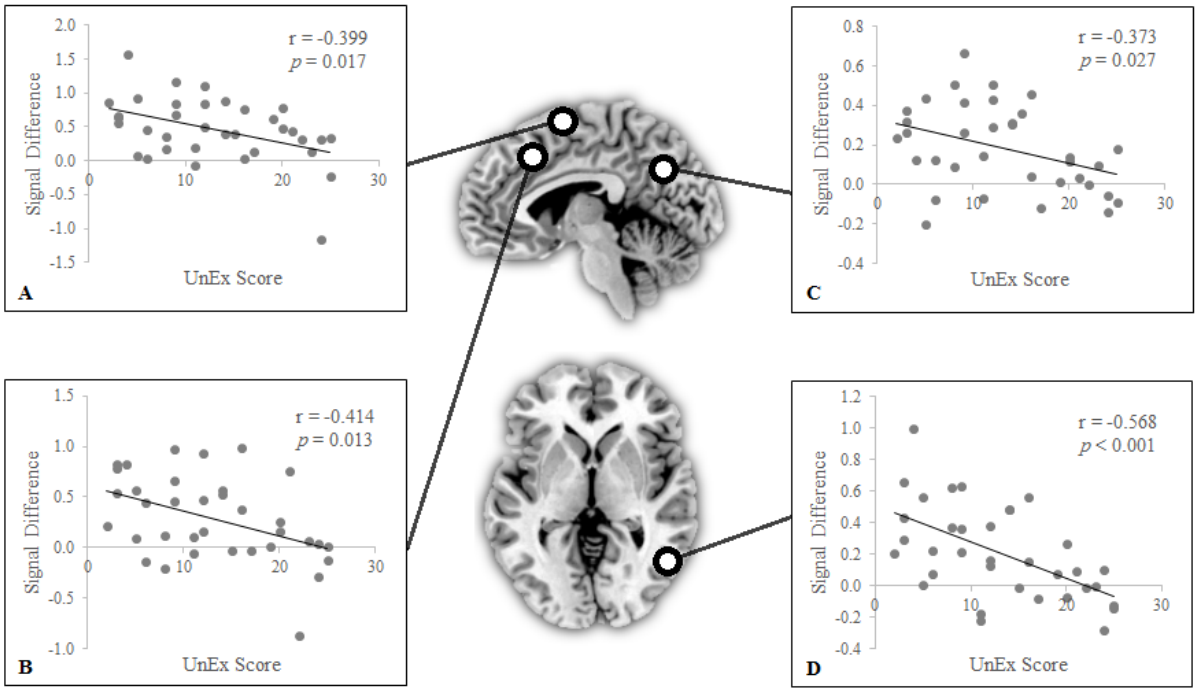

Figure 5.4 Significant correlations between the signal difference (Create – Trace; in arbitrary units) and the UnEx dimension of schizotypy in: A) left superior medial gyrus; B) left middle frontal gyrus; C) left inferior parietal lobule; and D) right inferior temporal gyrus.

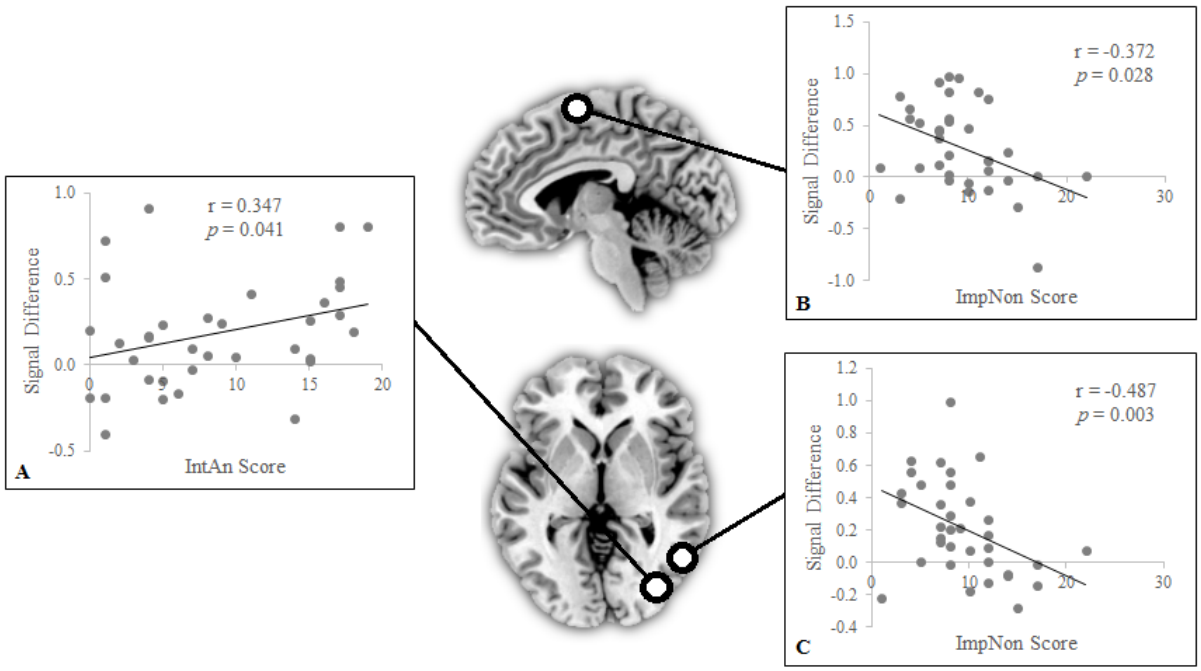

Figure 5.5 Significant correlations between the signal difference (Create – Trace; in arbitrary units) and the IntAn dimension of schizotypy in: A) right middle occipital gyrus; and the ImpNon dimension of schizotypy in B) left middle frontal gyrus; and C) right inferior temporal gyrus.

5.4 Discussion

The overall aim of the current study was to examine the link between creativity and schizotypy in a sample of nonclinical healthy young adults. Consistent with previous research, we found behavioural differences in creativity between high and low schizotypal individuals (e.g., Gibson, Folley, & Park, 2009; Nettle, 2006). We also utilised fMRI and PLS to further investigate this link; to the best of our knowledge, this is the first neuroimaging study to identify brain regions associated with creative thinking using a multivariate partial least squares method. These regions included bilateral inferior temporal gyrus, bilateral prefrontal cortex, left insular lobe, right angular gyrus, and right parahippocampal gyrus, which have all been implicated in creativity research (e.g., Goel & Vartanian, 2005; Howard-Jones, Blakemore, Samuel, Summers, & Claxton, 2005; Kowatari et al., 2009; Mashal, Faust, Hendler, & Jung-Beeman, 2007). Therefore, our fMRI findings corroborate with the slowly converging evidence of common cortical regions implicated in creative thinking.

In addition, this is the first study to correlate specific dimensions of schizotypy with the brain regions mentioned above: we found significant correlations between neural activations associated with creative thinking and three O-LIFE factors (unusual experiences, introvertive anhedonia, and impulsive nonconformity). In sum, our results add to the evidence of a link between the two constructs and support the hypothesis of a shared genetic basis for creative ability and schizotypal personality. These results will be further discussed below, with reference to the current understanding of the neural correlates of creativity.

5.4.1 Behavioural differences

Behaviourally, our results indicate that there are differences in figural creative performance between LS and HS groups, partially confirming our first hypothesis that the HS

group would display enhanced creativity as measured by the TTCT. A considerable amount of research has indicated DT to be the basis for creative production as it requires pursuing unconstrained ideas, which are influenced by fluent, original, and flexible thinking (Gibson et al., 2009; Runco & Acar, 2012). Although it is important to emphasise that DT is not the same as creative thinking, its strong concurrent validity makes it so far the best candidate to distinguish creative individuals from the less creative (Plucker, 1999).

Interestingly, in the present study, this difference was only significant in the figural form of the TTCT, suggesting that the verbal and figural tests are tapping into different aspects of creative thinking. This is further supported by the finding that these two measures only share 12.96% of their variance indicating a low association with each other (Clapham, 2004). A principal components analysis has also shown that various DT tasks load onto two separate factors, verbal and figural, rather than just one overall DT factor, suggesting that DT is a multidimensional construct (Baer, 1994; Clapham, 2004). Furthermore, the difference may be accentuated by the inclusion of "creative strengths" in the scoring of the TTCT-F, whereas the TTCT-V is assessed only on the traditional markers of DT such as fluency. Therefore, evaluating creativity may require more than a single DT test in order to fully assess creative thinking, as it may only provide a partial measure of creative aptitudes.

There was no significant IQ difference between the two groups, indicating that intelligence and creativity are two separate constructs, at least within our (educated, English-speaking) sample. This is further supported by the threshold hypothesis (Guilford, 1967), which predicts that measures of creativity and IQ are only correlated within low to average IQ populations, and not in groups with higher IQ (usually above 120; Jauk, Benedek, Dunst, & Neubauer, 2013). As both the HS and LS groups in the current study scored above 116 on average on the WASI, this could also explain the difference in creative aptitudes between the groups, but not in IQ. Although having only high-IQ individuals in our sample was a

limitation of this study, it also provided the opportunity to investigate the effect of creativity without the possible contribution of intellect.

Participants were required to have either a high or a low *global* schizotypy score (defined as the average of the four subscores in the O-LIFE) in the present study (regardless of their individual scores in each of the four factors). We used this score to ascertain whether having an overall high level of schizotypy could predict creativity, but we were also interested in which of the four dimensions were specifically related to creative thinking. Towards this end, the same group of participants were included in the fMRI analyses in order to investigate: 1) the cortical regions associated with creative thinking; and 2) the relationship between the schizotypy dimensions and the neural correlates of creativity.

5.4.2 Neural correlates of creativity

As hypothesised, we found one pattern that distinguished neural activity between the Create and Trace conditions. Overall, there was a bilateral spread of regions which correlated with greater activations for the Create condition, which encompassed the frontal, parietal, and temporal lobes. In the frontal regions, the left superior medial frontal gyrus and the right inferior frontal gyrus showed reduced task-induced deactivation, and the left middle frontal gyrus showed increased activation when engaged in the creative task compared to the control task.

These findings are in line with earlier creativity research, showing that the prefrontal cortex (PFC) is critically involved in DT which, in turn, is thought to be required for creative output (Heilman, Nadeau, & Beversdorf, 2003). As part of the executive network, PFC has been implicated in higher cognitive functions such as planning and problem solving, and numerous studies have shown that this region may be critical for cognitive flexibility (defined as the ability to disengage and switch to new solutions mid-task; Heilman et al., 2003;

Milner, 1984; Smith & Jonides, 1999). Bilateral PFC activation has also been found previously, which suggests that creativity is correlated with the interaction of the left and right PFC, rather than just one specific hemisphere (Kowatari et al., 2009).

Additionally, the left dorsolateral PFC (DLPFC) has been associated with visuospatial creativity (Aziz-Zadeh, Liew, & Dandekar, 2013), which is consistent with our finding of cortical activation in the left middle frontal gyrus. DLPFC is thought to play a role in the top-down organisation of creative cognition by being involved in the generation of complex ideas, goal-directed visual search, problem solving, and attentional control (Hampshire & Owen, 2006; Israel, Seibert, Black, & Brewer, 2010). Such involvement can be observed through studies that have investigated atypical DLPFC functioning. For example, Jahanshahi et al. (1998) showed that the disruption of the left DLPFC (using transcranial magnetic stimulation) resulted in the participants giving more stereotypical and unoriginal answers in their task, and patients with DLPFC damage also display strong perseveration to old information and a lack of cognitive flexibility. This further supports the role of this region in creative thinking (Dietrich, 2004).

Moreover, a study by de Manzano and Ullén (2012) found the DLPFC region to be involved in two different types of free generation tasks (Improvisation versus Pseudo-Random), where the participants were asked to either improvise or press keys at random on a keyboard. Although the PFC regions, including the DLPFC, were activated for both Improvisation and Pseudo-Random conditions when compared to the control task, there were no differences between the two experimental conditions, leading the authors to conclude that these regions are both utilised in free idea generation processes, regardless of the overall goal. This partly ties in with the process of mind wandering, which arises from internally focused thinking that is stimulus-independent, and has been implicated in the generation of creative solutions (Baird et al., 2012). Although it has mostly been associated with the default mode

network (DMN; Mason et al., 2007; McKiernan, D'Angelo, Kaufman, & Binder, 2006), Christoff, Gordon, Smallwood, Smith, and Schooler (2009) found that their mind wandering task recruited additional executive regions such as the DLPFC as well as the DMN. They postulated that the mind wandering process may prompt the co-operation of the executive *and* default mode networks, which have traditionally been thought to work in opposition, as the DMN represents a cluster of brain regions that are activated in the absence of external task demands (Raichle & Snyder, 2007). This co-activation of networks has also been found in a creative idea evaluation study, where specific regions in the networks showed positive functional connectivity during the task (Ellamil et al., 2012). As most of our regions show greater activation/smaller deactivation for the Create task relative to the control task, this suggests that the contribution of the DLPFC (and some regions of the PFC) may lead to greater flexibility in problem-solving and thought production, ultimately resulting in creative ideation. Our finding of cortical involvement of these key areas, therefore, strengthens the evidence of the role of the PFC in creative performance.

We also found significant task-induced correlations in the parietal and temporal lobes (areas responsible for the integration of multimodal sensory information). These regions are heavily interconnected with the frontal lobe, and it has been hypothesised that these connections are important for inhibiting familiar information and activating weak conceptual networks, leading to the development of novel ideas and solutions (Heilman et al., 2003; Villarreal et al., 2013). Studies show considerable involvement of these areas in various creativity tasks, with the temporal regions showing increased activation and the parietal regions showing reduced activation, or lower brain activity, compared to control tasks (e.g., Fink et al., 2009; Howard-Jones et al., 2005; Kowatari et al., 2009).

Again, we found both increased activation and reduced deactivation of these areas, similar to the prefrontal regions. Although the increase in activation in the bilateral inferior

temporal gyri is in agreement with earlier work, the parietal regions (in particular the left parietal lobule and the right parahippocampal gyrus) displayed decreased *de*activation (rather than activation), which was a surprising finding. More specifically, the creative task elicited reduced deactivation of these areas when compared to the control task, indicating a greater task-induced engagement of the regions regardless of the overall pattern of deactivation. As part of the DMN, this observation in the parietal lobule may be related to the concept of hyperconnectivity of the default network, which has been observed in schizophrenia patients and their relatives when performing a working memory task (Whitfield-Gabrieli et al., 2009). This suggests that the DMN is engaged for certain individuals even when they are performing a task, which again ties in with the idea that this network may work in conjunction with the executive network resulting in the linkage of unrelated ideas. This idea is further supported by Takeuchi et al. (2011)'s finding of a task-induced reduced deactivation in the precuneus (another region within the DMN) in a working memory task. When this was correlated with a behavioural measure of creativity, the results showed that a greater reduction of deactivation was associated with higher levels of creativity. Therefore, it may be that creative individuals are unable to suppress task-unrelated cognitive activity arising from the DMN which, when combined with the activations from the PFC regions, may lead to the association of two disparate ideas which are usually isolated.

Interestingly, reduced deactivation was also found in the insula lobe. As part of the salience network, bilateral insulae are thought to exert influence on the executive system via connections to the PFC (Ham, Leff, de Boissezon, Joffe, & Sharp, 2013). In particular, the anterior insula is considered to play a major role in the detection of salient stimuli, and facilitate in the processing of task-related information leading to the engagement of the executive network (Menon & Uddin, 2010; Sterzer & Kleinschmidt, 2010). Thus, this relationship between the salience and executive networks may explain the involvement of the

insula when performing a creative task. This is supported by a study by Villarreal and colleagues (2013), who found a positive correlation between the right insular activation and creativity level in a sample of musicians, leading them to conclude that this involvement reflects its capacity to integrate information and engage creative networks. Therefore, our finding in the current study further contributes to the understanding of extensive bilateral insular-PFC interactions, which trigger original and creative thinking.

Finally, we also found smaller deactivations for the Create task in regions associated with visuospatial processing and mental imagery, including the left inferior parietal lobule and the right middle occipital gyrus (Howard-Jones et al., 2005; Kosslyn, Ganis, & Thompson, 2001). These areas have been implicated in mental rotation tasks (Ng et al., 2001) and creative task evaluation (Ellamil et al., 2012), and may therefore correspond to our experimental paradigm, which required the participants to visually imagine and draw pictures.

In summary, the regions which were correlated with creative performance were mostly consistent with areas reported in the creativity literature. This included bilateral activation across the PFC, the temporal and parietal areas, as well as the left insula. In addition, both increased activation and reduced deactivation of these areas were observed, which was spread across three different neurocognitive networks. Such diversity of regions has led to a debate as to whether any conclusions can be made from creativity studies, with Arden, Chavez, Graziopene, and Jung (2010, p. 150) claiming that such results are "at present, uninterpretable" in their review of fMRI studies of creativity. However, the very nature of creativity and its complexity may be the reason behind such variability in neural regions within and across studies. More recently, there seems to be slow convergence of common neural areas associated with creative thinking (e.g., Vartanian, 2012). Although these common areas are still widespread across the brain and specific to the type of creative

task, it could be that creative production may be the result of collaboration between the networks, where the parieto-temporal regions initially integrate sensory information to interact with the salience network, initiating cognitive control. This would instigate the engagement of the executive network, which is responsible for frontal lobe mediated DT. This, in combination with task-unrelated ideas generated by the DMN and the inability to suppress these ideas, could lead to creative innovation which may only be possible with widespread cortical engagement.

Another interesting consequence of this decreased ability to suppress task-unrelated thoughts is the formation of creative associations that are not only novel but also bizarre (Carson et al., 2003). Such links are often seen in individuals who are on the schizophrenia spectrum, and creative behaviour has been consistently linked to individuals with high levels of schizotypy. Therefore, to answer our main question of a possible link between creativity and schizotypy, we examined the potential correlations between the neural regions found above and the schizotypy dimension scores.

5.4.3 Creativity and schizotypy

The activation differences between the two conditions (Create and Trace) were calculated from the regions identified in Section 5.4.2 for each individual and were correlated with their schizotypy dimension scores from the O-LIFE. The analyses revealed an interesting trend between the UnEx factor and creative behaviour, where UnEx was found to be correlated with four of the regions implicated in creative thinking. In addition, two of these regions were further correlated with the ImpNon factor. These correlations were all negative, indicating that individuals who scored the highest in these factors displayed the smallest activation difference between the Create and Trace conditions. The only significant positive correlation found was between IntAn, a negative factor, and the right middle

occipital gyrus. These results are in line with the idea that ‘less is more’ for creativity, which suggests that the deactivation of specific cortical areas may facilitate creative thinking (Jung et al., 2010).

As hypothesised, we found UnEx to be the dimension most strongly associated with the ROIs. This dimension includes perceptual aberrations, hallucinations, and magical ideation observed in healthy individuals to a varying degree, which is somewhat analogous to the positive symptoms of schizophrenia (Mason & Claridge, 2006). Scoring high on this dimension may result in a more overinclusive thinking style resulting in various behavioural manifestations that range from typical daydreaming to hallucinations; in fact, approximately 10% of the nonclinical population have been reported to experience at least one vivid, non-drug induced hallucinatory event (Verdoux & van Os, 2002). These anomalous experiences are thought to be due to cognitive disinhibition, possibly underpinned by weak sensory and cognitive gating leading to a flooding of ideas. Indeed, empirical studies have consistently shown a link between positive schizotypy and creative behaviour (Nettle, 2006; Schuldberg, 2001). Neurocognitively, such disinhibition may be explained by the deactivation and/or decreased activation of specific cortical areas, resulting in the release of inhibitory control these areas may have on other regions (Flaherty, 2005; Radel, Davranche, Fournier, & Dietrich, 2015).

In line with this, in a study of jazz musical improvisation, the authors found a widespread deactivation of the lateral prefrontal cortices, including in the DLPFC, when the participants were completing the improvising task compared to the control scale task (Limb & Braun, 2008). This presents a different hypothesis regarding the role of the DLPFC than that discussed earlier where, even though it is still involved in creative thinking, it could be the disengagement of this area of the executive network that leads to a more free-floating and defocused attention allowing for creative insights and original ideas. Although Limb and

Braun's (2008) study did not examine the personality characteristics of the participants, it could be that this neural deactivation could also lead to thought aberrations, which may manifest as UnEx-like traits. Therefore, our findings of lower activation in the prefrontal regions in those with high UnEx scores further provide evidence for a common neural basis for creativity and schizotypy.

More specifically, within the positive salience/pattern identified by our mean-centered PLS analysis, this negative correlation between activity in the prefrontal regions and UnEx was only found in the left superior medial and middle frontal gyri. Interestingly, this pattern of decreased engagement (where those with highest UnEx scores displayed the smallest activation difference between the two conditions) was not observed in the right inferior frontal gyrus. Although these results do not agree with other studies which have demonstrated increased bilateral PFC activity during creative tasks (e.g., Folley & Park, 2005; Howard-Jones et al., 2005), it could be that this difference stems from the type of creativity examined, as these findings mostly come from verbal experimental designs. This is supported by lesion studies which have reported increased levels of figural creativity in patients with left brain lesions (Mendez, 2004), and suppressive deep brain stimulation of the left hemisphere in Parkinson's disease patients have also shown elevated artistic production (Drago, Foster, Skidmore, & Heilman, 2009). Therefore, in view of the importance of PFC in creative behaviour, it could be that functional enhancement of the right hemispheric frontal regions may result in figural creativity when coupled with a corresponding disengagement of the left PFC.

However, this gives rise to the question of: why is there greater extent of engagement of the left frontal regions overall when the O-LIFE scores are not taken into account? Even though these regions are necessary for creative thinking, it may be that those who are able to translate creative thoughts into useful ideas paradoxically require less activity from the left

PFC areas. Therefore, across all participants, the regions involved in creative thinking are recruited: however, more creative individuals may actually need less of this recruitment. This may also be related with the concept of 'neural efficiency' (Haier et al., 1988), where lower cortical activation is observed in brighter individuals when engaged in a demanding cognitive task, compared to less intelligent individuals (Neubauer & Fink, 2009). Relating this back to the role of the left hemispheric inhibitory control, it could be that the disinhibition of such supervisory regulation could result in the release of more holistic functions and ideas mediated by the right prefrontal regions. Another consequence of this could be the emergence of positive schizotypal traits, which include paranormal and magical beliefs (Nelson & Rawlings, 2010). This difference may also explain our behavioural finding of higher TTCT-F scores in those with increased schizotypal traits.

Nonetheless, some frontally mediated control is necessary to harness these ideas appropriately, which could be why we observed increased activations/decreased deactivations in general for the Create condition compared to the control task. Indeed, research into schizotypal personality disorder (SPD; a clinically diagnosed disorder seen as an attenuated form of schizophrenia; Siever et al., 2002) has demonstrated that individuals with a diagnosis of SPD show greater abnormalities in frontal lobe activation than nonclinical schizotypal individuals, which behaviourally manifest as prefrontal impairments on tests assessing frontal executive function (Bergman et al., 1998; Diforio, Walker, & Kestler, 2000). Therefore, some degree of inhibitory control is still required for creative output to be coherent and useful, rather than nonsensical.

Similar to the left prefrontal regions, a negative correlation was found between UnEx scores and the left inferior parietal lobule. As mentioned previously, this association between the parietal lobule and creativity is in agreement with several findings of decreased parietal activity during creative cognition (e.g., Berkowitz & Ansari, 2010). Although this region

showed reduced deactivation across all participants when engaged in the creative task, surprisingly those with high levels of UnEx displayed the smallest difference between the two conditions. This is in contrast to the hypothesis of an increased engagement of the DMN during a cognitive task in creative individuals, which may lead to abstract thinking. However, research has shown that this region is frequently affected in schizophrenia and other related disorders, with structural studies showing reductions in grey matter volume overall including in the parietal regions (e.g., Buchanan et al., 2004; Kawasaki et al., 2004). Although no research has yet determined a direct link between parietal volume reduction and schizotypy, a spectrum pattern has been found between schizophrenia and schizotypal personality disorder where more widespread reduction of parietal gray matter is observed for schizophrenia patients compared to SPD (Zhou et al., 2007), which may possibly extend to nonclinical schizotypal individuals. Therefore, this may have contributed to the finding of decreased activation in the present study, although more research is needed to elucidate this possible structure-function relationship in schizotypy.

Another region frequently found to be atypical within the schizophrenia spectrum is the temporal lobe (e.g., Cobia, Smith, Wang, & Csernansky, 2012; Zipursky et al., 1994). We also found significant correlations between the right inferior temporal gyrus and both UnEx and ImpNon. Impulsive nonconformity is a dimension related to Eysenck's Psychoticism scale and measures impulsive-driven and disinhibited behaviour (Eysenck et al., 1985; Mason & Claridge, 2006). High-scoring individuals often display hypomanic traits, which have been linked to self-rated creativity (Furnham, Batey, Anand, & Manfield, 2008). This dimension may encourage creative output by lowering the threshold for unusual or strange ideas through disinbihition which, when coupled with their propensity for impulsive and reckless behaviour, may lead to more atypical or creative responses. Hughes, Furnham, and Batey (2013) found that individuals who rate themselves as being visually creative also rated highly

on impulsivity, and Burch et al. (2006) also found a higher level of ImpNon in visual artists when compared to non-artists, suggesting that this dimension is also important for creative output. Other studies have often found the involvement of both UnEx and ImpNon in creative thinking, albeit UnEx (or an equivalent positive dimension) being the most important factor in predicting creative behaviour (e.g., Nelson & Rawlings, 2010; O'Reilly et al., 2001). Burch and colleagues (2006) have suggested that scoring highly in psychometrically measured creativity tests could be due to two independent processes: formation of unique ideas; and being able to express an idea which may be deemed as unusual or inappropriate. However, our finding of common brain regions associated with both UnEx and ImpNon suggest that these factors work together, rather than independently, to produce overall creative output. This is also in line with the finding that these two dimensions often co-exist within a highly schizotypal individual (e.g., Batey & Furnham, 2008).

Lastly, a positive correlation was observed between the right middle occipital gyrus and IntAn, which is a negative factor measuring the inability to derive pleasure from social and physical interactions (Mason et al., 1995). Although this was unexpected finding, the direction of the correlation further support the multidimensional nature of schizotypy, where negative and positive factors tap into different aspects of the construct (Vollema & van den Bosch, 1995). Furthermore, some studies have shown a relationship between autistic-like traits and negative schizotypal traits indicating an overlap between the two (Hurst, Mitchell, Kimbrel, Kwapil, & Nelson-Gray, 2007; Rawlings & Locarnini, 2008), and this possible commonality is reflected in the O-LIFE questions measuring IntAn such as "do you like mixing with people?" and "have you often felt uncomfortable when your friends touch you?" (Mason & Claridge, 2006, p.210). Autism research has shown autistic-like qualities to be associated with increased attention to detail and heightened low-level visual and auditory sensory processing (Baron-Cohen, Ashwin, Ashwin, Tavassoli, & Chakrabarti, 2009).

Therefore, it is possible that these negative schizotypal and autistic-like traits share common processes, which could explain the increased level of activation in a primary sensory region in individuals with high IntAn scores.

To summarise thus far, these results support findings from earlier behavioural studies that indicate that positive schizotypy is the main contributor to creative thinking (e.g., Nettle, 2006). Being able to make loose associations may be the most essential factor in the generation of creative ideas, which may also manifest as positive schizotypal traits such as unusual perceptual experiences and paranormal beliefs. The neural regions found to be correlated with both creativity and UnEx included the left prefrontal areas, which is partly in line with Folley and Park's (2005) result of bilateral PFC involvement during DT in schizotypal individuals. Furthermore, two of the regions found to be associated with UnEx were further correlated with ImpNon, highlighting the possibility that these dimensions work in conjunction for maximum creative output. A surprising finding was the involvement of IntAn, a negative dimension, which may be related a deeper sensory processing mechanism consistent with withdrawn and introvertive personality traits. Altogether, our results further add to the very limited neuroimaging evidence of a relationship between schizotypal personality and creativity.

5.5 Limitations and future directions

The main limitations of the current study were related to handedness and gender. The recruited participants in the study were required to be right-handed, which was to limit any motor and laterality differences between the individuals during the drawing task. Considering the findings of greater ambidexterity and reduced lateralisation in psychopathology (Barnett & Corballis, 2002; Hirnstein & Hugdahl, 2014; Sommer et al., 2001), as well as increased

mixed-handedness in schizotypy (Jones et al., 2011), it could be that we omitted potential participants by excluding those who may have been the most appropriate to consider.

Furthermore, our study population was biased towards females, especially amongst the high schizotypy scoring participants. This bias is also observed across the general population, with females often scoring higher on the schizotypal spectrum compared to males, especially in the positive dimension (Badcock & Dragović, 2006; Bora & Baysan Arabaci, 2009). Therefore, having a high number of females in the study sample could have affected our main finding of an association between UnEx and creative thinking. However, it is unlikely that this result is solely due to gender effects as other studies have found similar associations between the two; nonetheless, this relationship should be explored further using a gender-balanced sample.

Another interesting question for future research is whether there are functional connectivity differences between high and low schizotypal individuals when engaged in creative thought. It seems likely that thinking creatively utilises multiple networks, and therefore using both functional and structural connectivity measures within the same sample of participants to examine this process could untangle the possible (dis)inhibitory influences between these networks and regions (e.g., Takeuchi et al., 2010).

5.6 Conclusions

Behavioural studies have shown robust associations between creativity and mild manifestations of subclinical psychopathology, such as schizotypy. Therefore the aim of the current study was to examine this relationship from a neuroimaging perspective, and to investigate possible associations between the different dimensions of schizotypy and neural correlates of creativity. By using a figural-based task which allowed the participants to draw in the scanner, we were able to characterise cortical areas pertinent to figural creativity which

has not been explored to the extent of verbal creativity. In addition, we utilised a multivariate analysis method, which allowed us to identify the best fitting pattern of neural activity associated with creativity. We also used correlational methods to investigate the relationship between schizotypy and creativity; by using a continuous measure rather than a high-low schizotypy dichotomy, we sought to increase the power to detect possible effects.

When the behavioural and fMRI results are taken together, they support the idea of a relationship between creativity and schizotypy. In particular, the regions found to be related to creative thinking were consistent with previous studies. However, there were also differences between this study and others examining the correlates of creativity, where the direction and magnitude of activations differed within the same regions across studies. Possible reasons for this may be due to the interpretation of the results depending on the method used (univariate versus multivariate) as well as the study design (continuous versus group). However, the biggest contributing reason is likely to be due to the fact that creativity itself is a complex construct that includes domains that may not necessarily be related (i.e., figural versus verbal creativity, artistic versus scientific creativity). Therefore, further research is needed to clarify the associations between these different domains and schizotypy, taking into account the multidimensionality of schizotypal personality. Nonetheless, the findings contribute to the growing evidence of a common neural basis between the two constructs, and may provide the motivation for future studies which could further illuminate our understanding of the complex nature of this relationship.

Chapter 6: Grey matter differences in schizotypy[4]

Abstract:

Earlier neuroimaging research into the brain structure of schizophrenia patients has shown consistent reductions in grey matter volume relative to healthy controls. Therefore, examining potential structural differences in individuals with high schizotypy may help elucidate the course of disorder progression and provide further support for the schizotypy-schizophrenia continuum. Thus far, schizotypy research investigating grey matter differences has been lacking and the findings have been inconsistent. Authors have reported both positive and negative associations between grey matter volume/cortical thickness and schizotypal personality. Therefore, the aim of the present study was to use a multivariate partial least squares approach to examine and clarify the relationship between psychometric schizotypy (measured by the O-LIFE) and grey matter volume in 35 healthy individuals. We found a significant association between high levels of schizotypy and reduced grey matter volume mainly in the frontal and temporal regions. Further analyses revealed that Unusual Experiences (UnEx; a positive dimension in the O-LIFE) was strongly correlated with reductions in the superior temporal gyrus, and the inferior and middle frontal gyri, which are all regions commonly found to be affected in paranoid schizophrenia (a positive clinical counterpart to UnEx). This indicates that there may be symptom-specific, structure-function abnormalities within the spectrum. These findings add to the evidence that healthy schizotypal individuals exhibit structural changes in regions associated with schizophrenia. Findings could also help to establish possible biological endophenotypes for the disorder.

Keywords: Schizotypy; Grey matter; MRI; Schizophrenia; Structural PLS; Neuroanatomy

[4] Material from this chapter has been submitted for publication:
Park, H.R.P., Wiebels, K., & Waldie, K.E. Grey matter differences in schizotypy using a multivariate partial least squares method. Submitted to *NeuroImage.*

6.1 Introduction

Schizophrenia is psychiatric disorder characterised by disturbances in cognition such as memory deficits, hallucinations, bizarre beliefs and behaviours, and impaired executive function (e.g., Danion, Rizzo, & Bruant, 1999; Engh et al., 2010; Hoffman, Rapaport, Mazure, & Quinlan, 1999; for a review, see Barch & Ceaser, 2012). Such behavioural symptoms may be broadly categorised into three factors: positive, which includes delusional thoughts and unusual perceptual experiences; negative, which describes social and physical anhedonia and introversion; and disorganised, which may lead to decreased sensory-motor functions and inappropriate affect (Basso, Nasrallah, Olson, & Bornstein, 1998; Cuesta, Ugarte, Coicoa, Eraso, & Peralta, 2007). More recently, studies have shown that these symptoms may partly be linked to subtle differences in brain structure observed in patients when compared to neurotypical individuals (Chua & McKenna, 1995; Gaser, Nenadic, Volz, Büchel, & Sauer, 2004; Salgado-Pineda et al., 2011). These abnormalities include reduced grey matter (GM) volume (Asami et al., 2012; Wright et al., 1999), atypical white matter integrity and connectivity (Agartz, Andersson, & Skare, 2001; Koch et al., 2013; Lee et al., 2013), as well as ventricular enlargement and cerebrospinal fluid differences (Chua et al., 2007; Coughlin et al., 2013; Sayo, Jennings, & Van Horn, 2012).

In particular, a large amount of research has indicated GM volume reductions in both first-episode and chronic schizophrenia patients (e.g., Kubicki et al., 2002; Olabi et al., 2011; Wright et al., 1999). Although there is substantial variability regarding which specific cortical areas contribute to reduced GM across empirical studies (stemming mainly from different methodologies and patient samples), recent meta-analyses and reviews have indicated a converging pattern of GM loss in frontal and temporal areas (e.g., Gupta et al., 2014). A meta-review by Shepherd, Laurens, Matheson, Carr, and Green (2012) found some overlap of regions across 32 reviews, with consistent decreases observed in frontal lobe gyri and

cingulate cortex, insula, thalamus, postcentral gyrus, and medial temporal areas, while a meta-analysis involving over 18000 subjects also found decreased intracranial and total brain volume in patients compared to healthy participants, with largest effect sizes seen for grey matter structures (Haijma et al., 2013).

Moreover, there seems to be a relationship between the degree of GM structural abnormality and illness duration, with chronic patients mostly showing a more widespread and severe pattern of reductions compared to first-episode patients (Whitford et al., 2006; for a review, see Hulshoff Pol & Kahn, 2008). However, this association is not strictly linear due to the confounding effects of pharmacological treatment, where it has been suggested that antipsychotic medication may have either attenuating (van Haren et al., 2007) or exacerbating (Ho et al., 2011) effects that contribute to GM reductions within schizophrenia patients.

Interestingly, such volumetric differences have also been found in healthy individuals with schizotypal personality, who display nonclinical traits that are similar to schizophrenia symptoms in the absence of psychosis (e.g., Chan, Di, McAlonan, & Gong, 2011; Lawrie et al., 2001). This suggests that these cortical abnormalities exist on a dimensional continuum across the schizophrenia spectrum, and may already be present prior to the onset of psychopathology (Ettinger et al., 2012). Although these psychologically healthy individuals present an opportunity to investigate the aetiology of schizophrenia and other related disorders, there is currently only a small number of studies examining the neuroanatomical correlates of the schizotypy (Nelson et al., 2013).

Schizotypy is characterised by a cluster of personality traits that are continually distributed within the general population, with psychosis and clinical illness at the extreme end (Claridge, 1997). It can be measured by using self-reported psychometric tests such as the Schizotypal Personality Questionnaire (SPQ; Raine, 1991) and the Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE; Mason et al., 1995), and is generally

organised into a three- or four-factor structure (positive, negative, disorganised, and impulsive), similar to schizophrenia (Ettinger, Meyhöfer, Steffens, Wagner, & Koutsouleris, 2014). A large number of behavioural, electrophysiological, and functional studies have examined the role of schizotypy in cognition, perception, and motor control, with the majority finding subtle, yet significant, deficits in individuals with high levels of schizotypy compared to those who score low on the measures (e.g., Aichert et al., 2012; Kumari et al., 2008; for a review, see Ettinger et al., 2014).

Neuroanatomical evidence also suggests structural differences in psychometric schizotypy; however, only a few empirical studies have investigated this relationship. An early study by Raine, Sheard, Reynolds, & Lencz (1992) used manual tracing methods to measure brain volumes in 17 healthy subjects, and also calculated both left and right prefrontal-temporal ratios, which was to control for any temporal lobe deficits contributing to prefrontal differences. They found negative correlations between high schizotypy scores and left prefrontal structures, as well as with the bilateral prefrontal-temporal ratios, leading the authors to suggest that schizotypal personality is associated with structural deficits that are already evident in nonclinical populations.

More recent studies have also indicated a decrease in regional GM volume in the frontal and temporal lobes of highly schizotypal individuals, including reductions in medial prefrontal, orbitofrontal, and temporal cortical regions (DeRosse et al., 2015; Ettinger et al., 2012). Furthermore, developments in neuroimaging have allowed researchers to determine cortical thickness measurements, with one study showing an association between high schizotypy and lower grey matter thickness in the temporal lobe (DeRosse et al., 2015). However, although these results are in line with the structural schizophrenia literature, other studies have reported mixed findings, both in brain volume and cortical thickness.

Kühn, Schubert, and Gallinat (2012) found that high schizotypy scores were associated with *increased* thickness in the right dorsolateral prefrontal cortex (DLPFC) and the right dorsal premotor cortex, and *reduced* volume in the thalamus. In addition, when they examined the positive and negative factors of schizotypy separately, they further found positive correlations between the right DLPFC and positive schizotypy, and also between the right temporo-parietal junction and negative schizotypy. Similarly, Wang et al. (2014a) also reported mixed results including reduced GM density in the left insula and the left DLPFC, but enhanced density in the right posterior medial temporal gyrus and the left cerebellum. In contrast, Modinos and colleagues (2010) only found *larger* global GM volumes in individuals with high positive schizotypy compared to those with low positive schizotypy, with regional differences also seen in the medial posterior cingulate cortex and the precuneus, where high schizotypy individuals again had greater regional volumes compared to those with low schizotypy. These increases in volume and cortical thickness have been explained in terms of a compensatory process of greater cortical recruitment, which may explain why those with high levels of schizotypy do not suffer from psychotic symptoms that define schizophrenia (Modinos et al., 2010). More specifically, Kühn et al. (2012) posited that the increased cortical thickness may be part of a protective mechanism for the observed reduced thalamus volume, preventing the possible onset of schizophrenia in these individuals.

Despite the variability of the results, there are two significant similarities within the literature; namely, the general cortical regions implicated in schizotypy (mainly frontal and temporal, which overlap those found in schizophrenia), and the overall finding of a difference (regardless of directionality) in GM structures between high and low schizotypal individuals. The specific disparities between studies may be due to the different methodology and recruitment of schizotypal individuals, which, in turn, could be attributed to the heterogeneity of the construct. An important consideration is the dimensional nature of schizotypy, which

usually consists of three or four factors. Psychometric measures of schizotypy take this into account by including a variety of questions from the different dimensions, and many studies use a composite score of positive, negative, and disorganised scales to define their schizotypy sample, while others only use a dimensional score (usually positive). This distinction is particularly important when generalising the overall results in terms of structural abnormalities in schizotypal individuals, as those with only high positive schizotypal traits may be tapping into a separate aspect of the construct, rather than schizotypy as a whole. Studies which have used a total schizotypy score all found reductions in GM volume (e.g., DeRosse et al., 2015; Raine et al., 1992; Wang et al., 2014a), including Kühn et al. (2012)'s study which reported reduced thalamus volume (despite increases in cortical thickness). However, when only the positive schizotypy factor is taken as the measure of schizotypal personality, positive correlations between GM structures and the schizotypy score are observed (e.g., Kühn et al., 2012; Modinos et al., 2010), with the exception of Ettinger et al. (2012) who found a negative association. Furthermore, the dimensionality of the construct may also have an effect in which particular regions are affected (within the frontal and temporal areas), as slight discrepancies are observed when studies that use an overall measure of schizotypy are compared to those which focus solely on positive schizotypy. This is also in line with schizophrenia research, as positive symptoms have been associated with specific structural changes in language and auditory perception regions, which may behaviourally manifest as hallucinations and atypical perceptual processes (Hirayasu et al., 1998; Steinmann, Leicht, & Mulert, 2014).

Therefore, the main objective of this study was to clarify the effect of nonclinical schizotypy on GM structure in young healthy individuals, and to further contribute to the evidence for a continuous relationship regarding brain structures in schizotypy and schizophrenia. The sample for the current study consisted of the 35 individuals from previous

chapters with a total O-LIFE score of half a standard deviation either above or below the mean, as we wanted to investigate possible structure changes in those who have already shown some functional differences as observed in Chapters 3 and 5.

Additionally, we utilised a multivariate method to identify the regions of GM correlated with the dimensional scores, which is a novel approach to examining structural differences in schizotypy. Thus far, one of the most widely used method to analyse structural data is voxel-based morphometry (VBM), which is based on a voxel-wise comparison of local tissue volume (Ashburner & Friston, 2000). Although it is a well-validated technique that is employed across a multitude of neuroimaging topics (e.g., schizophrenia, Honea et al., 2005; temporal lobe epilepsy, Keller & Roberts, 2008), it uses the general linear model framework to statistically compare the spatially processed images via parametric procedures (e.g., *t*-tests and ANOVAs). Aside from the assumptions that have to be met (e.g., normality and multicollinearity), massive-univariate tests (such as between all voxels in the brain) increase the probability of false positive findings and therefore require multiple comparison corrections that further decrease statistical power (Monti, 2011). Therefore, it has been suggested that a multivariate, non-parametric approach may be more appropriate when assessing patterns of information (rather than localised differences), such as changes in global tissue volume (Monti, 2011; Thirion et al., 2007).

Taking this into account, we decided to use a partial least squares (PLS) correlational method to identify potential GM changes in our participants. We entered all four dimensions of the O-LIFE into a behaviour PLS analysis to observe whether the four factors show any significant associations with GM differences. We expected to find a pattern of frontal and temporal regions that correlated with the factors, with some factors contributing more to the regional differences than others. We further hypothesised that the four factors would be associated with GM volume *reductions*, in line with the majority of schizotypy and

schizophrenia research. From here, we identified six key structures that have been consistently reported to be affected in schizophrenia and schizotypy, and extracted volume clusters in order to correlate the GM volume with each of the O-LIFE dimensional scores. Given the dimensional relationship between schizotypy and schizophrenia, and previous findings of positive symptoms playing a key role in structural changes in schizophrenia, we predicted that unusual experiences (UnEx; a positive factor) would be the strongest contributing factor to the cortical differences observed in high schizotypy.

6.2 Materials and methods

This chapter reports analysis of the structural data collected with the functional images analysed in the previous MRI chapters. Therefore participant information and image acquisition parameters are summarised in brief here.

6.2.1 Participants

A total of 35 participants (mean age = 23.26 years; SD = 4.88; 11 males) were included in the current study. Their level of schizotypy was measured using the O-LIFE (Mason et al., 1995), and the dimension scores from the four factors (UnEx, CogDis, IntAn, and ImpNon) were taken as behavioural measures. Participants gave their written informed consent to participate in the study and all experimental procedures were approved by the University of Auckland Human Participants Ethics Committee.

6.2.2 Image acquisition

Images were acquired using a 3T Siemens Magnetom Skyra scanner (Erlangen, Germany) at the Centre for Advanced MRI (CAMRI), Faculty of Medical and Health Sciences, Grafton, Auckland. Sagittal T1-weighted structural volumes were acquired from

each participant using a single shot 3D magnetisation-prepared rapidly acquired gradient echo (MP-RAGE) sequence with the following parameters: repetition time (TR) = 1900ms; echo time (TE) = 2.07ms; GRAPPA acceleration factor = 2; field of view (FOV) = 256mm^2; flip angle = 9 degrees; 176 sagittal slices; slice thickness = 1mm; matrix size = 256 × 256mm; voxel size = 1 × 1 × 1mm; scanning time = 4.26min.

6.2.3 Image preprocessing

The data were preprocessed using SPM8 software (Wellcome Trust Centre for Neuroimaging, London, UK; http://www.fil.ion.ucl.ac.uk/spm), which was implemented in MATLAB R2012b (MathWorks, Inc.). The raw structural images for all participants were first re-oriented manually with the origin set to anterior commissure using the Display function in SPM. The New Segment and DARTEL toolboxes were then utilised to preprocess the re-oriented images. New Segment is a more robust procedure that employs an improved registration model (Ashburner et al., 2013) compared to the default unified segmentation method (Ashburner & Friston, 2005), and was used to segment the images which resulted in six different tissue types (grey matter (GM), white matter (WM), cerebrospinal fluid (CSF), skull, soft tissue, and background/air). Only the first three (GM, WM, and CSF) were included for the DARTEL procedure.

DARTEL is based on the diffeomorphic registration algorithm (Ashburner, 2007) and allows for a more accurate inter-subject registration of brain images by creating study-specific templates. Using this method, the segmented images were aligned, normalised, modulated, and smoothed. The data were realigned to the template using default parameters. The images were then normalised to the standard Montreal Neurological Institute (MNI) space using a voxel size of 1.5 × 1.5 × 1.5mm. For the modulation step, 'Preserve Amount' option was selected in order to compare tissue volume rather than concentration in the

subsequent analyses. Lastly, the structural images were spatially smoothed using an isotropic Gaussian filter of 8 × 8 × 8mm at full-width half maximum (FWHM). The current study only reports analyses carried out on the preprocessed GM images.

6.2.4 Partial Least Squares analyses

Structural GM data were analysed using a multivariate statistical technique called PLS using a PLS graphical user interface (PLSgui; Rotman Research Institute of Baycrest Centre, Toronto, Canada; http://www.rotman-baycrest.on.ca), which was implemented in MATLAB R2012b (MathWorks, Inc.). This method is useful when looking at the overall distributed patterns in the data and therefore is particularly suited to detecting the distributed patterns of brain volume differences. A brief summary of the method can be found in Section 2.3.4 of Chapter 2.

In the present study, we conducted a behaviour PLS analysis to identify any significant latent variables (LV) associated with the GM data and all four dimensions of the O-LIFE. This analysis allowed us to examine the possible patterns of commonalities and/or differences within the brain-behaviour relationship, and the regions contributing to these patterns. First, a GM mask was created from the preprocessed images of all the participants using the ImCalc function in SPM. The threshold was set at 0.1 to exclude voxels representing WM and CSF. From here, the structural data were converted into a 35 × 2122945 matrix (with each row representing one participant and the columns containing grey matter voxels), which was then correlated with the four behaviours (the four dimensional scores from the O-LIFE) from each of the 35 participants[5]. The results allowed us to make

[5] For an example of another study using similar methods, see Ziegler et al. (2013). Here, the authors investigated brain structure in children and adolescents by performing manual PLS correlations with multiple cognitive ability measures, and calculated the structure-cognition covariance by entering 19 behaviours/test scores into one behaviour PLS analysis.

inferences about whether there is a pattern of GM differences that is associated with the schizotypy dimensions, and whether this pattern is representing GM increases or decreases in those regions. The significance and the reliability of the LV were determined by permutation testing and bootstrap resampling (McIntosh et al., 1996; Efron & Tibshirani, 1985). Clusters with bootstrap ratios (BSR) of ±3.3 were determined as reliable.

The data were also corrected for total incracranial volume (TICV) to minimise any brain volume effects between male and female participants. This was calculated by extracting the volume of each brain structure (GM, WM, and CSF) per voxel, which was then added together across all structures to give the final TICV for each participant. The variance of TICV was then removed from our MRI data by using multiple linear regression (Ziegler et al., 2013, further details by personal communication). This was performed manually in MATLAB by converting the structural image into a vector for each participant, which was then put into a data matrix consisting of 35 vectors. The covariate (TICV) was then regressed out of the matrix[6]. Finally, the corrected vectors were then reshaped and written back into the images for all participants.

From here, we compared the brain regions associated with high levels of schizotypy from our PLS analysis to those consistently found in schizophrenia (as established by Shepherd et al., 2012), as well as those reported in the previous schizotypy studies (DeRosse et al., 2015; Ettinger et al., 2012; Kühn et al., 2012; Modinos et al., 2009; Wang et al., 2014). There were six regions that overlapped across all studies, and the volume clusters from these areas were extracted using the multiple voxel extraction tool in PLSgui. Spearman's correlation coefficients were calculated for the four dimensions of schizotypy (UnEx,

[6] $Y_{corrected} = Y_{uncorrected} - Z \cdot B$
$= Y_{uncorrected} - Z \cdot inv(Z' \cdot Z) \cdot Z \cdot Y_{uncorrected}$
$= (I - Z \cdot inv(Z' \cdot Z) \cdot Z') \cdot Y_{uncorrected}$
Where $Y_{uncorrected}$ = original MRI images; $Y_{corrected}$ = corrected MRI images; Z = matrix containing the confounding variable (TICV); I = identity matrix (with vectors from all 35 participants); and B = regression coefficient.

CogDis, IntAn, and ImpNon) to investigate the relationship between these regions and each schizotypy dimension.

6.3 Results

6.3.1 Behavioural results

Mean scores and standard deviations (SD) for each of the four dimensions of the O-LIFE are shown in Table 6.1.

Spearman's correlations between age and each dimension indicated there was no effect of age on the subscale scores in the current sample. However, there was a significant gender effect for UnEx (U = 72.50, z = -2.12, p = .034, r = -.358) and CogDis (U = 76.00, z = -1.99, p = .046, r = -.336), with females (UnEx median = 14.5; CogDis median = 15.5) scoring significantly higher in these two subscales compared to the males (UnEx median = 8.00; CogDis median = 9.00). There were no gender effects for IntAn and ImpNon factors.

Table 6.1

Mean scores and standard deviations of each subscale within the O-LIFE for the total sample, as well as separate male and female samples.

O-LIFE dimension	Total (n=35)		Male (n=11)		Female (n=24)	
	Mean	SD	Mean	SD	Mean	SD
UnEx	12.94	7.25	9.18	6.52	14.67	7.02
CogDis	13.14	6.17	9.91	4.28	14.63	6.40
IntAn	8.57	6.21	10.27	5.88	7.79	6.32
ImpNon	9.29	4.46	7.55	3.01	10.08	4.84

Note: UnEx = unusual experiences; CogDis = cognitive disorganisation; IntAn = introvertive anhedonia; ImpNon = impulsive nonconformity; n = number of participants; SD = standard deviation.

6.3.2 Behaviour PLS analysis

The behaviour PLS analysis produced four LVs with LV1 reaching significance (using 1500 permutations and 1000 bootstraps; d = 228.78, p = .048). This LV explained

88.09% of the crossblock covariance ($p < .001$) and indicated an effect of schizotypy scores on the GM structure. There was a widespread pattern of regions found to be associated with differences in schizotypy (Figure 6.1). When the brain scores-behaviour correlation graph was examined, it was observed that only UnEx, CogDis, and ImpNon reliably contributed to this effect (even though IntAn shows an opposite trend, this was not reliable as indicated by the confidence intervals). Here, only negative saliences (cool regions) were observed with no significant positive brain-behaviour correlations at a threshold of BSR of ±3.3. This indicates that the three factors (UnEx, CogDis, and ImpNon) are *negatively* correlated with the cool regions, suggesting that *reductions* in grey matter volume for these regions are associated with increased scores on the three factors above. No associations between the schizotypy dimensions and *increased* grey matter volume were identified.

The O-LIFE measures showed associations with bilateral frontal, temporal, and parietal areas including bilateral inferior and middle temporal gyri, bilateral precentral and right postcentral gyri, left angular gyrus, right cerebellum, bilateral frontal regions, and bilateral precuneus. Co-ordinates of these regions are reported in Table 6.2.

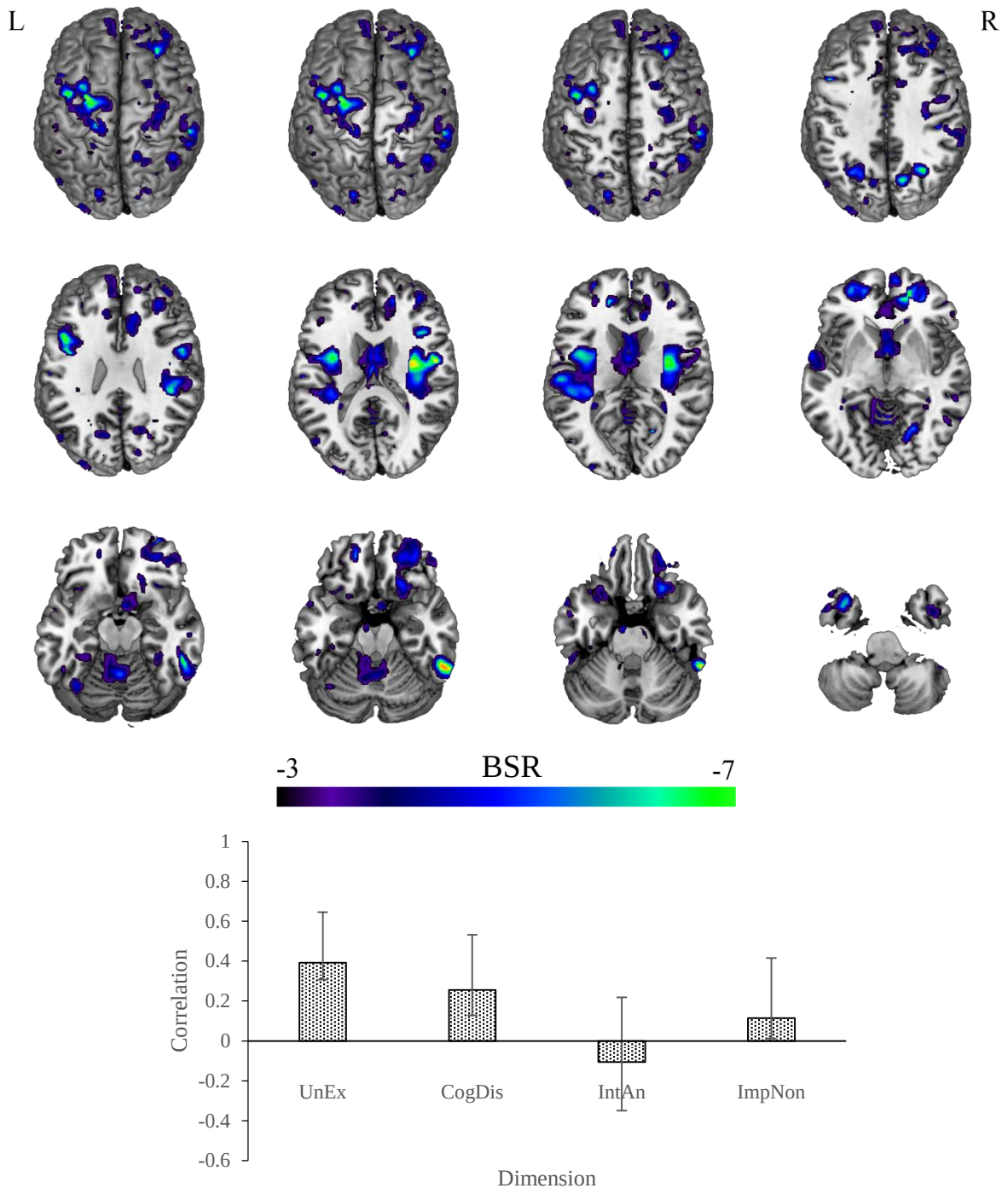

Figure 6.1 Singular image showing the areas of structural GM differences identified by the significant LV from the behaviour PLS analysis. Cool regions (corresponding to negative BSR scores) indicate regions which are negatively correlated with UnEx, CogDis, and ImpNon. The bar graph shows the overall level of correlation between each dimension and the brain scores of the participants (where brain scores indicate how strongly each participant contributes to the pattern expressed in the LV). Error bars reflect 95% confidence intervals. BSR = bootstrap ratio.

Table 6.2

Brain regions associated with the UnEx, CogDis, and ImpNon subscales in the latent variable identified by the behaviour PLS analysis.

	Brain region	*x*	*y*	*z*	BSR	Cluster size (*k*)
R	Precentral gyrus	63	6	24	-5.39	1719
R	Superior parietal lobule	18	-59	50	-6.62	1641
R	Precentral gyrus	39	-14	66	-4.62	1584
L	Superior temporal gyrus	-59	-27	12	-4.19	1424
R	Inferior temporal gyrus	56	-44	-20	-5.69	981
L	Precuneus	-8	-63	48	-4.58	775
R	Inferior parietal lobule	51	-26	32	-4.48	647
L	Middle frontal gyrus	-30	2	51	-4.10	349
L	Superior parietal lobule	-23	-47	77	-4.82	344
L	Middle occipital gyrus	-42	-78	12	-4.90	338
R	Inferior temporal gyrus	42	2	-47	-3.94	316
L	Angular gyrus	-50	-62	33	-4.09	308
R	IFG (p. Triangularis)	59	33	20	-4.73	278
L	IFG (p. Opercularis)	-33	8	29	-5.32	267
R	Lingual gyrus	20	-68	-3	-4.11	219
L	Middle temporal gyrus	-42	-60	-5	-4.32	211
R	Cerebellum (Lobule I IV)	9	-36	-24	-3.90	195
R	Inferior occipital gyrus	38	-74	-12	-5.31	181
R	Superior orbital gyrus	17	33	-15	-3.74	171
R	Cerebellum (Crus 1)	39	-81	-27	-3.64	165
R	Cuneus	15	-65	20	-3.77	95
L	Posterior medial frontal gyrus	-9	20	50	-3.94	88
R	Cuneus	20	-68	38	-3.93	86
R	Superior frontal gyrus	17	38	38	-4.27	78
R	Postcentral gyrus	27	-29	65	-3.67	78
R	Superior frontal gyrus	20	51	47	-4.07	77
R	Parahippocampal gyrus	33	-18	-27	-3.42	59
L	Superior occipital gyrus	-17	-89	45	-3.89	58
L	Precentral gyrus	-42	-6	44	-4.02	54

Note: Clusters evident with a bootstrap ratio of greater than -3.3 and a minimum cluster size of 50 voxels are reported. Cluster size indicates the number of voxels in the cluster. Co-ordinates are in MNI space and were anatomically labelled using the SPM Anatomy toolbox (Eickhoff et al., 2005; http://www.fz-juelich.de/inb/inb-3//spm_anatomy_toolbox). BSR = bootstrap ratio; L = left; R = right; IFG = inferior frontal gyrus.

6.3.3 Correlational analyses

We extracted volumes from the GM clusters in the left superior temporal gyrus, left middle frontal gyrus, bilateral inferior frontal gyri, left posterior medial frontal gyrus, and the right superior frontal gyrus, as these regions are observed to be consistently affected in both schizophrenia and schizotypy. Peak voxels with a BSR of -3.3 were considered to be reliable, and the minimum cluster size was set at 50 voxels. The volumes from these regions of interest (ROI) were then correlated with the four dimensional scores of O-LIFE, and results

were bootstrapped to assess reliability (Table 6.3). UnEx was found to be negatively correlated with all six ROIs, strongly suggesting that this dimension plays a key role in these volume changes. This is further supported by the fact that the other three dimensions (CogDis, IntAn, and ImpNon) showed no significant associations with these regions, except for a negative correlation between CogDis and right inferior frontal gyrus (r = -.439, p = .008).

Table 6.3

Spearman's correlations between extracted volumes and the four O-LIFE dimensions.

Region	UnEx		CogDis		IntAn		ImpNon	
	r	CI	*r*	CI	*r*	CI	*r*	CI
L Superior temporal gyrus	-.423*	[-.70, -.09]	-.269	[-.58, .10]	.281	[-.04, .57]	-.226	[-.50, .06]
L Middle frontal gyrus	-.452**	[-.70, -.11]	-.209	[-.53, .18]	.223	[-.12, .54]	-.198	[-.46, .11]
R Inferior frontal gyrus	-.465**	[-.70, -.14]	-.439**	[-.69, -.12]	.046	[-.31, .39]	-.275	[-.57, .06]
L Inferior frontal gyrus	-.552**	[-.75, -.26]	-.315	[-.57, .01]	.037	[-.29, .35]	-.260	[-.51, .04]
L Posterior med. frontal gyrus	-.378*	[-.66, -.04]	-.287	[-.58, .07]	.123	[-.20, .43]	-.068	[-.36, .23]
R Superior frontal gyrus	-.536**	[-.77, -.19]	-.313	[-.58, .03]	.049	[-.26, .37]	-.249	[-.50, .06]

Note: UnEx = unusual experiences; CogDis = cognitive disorganisation; IntAn = introvertive anhedonia; ImpNon = impulsive nonconformity; L = left; R = right; med. = medial; *r* = Spearman's correlation coefficient; CI = 95% confidence intervals (lower and upper bounds); * = $p < .05$; ** = $p < .01$.

6.4 Discussion

In this chapter, we invetigated the relationship between schizotypal personality traits and brain structure using a multivariate partial least squares technique. Consistent with previous research, we found a negative relationship between psychometric schizotypy and GM volume (e.g., DeRosse et al., 2015), where a widespread pattern of GM reductions was observed when correlated with the dimensions of the O-LIFE. However, our results differ

from other findings of a positive relationship between GM volume and schizotypy (e.g., Modinos et al., 2010; Wang et al., 2014a), as we did not see any evidence of an increase in GM regions that correlated with the schizotypy scores. These results will be discussed in context of what we currently know from studies of neuroanatomical correlates of schizophrenia and schizotypy.

The PLS analysis indicated GM volume differences in frontal and temporal areas such as the left superior temporal gyrus, the right superior frontal gyrus, bilateral inferior frontal and precentral gyri, the left posterior medial frontal gyrus, as well as some parietal areas such as the left angular gyrus and bilateral superior parietal lobes. From this, we were able to determine that using all four dimensions in one analysis could differentiate GM volume reductions in our sample, thus adding to the evidence that overall schizotypy can predict structural differences in schizotypal personality similar to what is found in the schizophrenia literature. By looking further into this association, we were able to conclude that the negative schizotypy factor (IntAn) did not play a significant role in this context.

Furthermore, when extracted volumes of the six ROIs were correlated to schizotypy scores in our analysis, it was found that only UnEx was significantly correlated to brain volume in all six regions, indicating this positive dimension as the only factor strongly associated with this pattern of grey matter reductions.

Interestingly, the affected areas found from the PLS analysis were confined to cortical regions in the current study. We did not find any associations between overall schizotypy behaviour and certain subcortical structures such as the thalamus, amygdala, and the hippocampus**,** which are commonly found to be affected in schizophrenia patients (Glahn et al., 2008). This may be explained in terms of the disconnection hypothesis of schizophrenia, which considers the symptoms of the disorder to be the direct result of abnormal functional and structural integration of brain processes (Camchong, MacDonald III, Bell, Mueller, &

Lim, 2011; Friston, 1998). In particular, studies have found decreased functional connectivity in multiple networks (e.g., the default mode network) arising from dysfunctional anatomical connections in schizophrenia patients (e.g., Skudlarski et al., 2010), which, in turn, has been attributed to localised grey matter and white matter abnormalities (Suzuki et al., 2002; Schmitt, Hasan, Gruber, & Falkai, 2011). The regions that are often affected in these neural circuits include the thalamus, caudate, and striatum (Welsh, Chen, & Taylor, 2010; Zhou et al., 2007), which are all subcortical structures with crucial roles in brain networks (Repovs, Csernansky, & Barch, 2011).

Relating this back to our results from the PLS analysis, it could be speculated that nonclinical schizotypal individuals may be affected by localised cortical structure differences, but do not exhibit any substantial cognitive and behavioural deficits due to seemingly intact subcortical regions. As our sample only consisted of young healthy adults, such regional differences could be the distinction between overall schizotypal traits and clinical psychopathology, where certain neuroanatomical structures remain unaffected in overall schizotypy until they change as a result of external risk factors. These changes may eventually lead to the development of schizotypal personality disorder (SPD; a clinically diagnosed disorder that is similar to schizophrenia but without overt psychotic symptoms; Siever et al., 2002) and schizophrenia. Research into SPD has also shown abnormalities in subcortical structures (Dickey et al., 2002), as well as volume reductions in the frontal and temporal lobes, with the decrease being only half of that observed in schizophrenia (Hazlett et al., 2008). This further supports the continuum model of the schizophrenia spectrum, where the gradual increase in neuroanatomical changes influences the level of symptom severity.

However, this interpretation must be taken with caution as these results are only in context of when we take all factors of the O-LIFE into account. By entering the four

dimensions into one analysis, we sought to find the maximum covariance between the four dimensions and structural differences. This was to investigate whether using all four scores could predict structural differences, even though there may be considerable variability between the dimensional scores across the same participants (e.g., individuals who score highly in the positive factor dimension may score low on the negative factor and vice versa). Although partial correlations between the four O-LIFE factors have been reported (Mason & Claridge, 2006), it was observed from the correlation graph (in Figure 6.1) that IntAn showed a trend of effect different to the other three factors relative to the observed pattern, at least within our sample. This is not surprising as various studies have consistently reported negative symptoms as a factor separate from other symptoms found in models of schizophrenia, regardless of how general (e.g., two dimensional; Kay et al., 1987) or specific (e.g., 11 factors; Peralta & Cuesta, 1999) the model may be (Blanchard & Cohen, 2006). In fact, research into the structural correlates of schizophrenia symptoms has shown symptom-specific regions as well as overlapping regions, which suggest that the different symptomology observed in patients may have a basis in the neuroanatomical regions affected in that particular person (e.g., Ha et al., 2004; Koutsouleris et al., 2008). This could also explain the heterogeneity of regions found to be affected in schizophrenia-spectrum disorders. Therefore, it is important to also examine whether there is a dimension that is most related to the structural deficits found in the schizophrenia and schizotypy, especially within regions that are consistently reported to be affected in patients and individuals with high levels of schizotypy.

By performing correlational analyses with specific ROI volumes and each dimension, we confirmed an association between UnEx and GM volume. The results indicated that UnEx plays a key role in structural changes seen in schizotypy (at least within our sample), in line with Ettinger et al. (2012)'s finding of a negative relationship between a positive schizotypy

factor and GM differences. Moreover, the regions implicated show an overlap with the cortical regions found to be affected in schizophrenia, including the inferior, medial, and middle frontal, as well as superior temporal regions (e.g., Kawasaki et al., 2004). It is interesting to note that most of these regions are highly significant with UnEx only, as fronto-temporal lobe deficits have been implicated in paranoid schizophrenia (e.g., García-Martí et al., 2008; Ha et al., 2004). This subtype of the disorder is characterised by persecutory delusions, perceptual disturbances, and hallucinations (5th Ed.; DSM-5; American Psychiatric Association, 2013) corresponding to the positive symptoms of the disorder (Fenton & McGlashan, 1991), and can be thought of as the clinical counterpart to the positive dimension of schizotypy (Mason et al., 1995). Furthermore, superior temporal gyrus has been suggested to be one of the key regions implicated in auditory hallucinations in schizophrenia (Gaser et al., 2004; Mechelli et al., 2007), and may also underlie auditory deficits that have been associated with schizotypy (Bates, 2005). Therefore, when only the positive schizotypal traits are taken into account, there is an overlap of regions that are also atypical in positive schizophrenia, in line with the idea that there are symptom-specific, structure-function abnormalities in the schizophrenia spectrum, which extends to include nonclinical schizotypy. This suggests that the positive factor of schizotypy is strongly related to schizophrenia, which could have clinical implications for schizotypal individuals, where UnEx may have a higher predictive power than the other dimensions in distinguishing those who may transition into a clinical disorder.

Overall, our main finding of an association between GM reductions and schizotypy adds to the increasing evidence of structural differences in those who exhibit more pronounced schizotypal personality traits, even when different types of psychometric schizotypy measures are used. Previous research which specifically investigated the relationship between GM volume and *overall* schizotypy have all found a negative

correlation (Raine et al., 1992; DeRosse et al., 2015; Wang et al., 2014a). One disparate subfinding regarding this particular relationship comes from Wang et al. (2014a) who found increased GM density in the right posterior MTG and the left cerebellum in their high global schizotypy group. They discussed this in the context of a compensatory mechanism in these individuals (as mentioned earlier in this chapter), especially as density reductions in the DLPFC and the insula were also observed in the same group, consistent with prior work.

On the other hand, there is less of an agreement within the literature when positive schizotypy is examined separately. The majority of the studies which have investigated the relationship between GM abnormalities and positive schizotypy have found increases in GM volume/thickness as well as reductions, in contrast to the findings of the current study which only found GM volume reductions. However, this may be in part due to the definition of 'positive schizotypy', which may differ depending on the psychometric measure used. Kühn et al. (2012) and Wang et al. (2014a) assessed the level of positive schizotypy in their participants by taking the score of the cognitive-perceptual factor in the SPQ, which include statements and questions such as 'I find it hard to communicate clearly what I want to say to people' and 'have you found that it is best not to let other people know too much about you?' (Raine, 1991, p. 558). When compared to the O-LIFE, similar questions ('do you ever feel that your speech is difficult to understand because the words are all mixed up and don't make sense?' and 'do you think having close friends is not as important as some people say?'; Mason & Claridge, 2006, pp. 209-210) are categorised into the CogDis and IntAn dimensions respectively, and therefore the high cognitive-perceptual scorers in the SPQ studies may not have exhibited the same positive profile as those in the current study. Moreover, these studies are consistent with our results when looking at the relationship between *overall* schizotypy and GM volume, providing further evidence that the classification of positive traits may influence the outcome of GM structure results.

There are two other studies which have directly examined positive schizotypy. Modinos et al. (2010) used the positive factor scores from the Community Assessment of Psychic Experiences (CAPE; Stefanis et al., 2002), while Ettinger et al. (2012) utilised the Rust Inventory of Schizotypal Cognitions (RISC; Rust, 1988) which solely measures paranoid aspects of schizotypy. Modinos et al. (2010) found greater GM volumes in the medial posterior cingulate cortex and the precuneus in subjects with high levels of positive schizotypy compared to those who scored low. Thus far, this is the only study which has not found any decreases in GM structures in highly schizotypal individuals, which may possibly be attributed to their study design of using dichotomous groups, where they used a subtraction method (based on the general linear model) to detect areas of structural differences between their high and low positive schizotypy groups. Our results are most similar to Ettinger et al. (2012)'s findings of GM reductions in positive schizotypy, possibly because the RISC strictly only contains items that tap into the general pananoid schizophrenia symptoms, most similar to the UnEx dimension of the O-LIFE (Rust, 1988).

Despite this variability in findings, there is a growing body of evidence which indicate GM differences in psychometric schizotypal personality. Importantly, the GM regions most implicated in schizophrenia were also found to be affected in the current study, including the frontal and temporal areas such as the left middle frontal gyrus and the left superior temporal gyrus. This was regardless of whether overall or positive schizotypy was examined, suggesting that a core pattern of abnormal regions may be responsible for generalised schizophrenia-spectrum symptoms and traits.

6.5 Limitations and future directions

The major limitation of this study was the gender imbalance in the sample. As observed in Section 6.3.1, there was a significant gender effect for both UnEx and CogDis

dimension scores of the O-LIFE, with females scoring significantly higher than males in the subscales. This trend is also observed across the schizophrenia spectrum, with females often showing higher levels of affective symptoms, including hallucinations and persecutory delusions (e.g., Leung & Chue, 2000). Additionally, brain morphology differences have been found between females and males, where the females have been found to show reduced grey matter volume in several brain regions compared to males (Good et al., 2001). Therefore, gender may have had a possible confounding effect on our finding of an association between schizotypy and GM reductions, although we attempted to minimise its role by controlling for the total intracranial volume in our sample.

Furthermore, the research into structural differences in schizotypy so far has focused largely on grey matter structures. As there is a large number of studies which indicate atypical white matter and ventricular structures in schizophrenia patients, this should be extended to include nonclinical populations for a more complete picture of the neuroanatomical relationship between schizotypy and schizophrenia. Although the more recent studies by DeRosse et al. (2015) and Wang et al. (2014a) have started examining neurobiological changes in psychometric schizotypy by utilising advanced methods such as graph theoretical analysis and white matter tractography, additional studies are needed to replicate their results, integrate findings, and establish a whole-brain picture regarding structural differences in schizotypy that eventually may lead to psychopathology. In particular, research into white matter tract abnormalities in individuals with high schizotypy may shed a light into possible cognitive network dysfunctions, involving tracts and pathways that connect the observed affected GM regions.

6.6 Conclusions

The aim of this study was to add to the existing literature of GM differences in schizotypal personality by using a novel multivariate method. This identified a pattern of volume reductions that maximally covaried with schizotypal personality. By looking at both the overall and positive schizotypy behaviours separately, we were able to make inferences about the possible symptom-specificity of affected cortical structures, and further link the regions to the areas implicated in schizophrenia. By establishing these structural differences in nonclinical populations without the confounding effects of medication, the affected cortical regions may be used as endophenotype candidates, and aid in elucidating the course and nature of possible clinical manifestations of the disorder. When taken together, these results support the notion of an overlap of phenotypic expression between schizotypy and schizophrenia, which extends across behavioural, cognitive, genetic, and also neuroanatomical domains.

Chapter 7: General discussion

The main aim of the current thesis was to examine the effect of schizotypy across functional and structural domains using behavioural and neuroimaging methods. Although a vast amount of research has investigated the neural basis of schizophrenia over the past century, its aetiology and pathophysiology remain largely unknown (Tandon et al., 2008). Thus, nonclinical schizotypy is a useful construct in which the phenomenological, genetic, cognitive, and neuropsychological overlaps with schizophrenia can be studied without any confounding factors such as psychosis and effects of treatment. Furthermore, its dimensional (normally distributed) nature allows for the identification of continuously distributed symptoms within the general population. This may be especially important when identifying at-risk individuals who might otherwise not have any other contributing risk factors, such as a family history of the disorder. Although the number of studies focusing on schizotypy has recently been increasing (Kwapil & Barrantes-Vidal, 2014), there is a need for a more unified picture of both the maladaptive and adaptive characteristics of the construct which may coexist in the same individual. Therefore, the behavioural and neuroimaging studies in this thesis were designed to provide a thorough examination of schizotypy within the same group of participants, and aimed to contribute towards formulating a more comprehensive and multidimensional model of the construct.

7.1 Summary

A brief summary of the study designs, participants, and main findings are seen in Table 7.1. In Study 1, it was found that individuals with high levels of psychometric schizotypy displayed sensory gating deficits compared to those with low schizotypy, confirming previous studies which have shown that highly schizotypal individuals already exhibit differences at a basic sensory level. This was demonstrated by comparing the ERP

amplitudes of the P50 response to paired auditory stimuli, where the high schizotypy group displayed a reduced attenuation to the second of the two stimuli in contrast to the low schizotypy group. This decreased gating was observed at both an overall schizotypy level and at a dimensional level (ImpNon), where the high impulsive nonconformity group also displayed a deficit similar to the result observed for the high overall O-LIFE group. This suggests that a reduction of sensory gating ability may lead to impulsive behaviour, possibly through a lack of self-control. This, in turn, may arise from the inability to discriminate relevant sensory information from the irrelevant stimuli. These results established that there were schizotypal differences in neural correlates within the current sample, and provided the rationale for Studies 2 and 3, which was based on the hypothesis that such early processing abnormalities may be responsible for higher cognitive deficits, such as disorganised thinking and language that are often observed in schizophrenia patients.

In Study 2, cerebral laterality for language was examined by using a lexical decision task ('go/no-go' with real words and nonwords) during fMRI with the same participants from Study 1. The rationale for this was based on the evidence of both language and functional imaging deficits observed in schizophrenia. Contrary to the study predictions, there were no differences in the pattern of laterality between the high and low schizotypal groups, suggesting that at least within this sample, language is strongly lateralised to the left hemisphere in both groups. That we found no laterality differences between groups likely reflects the possibility that there is no association between schizotypy and atypical laterality. This is supported by the fact that this result was found for both the behavioural dual-task and the lexical decision fMRI task in our study. Alternatively, our lack of association could have been due to methodological considerations. For example, we had a strict inclusion criteria of right handedness, as well as English being the first or only language (both left handers and bilingual individuals may deviate from the typical lateralisation for language though note that

reduced left hemispheric dominance for language has been found in right-handed schizophrenia patients; Dollfus et al., 2005). Moreover, our participant sample consisted of nonclinical schizotypal individuals, and therefore, it is possible that schizotypal individuals at risk for schizophrenia (either due to increased symptomology or first degree relatives with schizophrenia) may have shown left-right language differences.

In Study 3, we investigated the putative link between schizotypal personality and enhanced creativity using behavioural and fMRI methods. Behaviourally, the high schizotypy group showed greater figural creativity compared to the low schizotypy group. Interestingly, this difference was not observed in the verbal creativity task which, when taken with the null findings in Study 2, suggests that there are no linguistic differences associated with nonclinical schizotypy, at least with the current sample. When the neural activation differences between the figural creative and control trace conditions were correlated with the scores from the four dimensions of the O-LIFE, two factors (unusual experiences and impulsive nonconformity) were found to be associated with *decreased* activation in these regions. Thus we found a negative association between creative behaviour and neural activation. Although this result seems somewhat contradictory, this is in line with the idea of 'neural efficiency', where those who are better than others at a given task may require less cognitive effort and therefore less neural resources applied to the task (Haier et al., 1988). Although this decrease in cortical activity was a surprising finding, the association between unusual experiences (as well as impulsive nonconformity) and neural regions pertinent to creative thinking confirmed our hypothesis of a link between artistic creativity and schizotypal personality.

Finally, in Study 4 we illustrated that the differences between high and low schizotypal populations go beyond functional changes in the brain. We found noteworthy structural alterations between groups, where decreased regional grey matter volume was

correlated with high overall schizotypy. Each dimension score from the overall sample of 35 participants was further correlated with the grey matter volumes in six regions of interest. Our rationale for doing this was because different symptoms of schizophrenia have been associated with volume reductions in specific brain regions (e.g., Koutsouleris et al., 2008). Our correlational analyses revealed that only the positive factor (UnEx) was significantly correlated with all six regions.

Overall, the four studies demonstrated that there are certain characteristics significantly related to high schizotypal traits: perceptual gating deficits, higher figural (nonverbal) creativity, and grey matter reductions. These findings, if replicated, could be used to discriminate those who display presymptomatic schizophrenia symptoms from those without. However, while it seems that having a schizotypal personality results in subtle differences even within healthy individuals, it does not always have an observable effect on any higher-level cognitive functions, such as language deficits. And despite our observed differences between groups, it is likely that most of our schizotypal sample will never develop psychopathology. Taken together, longitudinal data are crucial to examine other external factors that may interact with and contribute to these existing deficits, potentially leading to the development of schizophrenia.

Furthermore, despite some similarities with schizotypal personality disorder and schizophrenia, there also appears to be beneficial aspects to having a schizotypal personality, such as enhanced creativity, which seems to be related to specific dimensions (such as unusual experiences). Therefore, when the results of the studies are taken together, they support the idea of schizotypy as a multidimensional construct, and that each dimension should be examined individually, as well as a part of the whole construct, to identify distinct developmental pathways that may lead to certain endophenotypic characteristics.

Table 7.1

Summary of the four experimental studies in the current thesis, including the participants, design and procedures, and the main findings of each study.

Study number	Total pool of participants (n=48)		Design and procedures (in the order the analyses were carried out)	Main findings
	Half a SD above/below the **overall O-LIFE** score mean	Half a SD above/below the mean of a specific **dimension**		
1: Sensory gating	Overall n=35	ImpNon n=33	<u>P50 ratio</u> 1. *t*-tests conducted for both Overall (high/low) and ImpNon (high/low) groups. <u>Spearman's correlations</u> 2. Each dimension score from the Overall group correlated with P50 ratio, difference, and S_1 and S_2 amplitudes.	<u>P50 ratio</u> 1. Significant gating deficits for both Overall and ImpNon as measured by P50 ratio. <u>Spearman's correlations</u> 2. Within the Overall group, CogDis and ImpNon correlated with the P50 ratio.
2: Language laterality	Overall n=35	UnEx n=27	<u>Dual-task</u> 1. *t*-tests conducted for both Overall (high/low) and UnEx (high/low) groups. <u>PLS</u> 2. Non-rotated PLS for both Overall and UnEx groups.	<u>Dual-task</u> 1. No behavioural differences between high/low groups for both Overall and UnEx. <u>PLS</u> 2. No laterality differences for either Overall or UnEx.
3: Creative thinking	Overall n=35	-	<u>PLS</u> 1. Mean-centering task PLS with one group (Overall). 2. Voxel signal extraction (for both Create and Trace) from regions within the Create salience map. <u>Spearman's correlations</u> 3. Create-Trace signal differences correlated with each dimension score.	<u>PLS</u> 1. Significant Create and Trace saliences. 2. Create condition elicited greater signal activation than Trace in all 12 regions (ROIs) within the salience map. <u>Spearman's correlations</u> 3. UnEx and ImpNon negatively correlated with 5 ROIs; IntAn positively correlated with 1 ROI.
4: Structural differences	Overall n=35	-	<u>PLS</u> 1. Behaviour PLS: all four dimension scores (behaviours) entered into a PLS analysis. <u>Spearman's correlations</u> 2. GM volumes extracted from 6 ROIs and correlated with each dimension score.	<u>PLS</u> 1. Behaviour PLS: grey matter volume reductions found to be correlated with schizotypy. <u>Spearman's correlations</u> 2. UnEx negatively correlated with all 6 ROIs; CogDis with 1 ROI.

7.2 Effects of schizotypy

The results from Studies 1, 3, and 4 further add to the current knowledge of the dimensional nature of psychometric schizotypy that exist within the general population. In particular, the findings of Studies 1 and 4 parallel those observed in schizophrenia patients, and therefore strengthen the evidence that schizotypal personality traits lie on the same continuum as schizophrenia-spectrum disorders. Sensory gating deficits, which were observed in Study 1, are in line with a large body of schizotypy and schizophrenia research that have also demonstrated similar deficits (e.g., Clementz et al., 1998; Croft et al., 2001), and seem to be one of the most reliable psychophysiological endophenotypes within the literature (Bramon et al., 2004). This is further supported by the findings of graded deficits across the spectrum, where at-risk and prodromal individuals show less marked P50 deficits compared to chronic schizophrenia patients (Brockhaus-Dumke et al., 2008), similar to patients with schizotypal personality disorder who also display less pronounced deficits than those with schizophrenia (Cadenhead et al., 2000; Hazlett et al., 2015). The fact that this gating abnormality was found in nonclinical individuals with high levels of self-reported schizotypy suggests that such preattentive differences may be one of the earliest developed markers that can be measured, and that can reliably differentiate low and high schizotypy individuals.

Interestingly, Studies 2 and 3 demonstrated different ways of how schizotypy may influence an individual's task performance. Despite previous findings of language differences, there was no evidence of this between the low and high schizotypy groups in Study 2. In contrast, there were significant associations between creative thinking and high levels of schizotypy in Study 3, and when taken together, these results suggest that nonclinical schizotypy may have adaptive effects such as increased creativity, perhaps especially when no maladaptive functional differences are present (such as reduced laterality

potentially leading to disorganised language, or lower scores in behavioural measures such as the WASI). As well as not showing any linguistic deficits, the highly schizotypal participants showed greater efficiency than those with low schizotypy scores when completing a figural creative task, as indicated by decreased activations of the regions implicated in creative thinking in Study 3. Therefore within this sample, it could be speculated that having a schizotypal personality has beneficial cognitive effects, despite the fact that basic sensory deficits still exist within these individuals. However, it may be that these 'deficits' are not always necessarily detrimental to cognitive function, and it could further be hypothesised that sensory overload, in this case, may encourage creative thinking through associations of two typically disparate ideas or thoughts.

Research examining the link between schizotypy and atypical language laterality has reported inconsistent findings, where some studies show a reduced left hemispheric dominance for language in highly schizotypal individuals compared to low, while others do not show this association. The null findings of Study 2 in the current thesis is suggestive of the fact that there may be potential developmental differences within the schizotypy construct, where some may eventually transition into the clinical spectrum at a later date (at-risk), while others, who possess similar levels of schizotypal traits, may never develop psychopathology (non-risk). More specifically, it could be that those with high levels of schizotypy who display atypical lateralisation have a higher chance of developing schizophrenia (where reduced laterality for language is consistently found in patients), while others who show typical laterality *despite* their high levels of schizotypy, may not have such a high risk of transition. This is particularly applicable when developing a possible cognitive endophenotype of schizophrenia, as it may be that only those who eventually develop psychosis show higher-level deficits, even when they are still on the nonclinical end of the spectrum.

Interestingly, research has also shown a direct link between cognitive functioning and P50 gating deficits in both first-episode and chronic schizophrenia patients, where both groups of patients displayed sensory gating *and* cognitive performance (e.g., working memory, reasoning, and processing speed) deficits, compared to healthy participants (Carolus et al., 2014). This suggests that cognitive impairments are already present in the early stages of clinical illness in conjunction with gating deficits, and therefore, cognitive deficits could be partly responsible for clinical psychosis, and may be utilised as a reliable marker for those at an immediate risk of developing a clinical disorder. Thus, when the results from Studies 1 and 2 are taken together, the P50 gating deficit could be used as a vulnerability marker, where it may be able to differentiate highly schizotypal individuals from the general population, providing a confirmatory measure of the psychometric schizotypal questionnaires. However, cognitive endophenotypes could potentially differentiate those at a higher risk for developing a clinical disorder *within* the schizotypal population, and therefore may have greater clinical implications compared to the P50 gating marker.

The different trajectories between the at-risk and the non-risk individuals within the schizotypy construct is also in line with the idea that schizotypal cognition may lead to two different outcomes, where one may lead to thought disturbances while the other may lead to creative thinking (Fisher, Heller, & Miller, 2013). And from this, it could be speculated that those who have a higher risk of developing psychosis may show cognitive abnormalities, while those who do not may display elevated creativity instead. In retrospect, further insight could have been gained if a specific cognitive task (such as working memory) had been included to directly compare executive functioning in the current sample of schizotypal individuals. However, the fact that there were no behavioural differences in the high and low groups in their WASI and the verbal TTCT performances indicate that these individuals did not differ in their higher cognitive (including linguistic) functions. Furthermore, those with

high levels of schizotypy were all either university students or graduates, which further demonstrates their intact cognitive functioning. From this, it could be hypothesised that in this group of individuals, there may have been a compensatory or buffering mechanism from major executive impairments, and this intact cognitive functioning may have a protective effect in the long-term despite the presence of schizotypal traits. Moreover, a compensatory mechanism may have allowed these individuals to adapt to more basic sensory deficits, and perhaps use these differences in a more constructive way (see Figure 7.1).

This was demonstrated by Study 3, which showed an association between schizotypal personality and enhanced creativity, when measured behaviourally by the figural TTCT. Functionally, it was found that UnEx was the factor most correlated with the regions implicated in creative thinking. As a positive factor of schizotypy, UnEx measures the level of perceptual aberrations and unusual thoughts, and as discussed in Chapter 5 (Study 3), this has been suggested to be due to cognitive disinhibition, which, in turn, may arise from weak sensory and cognitive gating mechanisms that lead to an overinclusive thinking style. Results from Study 1 support this hypothesis, as it was seen that the same group of individuals displayed weak sensory gating, which was further correlated with the cognitive disorganisation (CogDis) dimension, adding to the idea that UnEx traits arise from cognitive disinhibition. Interestingly however, within Study 3, CogDis score was not found to be associated to any regions pertinent to creative thinking. This could potentially be due to the fact that although gating deficits may result in disorganised thinking, when it comes to creative behaviour, the CogDis dimension does not have a specific effect on thinking *creatively*. This could perhaps be through adaptive mechanisms, in agreement with the idea that disorganised thinking is detrimental to the creative process **(**Batey & Furnham, 2008). Therefore, these findings add to the idea of 'healthy' schizotypy, which has been posited to describe individuals who experience psychosis-like symptoms (such as out-of-body

experiences) but do not suffer from any adverse effects from these thoughts (McCreery & Claridge, 2002). In fact, studies have shown that these individuals score higher on tests that measure subjective health and sense of well-being compared to those with low schizotypal traits (Kennedy & Kanthamani, 1995a; Schuldberg, 1990), with positive traits (such as UnEx) being particularly linked to psychological health (Goulding, 2004).

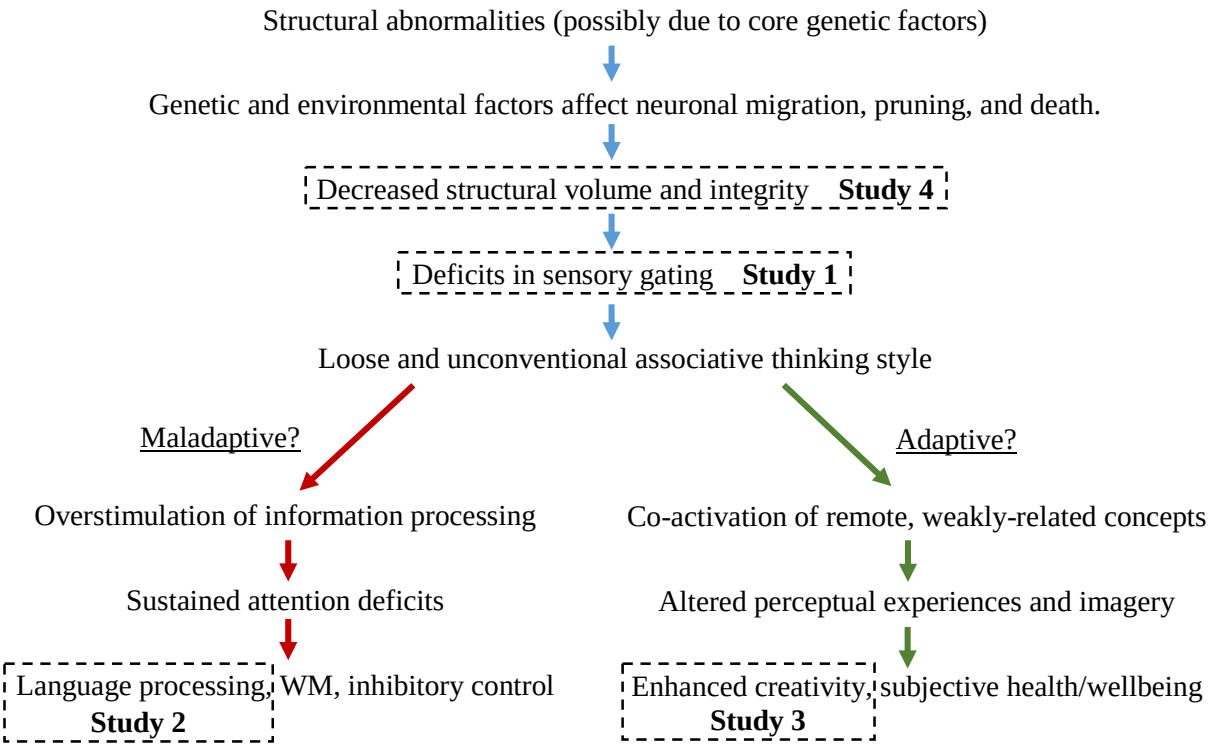

Figure 7.1 A flowchart showing two possible trajectories of an individual with high levels of schizotypy. Subtle changes in neuroanatomy may become exaggerated due to genetic and environmental factors, leading to inappropriate neuronal migration, pruning, and death. The resulting structural and sensory gating deficits have wider cognitive effects, which could lead to either a maladaptive route (negatively affecting higher-level cognitive processes) or an adaptive route (manifesting as positive imagery and enhanced creativity).

In summary, the results suggest that possessing a large number of schizotypal traits alone may not be sufficient for the transition into clinical disorders and psychosis. Importantly, it indicates that having a common aetiologial basis does not necessarily result in

the expression of the same endophenotypes, and therefore the underlying substrate may not always exert a similar influence across the spectrum.

7.3 Function-structure relationship in schizotypy

Study 4 showed significant associations between certain brain structures and schizotypy. Overall, grey matter reductions were found in the frontal and temporal regions, as well as the parietal lobules, and middle and superior occipital gyri. There was a diffuse pattern of affected structures within the fronto-temporal regions which, as noted earlier, is also observed in schizophrenia patients. However, no associations with the subcortical structures commonly associated with schizophrenia were found, leading to the possibility that cognitive deficits only arise when there are atypical connections between major structures and networks, due to the inadequate engagement of subcortical and limbic structures important for functional connectivity (e.g., Meyer-Lindenberg et al., 2001), as well as abnormal fronto-temporal structural connectivity (e.g., Hanlon et al., 2012).

From this, it may be hypothesised that extensive functional and structural dysfunction is necessary for the presentation of persistent overt psychosis, compared to regional deficits associated with schizotypy, which lead to schizotypal traits. In particular, it has been suggested that auditory hallucinations are a product of a failure to correctly recognise inner speech and thoughts as being self-generated (Waters, Woodward, Allen, Aleman, & Sommer, 2012), which suggests that language (frontal) and auditory perception (temporal) areas are affected. Moreover, when specific structures within the fronto-temporal regions are examined across schizophrenia and schizotypy, there is an overlap of regions that may be responsible for the manifestation of positive traits and symptoms. These include the inferior frontal and superior temporal gyri, which are responsible for verbal and auditory processes respectively, and were found to be reduced in volume in the high schizotypy group (Study 4).

Interestingly, the UnEx section of the O-LIFE includes questions which tap into these processes, such as “do you ever feel that your speech is difficult to understand because the words are all mixed up and don’t make sense?” and “have you ever thought you heard people talking only to discover that it was in fact some nondescript noise?” (Mason & Claridge, 2006, p. 209), which suggests that volume reductions in the frontal and temporal areas are associated with atypical verbal and auditory processing.

Therefore, it may be speculated that specific UnEx traits in schizotypy could be due to abnormalities in these regions, which are in line with positive symptoms in schizophrenia. However, for schizotypal individuals, these traits are unusual but not psychotic (e.g., “are your thoughts sometimes so strong that you can almost hear them?” where a positive answer would increase the UnEx score in the O-LIFE, Mason & Claridge, 1995, p. 209), whereas for schizophrenia patients, these become detached from the self, often resulting in second and third person hallucinations (e.g., ‘you are going to die’ and ‘he’s going to bed’ respectively, Waters, Badcock, & Maybery, 2007). This may be due to a communication failure between the frontal and temporal lobes (Ford, Mathalon, Whitfield, Faustman, & Roth, 2002), and this difference between self-awareness and self-detachment may be the one of the distinguishing features between nonclinical and clinical aspects of the schizophrenia spectrum.

However, it must be noted that hallucinations have also been reported in nonclinical populations, as previously mentioned in Chapter 5, and this suggests that they cannot be solely attributed to fronto-temporal connectivity deficits, which would also negatively affect other cognitive and perceptual processes. Interestingly, such hallucinatory experiences in nonclinical individuals have been described as being qualitatively different from those experienced by patients, where there is a higher perceived control of the hallucinations as well as the content being predominantly positive (Honig et al., 1998). This is in agreement with the finding that highly schizotypal individuals score higher on measures of subjective

health (as mentioned earlier in this chapter) and, therefore, there may be an association with nonclinical hallucinatory experiences and schizotypy (particularly the UnEx factor).

Furthermore, these anomalous experiences may also be linked with enhanced levels of creativity as found in Chapter 5. Questions suggesting this link are also found in the O-LIFE (e.g., “does it often happen that nearly every thought immediately and automatically suggests an enormous number of ideas?” and “no matter how hard you try to concentrate do unrelated thoughts creep into your mind?”, Mason & Claridge, 2006, p. 209) indicating that the decreased activations observed in highly schizotypal participants may give rise to specific traits such as unusual thoughts and experiences. Moreover, it has been suggested such deactivation of specific regions may result in a loss of inhibitory control, resulting in the disinhibition of other regions (Dias, Robbins, & Roberts, 1996; Radel et al., 2015). Results from Studies 3 and 4 could be seen to support this, as three out of the five regions related to creative thinking and schizotypy from Study 3 (namely the left middle frontal gyrus, left inferior parietal lobule, and the right inferior temporal gyrus) are close in proximity to the inferior frontal and superior temporal areas found to be affected in Study 4. Therefore, grey matter reductions in these regions could have led to the disinhibition of neighbouring areas ultimately resulting in manifestations of atypical behaviour, such as unusual experiences and increased creativity.

Finally, a neurocognitive model of hallucinations proposed by Allen, Larøi, McGuire, and Aleman (2008) may potentially be used to build a more cohesive picture of schizotypy processes. This model posits that perceptual aberrations and hallucinatory experiences are a result of a combination of bottom-up and top-down processing dysfunctions. Bottom-up deficits have been hypothesised to be caused by an overactivation of primary and secondary sensory cortices, leading to the experience of perception in the absence of relevant stimuli. When coupled with a weakened top-down control (due to abnormalities in the cortical and

subcortical regions, as well as connectivity deficits), it may lead to the breakdown of higher-level cognitive processes, resulting in a variety of schizophrenia symptoms (Allen et al., 2008).

In the context of the current findings, it seems that the schizotypal participants' bottom-up processes may have been affected, as indicated by their sensory gating deficits observed in Study 1, as well as the finding of increased activation in the middle occipital gyrus (a primary sensory region) in Study 3 (compared to the other four regions which all showed decreased activation). However, their cognitive processes remain largely intact, as observed by their high level of cognitive functioning, even with the finding of reduced grey matter regions (a top-down deficit) in Study 4. Therefore, it may potentially be that the *extent* to which these top-down processes are adversely affected is important in determining schizotypal individuals who could be at-risk of developing a clinical disorder. It may further be speculated that all highly schizotypal individuals are vulnerable to becoming at-risk (indicated by their bottom-up processing deficits), and this transition may depend on additional environmental factors (such as stress, drug use, and trauma) that may instigate further changes, leading the individual to shift from adaptive to maladaptive schizotypal traits, increasing the risk of clinical psychosis.

7.4 Limitations, applications, and future directions

There were a number of limitations that were identified in the current thesis. The main limitation is related to the participant sample, in which the majority of the participants in the studies were either university students or graduates. Furthermore, their above average IQ scores reflect their high functioning, which may mask any subtle cognitive deficits that may be related to schizotypy. Interestingly however, the results from Studies 1 and 4 (which did not measure performance) indicate that there are quantitative abnormalities even in those

individuals who may not show any overt deficits otherwise, which further add to the evidence that the fully dimensional model of schizotypy applies to the general population, with those scoring highly on schizotypal traits showing certain related deficits observed in the schizophrenia spectrum. Therefore, future studies should include tasks which test higher-level cognition explicitly (such as working memory or cognitive flexibility tasks) in conjunction with those that test lower-level processes (such as pattern recognition tasks), to see whether (and to what extent) cognitive processes are affected in highly functional schizotypal individuals, in order to construct a schizotypy profile that is most associated with high cognitive deficits.

Following from this, the results of Study 2 indicate the task could have been too simple (seen by the ceiling effects) to detect any laterality differences in these individuals. Previous studies reporting differences in language laterality between high and low schizotypy have mostly employed more complex tasks that have included other components other than pure lexical decision, such as priming (Kravetz et al., 1998), verbal fluency (Hori et al., 2008), irony comprehension (Rapp et al., 2010), emotional prosody (Najt et al., 2012), and emotional Stroop (Van Strien & Kampen, 2009). This suggests that the findings from these studies may potentially have been influenced by other cognitive processing differences, rather than purely language. Therefore, an interesting approach may be to examine language laterality utilising two different tasks, such as a lexical decision task and an emotional prosody task (which combines emotion and language processes), in order to make inferences about to what extent language laterality is affected in schizotypy, and whether differences are only evident when there is an influence of another process (such as emotion, which has been implicated in both schizotypy and schizophrenia; Aguirre, Sergi, & Levy, 2008; Brüne, 2005).

Another limitation regarding the participant sample is the overrepresentation of female participants, which may have led to gender effects in the studies. Due to time restraints and resources, it was not possible to recruit enough participants to conduct gender-balanced studies. This is a common limitation within psychology research, and also within schizotypy, where studies show that females score higher on psychometric measures of positive schizotypy compared to men, as mentioned previously in Chapters 5 and 6 (e.g., Bora & Baysan Arabaci, 2009; Miller & Burns, 1995). As there are neuroanatomical differences between females and males, this limitation is especially pertinent to Study 4, which compared brain volumes between the participants. Although total intracranial volume was controlled for, gender itself was not. Therefore, future studies explore the effect of schizotypy using a balanced sample, and/or control for the effects by entering gender as a covariate in functional and structural analyses.

Regarding data analyses, a dichotomous design was utilised in Studies 1 and 2, where the participants were categorised into high and low groups in order to examine group differences. Furthermore, even in the correlational analyses (including PLS), the 35 participants in the group were chosen on the basis of their scores being half a standard deviation above or below the mean of the overall O-LIFE score. Such a design is often observed to be problematic mostly due to the imposition of artificial boundaries between categories that lead to the discarding of information and loss of power (Fernandes-Taylor, Hyun, Reeder, & Harris, 2011). Despite the problems associated with dichotomising the sample, we chose this design as we were interested in examining possible endophenotypes associated with schizotypy, with the aim of finding specific markers which may be used to differentiate at-risk individuals as a group from those with a low risk. To minimise the effect of an arbitrary divide, we decided to exclude individuals who scored in the middle range of the scale-of-interest (overall O-LIFE in all four studies, ImpNon in Study 1, and UnEx in

Study 3), so that any group design would consist of participants who did not overlap across groups. Furthermore, we included the same 35 participants from the group analyses (in Studies 1 and 2) across all four studies, as we were particularly interested in the effect of schizotypy across different tasks in the same group of individuals.

There are several other implications from these studies that may be applicable for future research. Although speculations have been made about the possible function-structure relationship in this chapter, studies focusing specifically on this link may be able to shed light on the determining those who are at a high risk for developing a clinical disorder. Studies using white matter tractography via diffusion tensor imaging methods can elucidate connectivity dysfunction that is present in schizophrenia and schizotypal personality disorder patients (e.g., Hazlett, Goldstein, & Kolaitis, 2012), and also in some nonclinical schizotypal individuals (e.g., DeRosse et al., 2015). By combining such neuroanatomical differences with various low- and high-level cognitive tests, a profile of an individual-at-risk may tentatively be formed, with the aim of providing information that may predict future transition into illness. Furthermore, the development of a continuum which combines personality, behavioural, functional, and structural changes may be beneficial in understanding the aetiology of clinical manifestations of the schizophrenia construct. If demographical and environmental background information can be gathered, this may also help in elucidating the external factors that make a schizotypal individual more likely to transition into the clinical spectrum, and to design specific interventions that may be able to influence this outcome.

On this note, another line of research could focus on examining possible differences between high schizotypal individuals *without* a family history of schizophrenia, high schizotypal individuals *with* a family history of schizophrenia, and individuals at ultra-high risk (defined as those with a family history of psychotic disorder *and* displaying subclinical symptoms/functional decline, Yung, Phillips, Yuen, & McGorry, 2004), to further clarify

functional and structural endophenotypes that may predict future transition. Although background information on family history of mental disorders was recorded for this research, due to time constraints, only a few highly schizotypal participants with a family history were recruited, which were not enough to separate them from others with high levels of schizotypy but without a family history[7].

Finally, longitudinal data may be especially valuable in elucidating: 1) the progression of the schizotypy-schizophrenia spectrum; 2) the functional and structural endophenotypes that clarify those at a high risk of developing a clinical disorder from those with a low risk, *despite* the similarities in their schizotypy phenotype; 3) potential compensatory mechanisms and mediating factors that diffuse any negative effects induced by high levels of schizotypy; and 4) the specificity of the dimensions leading to a subtype of schizophrenia (e.g., whether UnEx can predict positive schizophrenia or IntAn with negative schizophrenia).

7.5 General conclusion

In conclusion, the empirical studies in the thesis suggest that there are specific functional and structural changes in schizotypy that are evident early on within the schizotypy-schizophrenia spectrum. These changes mirror those observed in clinical patients, albeit in a less severe manner, further adding to the evidence that support the dimensional model of schizotypy. These findings indicate that the schizotypy spectrum can provide an integrative construct to investigate the developmental pathways linking schizotypal personality traits to subclinical schizotypy to the manifestation of clinical symptoms, and may provide a vulnerability marker for populations that are at a potential risk to schizophrenia-spectrum disorders. The differences observed across the four dimensions of

[7] This was balanced out in the analyses by the inclusion of a similar number of participants with low levels of schizotypy who had a family history of mental disorders.

schizotypy further suggest that the multidimensionality of schizotypy is a complex construct, and more research is needed to disentangle other external factors that affect the overall schizotypal expression as well as the interactions between the different dimensions. This may provide insight into the adaptive and maladaptive developmental pathways in nonclinical populations, where compensatory and protective mechanisms could result in the expression of schizotypy as positive personality and cognitive traits, rather than as a possible precursor to schizophrenia-spectrum psychopathology.

References

Addis, D.R., McIntosh, A.R., Moscovitch, M., Crawley, A.P., & McAndrews, M.P. (2004). Charaterizing spatial and temporal features of autobiographical memory retrieval networks: a partial least squares approach. *NeuroImage, 23(4),* 1460-1471. doi:10.1016/j.neuroimage.2004.08.007

Adler, L.E., Oliney, A., Waldo, M., Harris, J.G., Griffith, J., Stevens, K., . . . Freedman, R. (1998). Schizophrenia, sensory gating, and nicotinic receptors. *Schizophrenia Bulletin, 24,* 189-202. doi:10.1093/oxfordjournals.schbul.a033320

Adler, L.E., Pachtman, E., Franks, R.D., Pecevich, M., Waldo, M.C., & Freedman, R. (1982). Neurophysiological evidence for a defect in neuronal mechanisms involved in sensory gating in schizophrenia. *Biological Psychiatry, 17,* 639-654.

Agartz, I., Andersson, J.L.R., & Skare, S. (2001). Abnormal brain white matter in schizophrenia: a diffusion tensor imaging study. *Neuroreport, 12(10),* 2251-2254. doi:10.1097/00001756-200107200-00041

Aguirre, F., Sergi, M.J., & Levy, C.A. (2008). Emotional intelligence and social functioning in persons with schizotypy. *Schizophrenia Research, 104(1-3),* 255-264. doi:10.1016/j.schres.2008.05.007

Aguirre, G.K., Zarahn, E., & D'Esposito, M. (1998). The variability of human, BOLD hemodynamic responses. *NeuroImage, 8,* 360-369. doi:10.1006/nimg.1998.0369

Aichert, D.S., Williams, S.C.R., Möller, H.-J., Kumari, V., & Ettinger, U. (2012). Functional neural correlates of psychometric schizotypy: An fMRI study of antisaccades. *Psychopathology, 49(3),* 345-356. doi:10.1111/j.1469-8986.2011.01306.x

Akinola, M., & Mendes, W.B. (2008). The Dark Side of Creativity: Biological Vulnerability and Negative Emotions Lead to Greater Artistic Creativity. *Personality and Social Psychology Bulletin, 34(12),* 1677-1686. doi:10.1177/0146167208323933

Allen, P., Larøi, F., McGuire, P.K., & Aleman, A. (2008). The hallucinating brain: A review of structural and functional neuroimaging studies of hallucinations. *Neuroscience & Biobehavioral Reviews, 32(1),* 175-191. doi:10.1016/j.neubiorev.2007.07.012

American Psychiatric Association. (1987). Diagnostic and statistical manual of mental disorders (3rd Ed.).

American Psychiatric Association. (2013). Schizophrenia Spectrum and Other Psychotic Disorders. In *Diagnostic and statistical manual of mental disorders* (5th Ed.). doi:10.1176/appi.books.9780890425596.dsm02

Andreasen, N.C. (1987). Creativity and Mental Illness: Prevalence Rates in Writers and Their First-Degree Relatives. *American Journal of Psychiatry, 144,* 1288-1292. doi:10.1176/ajp.144.10.1288

Andreasen, N.C., & Olsen, S. (1982). Negative v Positive Schizophrenia: Definition and Validation. *Archives of General Psychiatry, 39,* 789-794. doi:10.1001/archpsyc.1982.04290070025006

Andreasen, N.C., & Powers, P.S. (1975). Creativity and psychosis: An examination of conceptual style. *Archives of General Psychiatry, 32,* 70-73. doi:10.1001/archpsyc.1975.01760190072008

Andreasen, N.C., Nopoulos, P., O'Leary, D.S., Miller, D.D., Wassink, T., & Flaum, M. (1999). Defining the phenotype of schizophrenia: cognitive dysmetria and its neural mechanisms. *Biological Psychiatry, 46,* 908-920. doi:10.1016/S0006-3223(99)00152-3

Angrilli, A., Spironelli, C., Elbert, T., Crow, T.J., Marno, G., & Stegagno, L. (2009). Schizophrenia as Failure of Left Hemispheric Dominance for the Phonological Component of Language. *PLoS ONE, 4(2),* e4507. doi:10.1371/journal.pone.0004507

Arden, R., Chavez, R.S., Graziopene, R., & Jung, R.E. (2010). Neuroimaging creativity: A psychometric view. *Behavioural Brain Research, 214,* 143-156. doi:10.1016/j.bbr.2010.05.015

Arnt, S., Alliger, R.J., & Andreasen, N.C. (1991). The distinction of positive and negative symptoms: The failure of a two-dimensional model. *The British Journal of Psychiatry, 158,* 317-322. doi:10.1192/bjp.158.3.317

Artiges, E., Martinot, J.-L., Verdys, M., Attar-Levy, D., Mazoyer, B., Tzourio, N., . . . Paillère-Martinot, M.-L. (2000). Altered Hemispheric Functional Dominance During Word Generation in Negative Schizophrenia. *Schizophrenia Bulletin, 26(3),* 709-721. doi:10.1093/oxfordjournals.schbul.a033488

Asai, T., Sugimori, E., & Tanno, Y. (2009). Schizotypal personality traits and atypical lateralization in motor and language functions. *Brain and Cognition, 71,* 26-37. doi:10.1016/j.bandc.2009.03.007

Asai, T., Sugimori, E., Bando, N., & Tanno, Y. (2011). The hierarchic structure in schizotypy and the five-factor model of personality. *Psychiatry Rsearch, 185(1-2),* 78-83. doi:10.1016/j.psychres.2009.07.018

Asami, T., Bouix, S., Whitford, T.J., Shenton, M.E., Salisbury, D.F., & McCarley, R.W. (2012). Longitudinal loss of gray matter volume in patients with first-episode schizophrenia: DARTEL automated analysis and ROI validation. *NeuroImage, 59(2),* 986-996. doi:10.1016/j.neuroimage.2011.08.066

Ashburner, J. (2007). A fast diffeomorphic image registration algorithm. *NeuroImage, 38(1),* 95-113. doi:10.1016/j.neuroimage.2007.07.007

Ashburner, J., & Friston, K.J. (2000). Voxel-Based Morphometry – The Methods. *NeuroImage, 11,* 805-821. doi:10.1006/nimg.2000.0582

Ashburner, J., & Friston, K.J. (2005). Unified segmentation. *NeuroImage, 26(3),* 839-851. doi:10.1016/j.neuroimage.2005.02.018

Ashburner, J., Barnes, G., Chen, C.-C., Daunizeau, J., Flandin, G., Friston, K., … Phillips, C. (2013). SPM8 Manual. *Functional Imaging Laboratory, Wellcome Trust Centre for Neuroimaging, Institute of Neurology, UCL, UK.* Retrieved from http://www.fil.ion.ucl.ac.uk/spm

Aziz-Zadeh, L., Liew, S.-L., & Dandekar, F. (2013). Exploring the neural correlates of visual creativity. *Social Cognitive & Affective Neuroscience, 9(11),* 475-480. doi:10.1093/scan/nss021

Badcock, J.C., & Dragović, M. (2006). Schizotypal personality in mature adults. *Personality and Individual Differences, 40,* 77-85. doi:10.1016/j.paid.2005.06.015

Badzakova-Trajkov, G., Häberling, I.S., & Corballis, M.C. (2011). Magical ideation, creativity, handedness, and cerebral asymmetries: A combined behavioural and fMRI study. *Neuropsychologia, 49,* 2896-2903. doi:10.1016/j.neuropsychologia.2011.06.016

Badzakova-Trajkov, G., Kirk, I.J., & Waldie, K.E. (2008). Dual-task performance in late proficient bilinguals. *Laterality: Asymmetries of Body, Brain and Cognition, 13(3),* 201-216. doi:10.1080/13576500701801140

Baer, J. (1994). Divergent thinking is not a general trait: A multidomain training experiment. *Creativity Research Journal, 7(1),* 35-46. doi:10.1080/10400419409534507

Baird, B., Smallwood, J., Mrazek, M.D., Kam, J.W.Y., Franklin, M.S., & Schooler, J.W. (2012). Inspired by Distraction: Mind Wandering Facilitates Creative Incubation. *Psychological Science, 23(10),* 1117-1122. doi:10.1177/0956797612446024

Balconi, M., & Pozzoli, U. (2003). Face-selective processing and the effect of pleasant and unpleasant emotional expressions on ERP correlates. *International Journal of Psychophysiology, 49(1),* 67-74. doi:10.1016/S0167-8760(03)00081-3

Barch, D.M., & Ceaser, A. (2012). Cognition in schizophrenia: core psychological and neural mechanisms. *Trends in Cognitive Sciences, 16(1),* 27-34. doi:10.1016/j.tics.2011.11.015

Barch, D.M., Carter, C.S., Perlstein, W., Baird, J., Cohen, J.D., & Schooler, N. (1999). Increased Stroop facilitation effects in schizophrenia are not due to increased automatic spreading activation. *Schizophrenia Research, 39,* 51-64. doi:10.1016/S0920-9964(99)00025-0

Barnett, K.J., & Corballis, M.C. (2002). Ambidexterity and magical ideation. *Laterality: Asymmetries of Body, Brain and Cognition, 7(1),* 75-84. doi:10.1080/13576500143000131

Baron-Cohen, S., Ashwin, E., Ashwin, C., Tavassoli, T., & Chakrabarti, B. (2009). Talent in autism: hyper-systemizing, hyper-attention to detail and sensory hypersensitivity. *Philosophical Transactions of the Royal Society B: Biological Sciences, 364(1522),* 1377-1383. doi:10.1098/rstb.2008.0337

Barrantes-Vidal, N. (2004). Creativity & Madness Revisited from Current Psychological Perspectives. *Journal of Consciousness Studies, 11(3-4),* 58-78.

Barrantes-Vidal, N., Ros-Morente, A., & Kwapil, T.R. (2009). An examination of neuroticism as a moderating factor in the association of positive and negative schizotypy with psychopathology in a nonclinical sample. *Schizophrenia Research, 115,* 303-309. doi:10.1016/j.schres.2009.09.021

Barron, F., & Harrington, D.M. (1981). Creativity, Intelligence, and Personality. *Annual Review of Psychology, 32,* 439-476. doi:10.1146/annurev.ps.32.020181.002255

Basso, M.R., Nasrallah, H.A., Olson, S.C., & Bornstein, R.A. (1998). Neuropsychological correlates of negative, disorganized and psychotic symptoms in schizophrenia. *Schizophrenia Research, 31(2-3),* 99-111. doi:10.1016/S0920-9964(98)00023-1

Bates, T.C. (2005). The panmodal sensory imprecision hypothesis of schizophrenia: reduced auditory precision in schizotypy. *Personality and Individual Differences, 38,* 437-449. doi:10.1016/j.paid.2004.04.021

Batey, M., & Furnham, A. (2006). Creativity, intelligence, and personality: A critical review of the scattered literature. *Genetic, Social, and General Psychology Monographs, 132,* 355-429. doi:10.3200/mono.132.4.355-430

Batey, M., & Furnham, A. (2008). The relationship between measures of creativity and schizotypy. *Personality and Individual Differences, 45,* 816-821. doi:10.1016/j.paid.2008.08.014

Batey, M., & Furnham, A. (2009). The Relationship between Creativity, Schizotypy and Intelligence. *Individual Differences Research, 7(4),* 272-284.

Becker, G. (2001). The Association of Creativity and Psychopathology: Its Cultural-Historical Origins. *Creativity Research Journal, 13(1),* 45-53. doi:10.1207/S15326934CRJ1301_6

Beech, A., Powell, T., McWilliam, J., & Claridge, G. (1989). Evidence of reduced 'cognitive inhibition' in schizophrenia. *British Journal of Clinical Psychology, 28,* 109-116. doi:10.1111/j.2044-8260.1989.tb00821.x

Bell, M.D., Lysaker, P.H., Milstein, R.M., & Beam-Goulet, J.L. (1994). Concurrent validity of the cognitive component of schizophrenia: Relationship of PANSS scores to neuropsychological assessments. *Psychiatry Research, 54(1),* 51-58. doi:10.1016/0165-1781(94)90064-7

Benes, F.M. (2000). Emerging principles of altered neural circuitry in schizophrenia. *Brain Research Reviews, 31,* 251-269. doi:10.1016/S0165-0173(99)00041-7

Bergida, H., & Lenzenweger, M.F. (2006). Schizotypy and sustained attention: confirming evidence from an adult community sample. *Journal of Abnormal Psychology, 115,* 545-551. doi:10.1037/0021-843X.115.3.545

Bergman, A.J., Harvey, P.D., Roitman, S.L., Mohs, R.C., Marder, D., Silverman, J.M., & Siever, L.J. (1998). Verbal learning and memory in schizotypal personality disorder. *Schizophrenia Bulletin, 24,* 635-641. doi:10.1093/oxfordjournals.schbul.a033355

Berkowitz, A.L., & Ansari, D. (2010). Expertise-related deactivation of the right temporoparietal junction during musical improvisation. *NeuroImage, 49(1),* 712-719. doi:10.1016/j.neuroimage.2009.08.042

Bertrand, O., Perrin, F., & Pernier, J. (1985). A theoretical justification of the average reference in topographic evoked potential studies. *Electroencephalography & Clinical Neurophysiology, 62*(6), 462-464. doi:10.1016/0168-5597(85)90058-9

Bialystok, E., Craik, F.I.M., Grady, C., Chau, W., Ishii, R., Gunji, A., & Pantev, C. (2005). Effect of bilingualism on cognitive control in the Simon task: evidence from MEG. *NeuroImage, 24(1),* 40-49. doi:10.1016/j.neuroimage.2004.09.044

Binder, J.R., Frost, J.A., Hammeke, T.A., Cox, R.W., Rao, S.M., & Prieto, T. (1997). Human Brain Language Areas Identified by Functional Magnetic Resonance Imaging. *The Journal of Neuroscience, 17(1),* 353-362.

Binder, J.R., McKiernan, K.A., Parsons, M.E., Westbury, C.F., Possing, E.T., Kaufman, J.N., & Buchanan, L. (2003). Neural correlates of lexical access during visual word recognition. Journal of Cognitive Neuroscience, 15(3), 372-393. doi:10.1162/089892903321593108

Birchwood, M., Todd, P., & Jackson, C. (1998). Early intervention in psychosis. The critical period hypothesis. *The British Journal of Psychiatry – Supplement, 172(33),* 53-59. doi:10.1097/00004850-199801001-00006

Bishop, D.V.M., Ross, V.A., Daniels, M.S., & Bright, P. (1996). The measurement of hand preference: A validation study comparing three groups of right-handers. *The British Journal of Psychology, 87,* 269-285. doi:10.1111/j.2044-8295.1996.tb02590.x

Blackwood, D.H.R., Glabus, M.F., Dunan, J., O'Carroll, R.E., Muir, W.J., & Ebmeier, K.P. (1999). Altered cerebral perfusion measured by SPECT in relatives of patients with schizophrenia: Correlations with memory and P300. *British Journal of Psychiatry, 175,* 357-366. doi:10.1192/bjp.175.4.357

Blanchard, J.J., & Cohen, A.S. (2006). The Structure of Negative Symptoms Within Schizophrenia: Implications for Assessment. *Schizophrenia Bulletin, 32(2),* 238-245. doi:10.1093/schbul/sbj013

Bleuler, E. (1950). *Dementia praecox or the group of schizophrenias.* (J. Zinkin, Trans.). New York: International Universities Press. (Original work published 1911).

Boatman, D. (2004). Cortical bases of speech perception: evidence from functional lesion studies. *Cognition, 92(1-2),* 47-65. doi:10.1016/j.cognition.2003.09.010

Boder, E., & Jarrico, S. (1982). The Boder test of reading-spelling patterns: A diagnostic screening test for subtypes of reading disability. New York: Grune & Stratton.

Bogen, J.E., & Bogen, G.M. (1969). The other side of the brain III: The corpus callosum and creativity. *Bulletin of the Los Angeles Neurological Societies, 64,* 191-220.

Booth, J.R., Burman, D.D., Meyer, J.R., Gitelman, D.R., Parrish, T.B., & Mesulam, M.M. (2002). Modality Independence of Word Comprehension. *Human Brain Mapping, 16,* 251-261. doi:10.1002/hbm.10054

Bora, E., & Baysan Arabaci, L. (2009). Effect of age and gender on schizotypal personality traits in the normal population. *Psychiatry and Clinical Neurosciences, 63(5),* 663-669. doi:10.1111/j.1440-1819.2009.02011.x

Boutros, N.N., Belger, A., Campbell, D., D'Souza, C., & Krystal, J. (1999). Comparison of four components of sensory gating in schizophrenia and normal subjects: a preliminary report. *Psychiatry Research, 88,* 119-130. doi:10.1016/S0165-1781(99)00074-8

Braff, D. L. (1993). Information processing and attention dysfunctions in schizophrenia. *Schizophrenia Bulletin, 19,* 233-259. doi:10.1093/schbul/19.2.233

Braff, D.L., Geyer, M.A., & Swerdlow, N.R. (2001). Human studies of prepulse inhibition of startle: Normal subjects, patient groups, and pharmacological studies. *Psychopharmacology, 156,* 234-258.doi:10.1007/s002130100810

Bramon, E., Rabe-Hesketh, S., Sham, P., Murray, R.M., & Frangou, S. (2004). Meta-analysis of the P300 and P50 waveforms in schizophrenia. *Schizophrenia Research, 70,* 315-329. doi:10.1016/j.schres.2004.01.004

Braunstein-Bercovitz, H., Rammsayer, T., Gibbons, H., & Lubow, R.E. (2002). Latent inhibition deficits in high-schizotypal normals: symptom-specific or anxiety-related? *Schizophrenia Research, 53,* 109-121. doi:10.1016/S0920-9964(01)00166-9

Brockhaus-Dumke, A., Mueller, R., Faigle, U., & Klosterkoetter, J. (2008). Sensory gating revisited: Relation between brain oscillations and auditory evoked potentials in schizophrenia. *Schizophrenia Research, 99,* 238-249. doi:10.1016/j.schres.2007.10.034

Brockhaus-Dumke, A., Schultze-Lutter, F., Mueller, R., Tendolkar, I., Bechdolf, A., Pukrop, R., . . . Ruhrmann, S. (2008). Sensory Gating in Schizophrenia: P50 and N100 Gating

in Antipsychotic-Free Subjects at Risk, First-Episode, and Chronic Patients. *Biological Psychiatry, 64(5),* 376-384. doi:10.1016/j.biopsych.2008.02.006

Broks, P. (1984). Schizotypy and hemisphere function – II. Performance asymmetry on a verbal divided visual field task. *Personality and Individual Differences, 5,* 649-656.

Brown, L.A., & Cohen, A.S. (2010). Facial emotion recognition in schizotypy: the role of accuracy and social cognitive bias. *Journal of the International Neuropsychological Society, 16,* 474-483. doi:10.1017/S135561771000007X

Brownell, H.H., Simpson, T.L., Bihrie, A.M., Potter, H.H., & Gardner, H. (1990). Appreciation of metaphoric alternative word meanins by left and right brain-damaged patients. *Neuropsychologia, 28(4),* 375-383. doi:10.1016/0028-3932(90)90063-T

Bruder, G., Rabinowicz, E., Towey, J., Brown, A., Kaufmann, C.A., Amador, X., . . . Gorman, J.M. (1995). Smaller Right Ear (Left Hemisphere) Advantage for Dichotic Fused Words in Patients With Schizophrenia. *American Journal of Psychiatry, 152(6),* 932-935. doi:10.1176/ajp.152.6.932

Brugger, P., & Regard, M. (1995). Rorschach inkblots in the peripheral visual fields: enhanced associative quality to the left of fixation. *Journal of Genetic Psychology, 156,* 385-387. doi:10.1080/00221325.1995.9914831

Brüne, M. (2005). Emotion recognition, 'theory of mind,' and social behavior in schizophrenia. Psychiatry Research, 133(2-3), 135-147. doi:10.1016/j.psychres.2004.10.007

Buchanan, R.W., Francis, A., Arango, C., Miller, K., Lefkowitz, D.M., McMahon, R.P., . . . Pearlson, G.D. (2004). Morphometric assessment of the heteromodal association cortex in schizophrenia. *American Journal of Psychiatry, 161,* 322-331. doi:10.1176/appi.ajp.161.2.322

Buchsbaum, M.S., Trestman, R.L., Hazlett, E., Siegel Jr., B.V., Schaefer, C.H., Luu-Hsia, C., . . . Siever, L.J. **(**1997). Regional cerebral blood flow during the Wisconsin Card Sort Test in schizotypal personality disorder. *Schizophrenia Research, 27,* 21-28. doi:10.1016/S0920-9964(97)00081-9

Bullen, J.G., & Hemsley, D.R. (1987). Schizophrenia: A failure to control the contents of consciousness. *British Journal of Psychology, 26,* 25-33. doi:10.1111/j.2044-8260.1987.tb00720.x

Burch, G.S., Pavelis, C., Hemsley, D.R., & Corr, P.J. (2006). Schizotypy and creativity in visual artists. *British Journal of Psychology, 97(2),* 177-190. doi:10.1348/000712605X60030

Burch, G.S., Steel, C., & Hemsley, D.R. (1998). Oxford-Liverpool Inventory of Feelings and Experiences: Reliability in an experimental population. *British Journal of Clinical Psychology, 37(1),* 107-108. doi:10.1111/j.2044-8260.1998.tb01284.x

Burns, J., Bastin, M.E., Whalley, H., Macgillivray, T., Johnstone, E.C., & Lawrie, S.M. (2003). Structural disconnectivity in schizophrenia: a diffusion tensor magnetic resonance imaging study. *The British Journal of Psychiatry,182,* 439-443. doi:10.1192/bjp.182.5.439

Cadenhead, K.S., Geyer, M.A., & Braff, D.L. (1993). Impaired startle prepulse inhibition and habituation in patients with schizotypal personality disorder. *American Journal of Psychiatry, 150,* 1862-1867. doi:10.1176/ajp.150.12.1862

Cadenhead, K.S., Light, G.A., Geyer, M.A., & Braff, D.L. (2000). Sensory Gating Deficits Assessed by the P50 Event-Related Potential in Subjects With Schizotypal Personality Disorder. *American Journal of Psychiatry, 157,* 55-59. doi:10.1176/ajp.157.1.55

Cadenhead, K.S., Light, G.A., Geyer, M.A., McDowell, J.E., & Braff, D.L. (2002). Neurobiological Measures of Schizotypal Personality Disorder: Defining an

Inhibitory Endophenotype? *Americal Journal of Psychiatry, 159,* 869-871. doi:10.1176/appi.ajp.159.5.869

Callicott, J.H., Egan, M.F., Mattay, V.S., Bertolino, A., Bone, A.D., Verchinksi, B., . . . Weinberger, D.R. (2003). Abnormal fMRI response of the dorsolateral prefrontal cortex in cognitively intact siblings of patients with schizophrenia. *American Journal of Psychiatry, 160(4),* 709-719. doi:10.1176/appi.ajp.160.4.709

Camchong, J., MacDonald III, A.W., Bell, C., Mueller, B.A., & Lim, K.O. (2011). Altered Functional and Anatomical Connectivity in Schizophrenia. *Schizophrenia Bulletin, 37(3),* 640-650. doi:10.1093/schbul/sbp131

Cannon, T.D., Kaprio, J., Lonnqvist, J., Huttunen, M., & Koskenvuo, M. (1998). The genetic epidemiology of schizophrenia in a Finnish twin cohort: a population-based modelling study. *Archives of General Psychiatry, 55,* 67-74. doi:10.1001/archpsyc.55.1.67

Cardno, A.G., Marshall, E.J., Coid, B., Macdonald, A.M., Ribchester, T.R., Davies, N.J., . . . Murray, R.M. (1999). Heritability estimates for psychotic disorders: the Maudsley twin psychosis series. *Archives of General Psychiatry, 56,* 162-168. doi:10.1001/archpsyc.56.2.162

Carlin, J.L., & Lindell, A.K. (2015). Schizotypal traits do not influence behavioral asymmetries for language processing in the non-clinical population. *Personality and Individual Differences, 85,* 25-29. doi:10.1016/j.paid.2015.04.037

Carolus, A.M., Schubring, D., Popov, T.G., Popova, P., Miller, G.A., & Rockstroh, B.S. (2014). Function cognitive and cortical abnormalities in chronic and first-admission schizophrenia. *Schizophrenia Research, 157,* 40-47. doi:10.1016/j.schres.2014.05.012

Carson, S.H., Peterson, J.B., & Higgins, D.M. (2003). Decreased latent inhibition is associated with increased creative achievement in high-functioning individuals.

Journal of Personality and Social Psychology, 85, 499-506. doi:10.1037/00223514.85.3.499

Carter, C.S., Robertson, L.C., & Nordahl, T.E. (1992). Abnormal processing of irrelevant information in chronic schizophrenia: selective enhancement of Stroop facilitation. *Psychiatry Research, 41*, 137-146. doi:10.1016/0165-1781(92)90105-C

Castro, A., & Pearson, R. (2011). Lateralisation of language and emotion in schizotypal personality: Evidence from dichotic listening. *Personality and Individual Differences, 51*, 726-731. doi:10.1016/j.paid.2011.06.017

Chan, R.C.K., Di, X., McAlonan, G.M., & Gong, Q.-Y. (2011). Brain Anatomical Abnormalities in High-Risk Individuals, First-Episode, and Chronic Schizophrenia: An Activation Likelihood Estimation Meta-analysis of Illness Progression. *Schizophrenia Bulletin, 37(1),* 177-188. doi:10.1093/schbul/sbp073

Chang, W.-P., Arfken, C.L., Sangal, M.P., & Boutros, N.N. (2011). Probing the relative contribution of the first and second responses to sensory gating indices: A meta-analysis. *Psychophysiology, 48(7),* 980-992. doi:10.1111/j.1469-8986.2010.01168.x

Chapman, H.L., Grimshaw, G.M., & Nicholls, M.E.R. (2011). Going beyond students: An association between mixed-hand preference and schizotypy subscales in a general population. *Psychiatry Research, 187(1-2),* 89-93. doi:10.016/j.psychres.2010.11.019

Chapman, L.J., Chapman, J.P., & Kwapil, T.R. (1995). Scales for the measurement of schizotypy. In A. Raine, T. Lencz, & S.A. Mednick (Eds.), *Schizotypal Personality* (pp. 79-106). New York: Cambridge University Press. doi:10.1017/CBO9780511759031.006

Christoff, K., Gordon, A.M., Smallwood, J., Smith, R., & Schooler, J.W. (2009). Experience sampling during fMRI reveals default network and executive system contributions to

mind wandering. *Proceedings of the National Academy of Sciences, 106(21),* 8719-8724. doi:10.1079/pnas.0900234106

Chua, S.E., & McKenna, P.J. (1995). Schizophrenia – a brain disease? A critical review of structural and functional cerebral abnormality in the disorder. *The British Journal of Psychiatry, 166,* 563-582. doi:10.1192/bjp.166.5.563

Chua, S.E., Cheung, C., Cheung, V., Tsang, J.T.K., Chen, E.Y.H., Wong, J.C.H., . . . McAlonan, G.M. (2007). Cerebral grey, white matter and csf in never-medicated, first-episode schizophrenia. *Schizophrenia Research, 89(1-3),* 12-21. doi:10.1016/j.schres.2006.09.009

Clapham, M.M. (2004). The Convergent Validity of the Torrance Tests of Creative Thinking and Creativity Interest Inventories. *Educational and Psychological Measurement, 64,* 828-841. doi:10.1177/0013164404263883

Claridge, G. (1997). Theoretical background and issues. In G. Claridge (Ed.), *Schizotypy: Implications for illness and health.* Oxford: Oxford University Press.

Claridge, G., & Beech, T. (1995). Fully and quasi-dimensional constructions of schizotypy. In A. Raine, T. Lencz, & S.A. Mednick (Eds.), *Schizotypal Personality,* pp. 192-216. Cambridge: Cambridge University Press. doi:10.1017/CBO9780511759031.010

Claridge, G., & Broks, P. (1984). Schizotypy and hemisphere function – I. *Personality and Individual Differences, 5,* 633-648. doi:10.1016/0191-8869(84)90111-9

Claridge, G., & McDonald, A. (2009). An investigation into the relationships between convergent and divergent thinking, schizotypy, and autistic traits. *Personality and Individual Differences, 46,* 794-799. doi:10.1016/j.paid.2009.01.018

Claridge, G., McCreery, C., Mason, O., Bentall, R., Boyle, G., Slade, P., & Popplewell, D. (1996). The factor structure of 'schizotypal' traits: a large replication study. *British*

Journal of Clinical Psychology, 35, 103-115. doi:10.1111/j.2044-8260.1996.tb01166.x

Clark, D.G., Guiar, B., & Hoffman, P.R. (1985). Reliability of verbal-manual interference. *Brain and Cognition, 4(4),* 486-491. doi:10.1016/0278-2626(85)90036-3

Clementz, B.A., Geyer, M.A., & Braff, D.L. (1998). Poor P50 Suppression Among Schizophrenia Patients and Their First-Degree Biological Relatives. *The American Journal of Psychiatry, 155(12),* 1691-1694. doi:10.1176/ajp.155.12.1691

Cline, V.B., Richards, J.M., & Needham, W.E. (1963). DT tests and achievement in high school science. *Journal of Applied Psychology, 47,* 184-189. doi:10.1037/h0041145

Cobia, D.J., Smith, M.J., Wang, L., & Csernansky, J.G. (2012). Longitudinal progression of frontal and temporal lobe changes in schizophrenia. *Schizophrenia Research, 139(1-3),* 1-6. doi:10.1016/j.schres.2012.05.002

Cochrane, M., Petch, I., & Pickering, A.D. (2012). Aspects of cognitive functioning in schizotypy and schizophrenia: evidence for a continuum model. *Psychiatry Research, 196,* 230-234. doi:10.1016/j.psychres.2012.02.010

Coleman, M.J., Levy, D.L., Lenzenweger, M.F., & Holzman, P.S. (1996). Thought disorder, perceptual aberrations, and schizotypy. *Journal of Abnormal Psychology, 105,* 469-473. doi:10.1037/0021-843X.105.3.469

Coles, M.G.H., & Rugg, M.D. (1995). Event-related brain potentials: an introduction. In M.D. Rugg & M.G.H. Coles (Eds.), *Electrophysiology of mind: Event-related brain potentials and cognitivion.* Oxford, New York: Oxford University Press.

Corballis, P.M., Funnell, M.G., & Gazzaniga, M.S. (2000). An Evolutionary Perspective on Hemispheric Asymmetries. *Brain and Cognition, 43(1-3),* 112-117.

Costa, P.T., & McCrae, R.R. (1992). Normal personality assessment in clinical practice: The NEO Personality Inventory. *Psychological Assessment, 4(1),* 5-13. doi:10.1037/1040-3590.4.1.5

Coughlin, J.M., Ishizuka, K., Kano, S.I., Edwards, J.A., Seifuddin, F.T., Shimano, M.A., . . . Sawa, A. (2013). Marked reduction of soluble superoxide dismutase-1 (SOD1) in cerebrospinal fluid of patients with recent-onset schizophrenia. *Molecular Psychiatry, 18,* 10-11. doi:10.1038/mp.2012.6

Covington, M.A., He, C., Brown, C., Naçi, L., McClain, J.T., Fjordback, B.S., . . . Brown, J. (2005). Schizophrenia and the structure of language: The linguist's view. *Schizophrenia Research, 77(1),* 85-98. doi:10.1016/j.schres.2005.01.016

Cox, A.J., & Leon, J.L. (1999). Negative Schizotypal Traits in the Relation of Creativity to Psychopathology. *Creativity Research Journal, 12(1),* 25-36. doi:10.1027/s15326934crj1201_4

Cramond, B., Matthews-Morgan, J., Bandalos, D., & Zuo, L. (2005). A Report on the 40 Year Follow-Up of the Torrance Tests of Creative Thinking: Alive and Well in the New Millennium. *Gifted Child Quarterly, 49(4),* 283-291. doi:10.1177/001698620504900402

Croft, R.J., Dimoska, A., Gonsalvez, C.J., & Clarke, A.R. (2004). Suppression of P50 evoked potential component, schizotypal beliefs and smoking. *Psychiatry Research, 128,* 53-62. doi:10.1016/j.psychres.2004.05.009

Croft, R.J., Lee, A., Bertolot, J., & Gruzelier, J.H. (2001). Associations of P50 Suppression and Desensitization with Perceptual and Cognitive Features of "Unreality" in Schizotypy. *Biological Psychiatry, 50,* 441-446. doi:10.1016/S0006-3223(01)01082-4

Crow, T.J. (1990). Temporal Lobe Asymmetries as the Key to the Etiology of Schizophrenia. *Schizophrenia Bulletin, 16(3),* 432-443. doi:10.1093/schbul/16.3.433

Crow, T.J. (1997). Is schizophrenia the price that *Homo sapiens* pays for language? *Schizophrenia Research, 28,* 127-141. doi:10.1016/S0920-9964(97)00110-2

Crow, T.J. (2008). The 'big bang' theory of the origin of psychosis and the faculty of language. *Schizophrenia Research, 102(1-3),* 31-52. doi:10.1016/j.schres.2008.03.010

Cuesta, M.J., Ugarte, M.D., Goicoa, T., Eraso, S., & Peralta, V. (2007). A taxometric analysis of schizophrenia symptoms. *Psychiatry Research, 150(3),* 245-253. doi:10.1016/j.psychres.2006.01.019

Damoiseaux, J.S., Rombouts, S.A.R.B., Barkhof, F., Sheltens, P., Stam, C.J., Smith, S.M., & Beckmann, C.F. (2006). Consistent resting-state networks across healthy subjects. *Proceedings of the National Academy of Sciences of the United States of America, 103(37),* 13848-13853. doi:10.1073/pnas.0601417103

Danion, J.-M., Rizzo, L., & Bruant, A. (1999). Functional Mechanisms Underlying Impaired Recognition Memory and Conscious Awareness in Patients With Schizophrenia. *Archives of General Psychiatry, 56(7),* 639-644. doi:10.1001/archpsyc.56.7.639

Daskalakis, Z.J., & Fitzgerald, P.B. (2002). Evidence for Impaired Cortical Inhibition in Schizophrenia Using Transcranial Magnetic Stimulation. *Archives of General Psychiatry, 59,* 347-354. doi:10.1001/archpsyc.59.4.347

De la Casa, L.G., & Ruiz, G., & Lubow, R.E. (1993). Latent inhibition and recall/recognition of irrelevant stimuli as a function of preexposure duration in high and low psychotic-prone normal subjects. *British Journal of Psychology, 84,* 119-132. doi:10.1111/j.2044-8295.1993.tb02467.x

de Manzano, Ö, & Ullén, F. (2012). Goal-independent mechanisms for free response generation: Creative and pseudo-random performance share neural substrates. *NeuroImage, 59(1),* 772-780. doi:10.1016/j.neuroimage.2011.07.016

de Souza, L.C., Volle, E., Bertoux, M., Czernecki, V., Funkiewiez, A., Allali, G., . . . Levy, R. (2010). Poor creativity in frontotemporal dementia: A window into the neural bases of the creative mind. *Neuropsychologia, 48(13),* 3733-3742. doi:10.1016/j.neuropsychologia.2010.09.010

Debbané, M., Eliez, S., Badoud, B., Conus, P., Flückiger, R., & Schultze-Lutter, F. (2014). Developing Psychosis and Its Risk States Through the Lens of Schizotypy. *Schizophrenia Bulletin.* Advance online publication. doi:10.1093/schbul/sbu176

DeLisi, L.E. (2001). Speech Disorder in Schizophrenia: Review of the Literature and Exploration of Its Relation to the Uniquely Human Capacity for Language. *Schizophrenia Bulletin, 27(3),* 481-496. doi:10.1093/oxfordjournals.schbul.a006889

DeRosse, P., Nitzburg, G.C., Ikuta, T., Peters, B.D., Malhotra, A.K., & Szeszko, P.R. (2015). Evidence From Structural and Diffusion Tensor Imaging for Frontotemporal Deficits in Psychometric Schizotypy. *Schizophrenia Bulletin, 41(1),* 104-114. doi:10.1093/schbul/sbu150

Dias, R., Robbins, T.W., & Roberts, A.C. (1996). Dissociation in prefrontal cortex of affective and attentional shifts. *Nature, 380,* 69-72. doi:10.1038/380069a0

Dickey, C.C., McCarley, R.W., & Shenton, M.E. (2002). The Brain in Schizotypal Personality Disorder: A Review of Structural MRI and CT Findings. *Harvard Review of Psychiatry, 10,* 1-15. doi:10.1080/10673220216201

Dietrich, A. (2004). The cognitive neuroscience of creativity. *Psychonomic Bulletin & Review, 11(6),* 1011-1026. doi:10.3758/BF03196731

Diforio, D., Walker, E.F., & Kestler, L.P. (2000). Executive functions in adolescents with schizotypal personality disorder. *Schizophrenia Research, 42,* 125-134. doi:10.1016/S0920-9964(99)00119-X

Dinn, W.M., Harris, C.L., Aycicegi, A., Greene, P., & Andover, M.S. (2002). Positive and negative schizotypy in a student sample: neurocognitive and clinical correlates. *Schizophrenia Research, 56,* 171-185. doi:10.1016/S0920-9964(01)00230-4

Dollfus, S., Razafimandimby, A., Delamillieure, P., Brazo, P., Joliot, M., Mazoyer, B., & Tzourio-Mazoyer, N. (2005). Atypical hemispheric specialization for language in right-handed schizophrenia patients. *Biological Psychiatry, 57,* 1020-1028. doi:10.1016/j.biopsych.2005.01.009

Drago, V., Foster, P.S., Skidmore, F.M., & Heilman, K.M. (2009). Creativity in Parkinson's disease as a function of right versus left hemibody onset. *Journal of Neurological Sciences, 276(1-2),* 179-183. doi:10.1016/j.jns.2008.09.026

Edell, W.S. (1987). Role of structure in disordered thinking in borderline and schizophrenic disorders. *Journal of Personality Assessment, 51,* 23-41. doi:10.1207/s15327752jpa5101_3

Edgar, J.C., Huang, M.X., Weisend, M.P., Sherwood, A., Miller, G.A., Adler, L.E., & Cañive, J.M. (2003). Interpreting abnormality: an EEG and MEG study of P50 and the auditory paired-stimulus paradigm. *Biological Psychology, 65(1),* 1-20. doi:10.1016/S0301-0511(03)00094-2

Efron, B., & Tibshirani, R. (1985). The bootstrap method for assessing statistical accuracy. *Behaviormetrika, 17,* 1-35. doi:10.2333/bhmk.12.17_1

Eickhoff, S., Stephan, K.E., Mohlberg, H., Grefkes, C., Fink, G.R., Amunts, K., & Zillies, K. (2005). A new SPM toolbox for combining probabilistic cytoarchitectonic maps and functional imaging data. *NeuroImage, 25(4),* 1325-1335. doi:10.1016/j.neuroimage.2004.12.034

Ellamil, M., Dobson, C., Beeman, M., & Christoff, K. (2012). Evaluative and generative modes of thought during the creative process. *NeuroImage, 59,* 1783-1794. doi:10.1016/j.neuroimage.2011.08.008

Engh, J.A., Friis, S., Birkenaes, A.B., Jónsdóttir, H., Klungsøyr, O., Ringen, P.A., . . . Andreassen, O.A. (2010). Delusions Are Associated With Poor Cognitive Insight in Schizophrenia. *Schizophrenia Bulletin, 36(4),* 830-835. doi:10.1093/schbul/sbn193

Ettinger, U., Kumari, V., Crawford, T.J., Flak, V., Sharma, T., Davis, R.E., & Corr, P.J. (2005). Saccadic eye movements, schizotypy, and the role of neuroticism. *Biological Psychology, 68(1),* 61-78. doi:10.1016/j.biopsycho.2004.03.014

Ettinger, U., Meyhöfer, I., Steffens, M., Wagner, M., & Koutsouleris, N. (2014). Genetics, cognition, and neurobiology of schizotypal personality: a review of the overlap with schizophrenia. *Frontiers in Psychiatry, 5(18),* 1-16. doi:10.3389/fpsyt.2014.00018

Ettinger, U., Williams, S.C.R., Meisenzahl, E.V., Möller, H.-J., Kumari, V., & Koutsouleris, N. (2012). Association between brain structure and psychometric schizotypy in healthy individuals. *The World Journal of Biological Psychiatry, 13(7),* 544-549. doi:10.3109/15622975.2011.559269

Evans, L.H., Gray, N.S., & Snowden, R.J. (2007). Reduced P50 suppression is associated with the cognitive disorganisation dimension of schizotypy. *Schizophrenia Research, 97,* 152-162. doi:10.1016/j.schres.2007.07.019

Eysenck, H.J. (1993). Creativity and personality: suggestions for a theory. *Psychological Inquiry, 4,* 147-178. doi:10.1207/s15327965pli0403_1

Eysenck, H.J., & Furnham, A. (1993). Personality and the Barron-Welsh Art Scale. *Psychological Reports, 76,* 837-838. doi:10.2466/pms.1993.76.3.837

Eysenck, S.B.G., Eysenck, H.J., & Barrett, P. (1985). A revised version of the psychoticism scale. *Personality and Individual Differences, 6(1),* 21-29. doi:10.1016/0191-8869(85)90026-1

Fanous, A., Gardner, C., Walsh, D., & Kendler, K.S. (2001). Relationship Between Positive and Negative Symptoms of Schizophrenia and Schizotypal Symptoms in Nonpsychotic Relatives. *Archives of General Psychiatry, 58,* 669-673. doi:10.1001/archpsyc.58.7.669

Fanous, A., Neale, M.C., Gardner, C.O., Webb, B.T., Straub, R.E., O'Neill, F.A., . . . Kendler, K.S. (2007). Significant correlation in linkage signals from genome-wide scans of schizophrenia and schizotypy. *Molecular Psychiatry, 12,* 958-965. doi:10.1038/sj.mp.4001996

Fenton, W.S., & McGlashan, T.H. (1991). Natural History of Schizophrenia SubtypesII. Positive and Negative Symptoms and Long-term Course. *Archives of General Psychiatry, 48(11),* 978-986. doi:10.1001/archpsyc.1991.01810350018003.

Fernandes-Taylor, S., Hyun, J.K., Reeder, R.N., & Harris, A.H.S. (2011). Common statistical and research design problems in manuscripts submitted to high-impact medical journals. *BMC Research Notes, 4,* 304. doi:10.1186/1756-0500-4-304

Fink, A., Grabner, R.H., Benedek, M., Reishofer, G., Hauswirth, V., Fally, M., . . . Neubauer, A.C. (2009). The creative brain: investigation of brain activity during creative problem solving by means of EEG and fMRI. *Human Brain Mapping, 30,* 734-748. doi:10.1002/hbm.20538

Fink, A., Weber, B., Koschutnig, K., Benedek, M., Reishofer, G., Ebner, F., . . . Weiss, E.M. (2014). Creativity and schizotypy from the neuroscience perspective. *Cognitive, Affective, & Behavioral Neurocience, 14(1),* 378-387. doi:10.3758/s13415-013-0210-6

Fisher, J.E., Heller, W., & Miller, G.A. (2013). Neuropsychological differentiation of adaptive creativity and schizotypal cognition. *Personality and Individual Differences, 54(1),* 70-75. doi:10.1016/j.paid.2012.08.003

Fisher, J.E., Mohanty, A., Herrington, J.D., Koven, N.S., Miller, G.A., & Heller, W. (2004). Neuropsychological evidence for dimensional schizotypy: Implications for creativity and psychopathology. *Journal of Research in Personality, 38(1),* 24-31. doi:10.1016/j.jrp.2003.09.014

Flaherty, A.W. (2005). Frontotemporal and Dopaminergic Control of Idea Generation and Creative Drive. *The Journal of Comparative Neurology, 493,* 147-153. doi:10.1002/cne.20768

Floden, D., Vallesi, A., & Stuss, D.T. (2011). Task Context and Frontal Lobe Activation in the Stroop Task. *Journal of Cognitive Neuroscience, 23(4),* 867-879. doi:10.1162/jocn.2010.21492

Folley, B.S., & Park, S. (2005). Verbal creativity and schizotypal personality in relation to prefrontal hemispheric laterality: A behavioural and near-infrared optical imaging study. *Schizophrenia Research, 80(2-3),* 271-282. doi:10.1016/j.schres.2005.06.016

Folstein, J.R., & Van Petten, C. (2008). Influence of cognitive control and mismatch on the N2 component of the ERP: A review. *Psychophysiology, 45,* 152-170. doi:10.1111/j.1469-8986.2007.00602.x

Fonseca-Pedrero, E., Paíno, M., Lemos-Giráldez, García-Cueto, E., Campillo-Álvarez, A., Villazón-García, & Muñiz, J. (2008). Schizotypy assessment: State of the art and future prospects. *International Journal of Clinical and Health Psychology, 8(2),* 577-593.

Ford, J.M., Mathalon, D.H., Whitfield, S., Faustman, W.O., & Roth, W.T. (2002). Reduced communication between frontal and temporal lobes during talking in schizophrenia. *Biological Psychiatry, 51(6),* 485-492. doi:10.1016/S0006-3223(01)01335-X

Fossati, A., Raine, A., Carretta, I., Leonardi, B., & Maffei, C. (2003). The three-factor model of schizotypal personality: invariance across age and gender. *Personality and Individual Differences, 35(5),* 1007-1019. doi:10.1016/S0191-8869(02)00314-8

Freedman, R., Adler, L.E., & Leonard, S. (1999). Alternative phenotypes for the complex genetics of schizophrenia. *Biological Psychiatry, 45,* 551-558. doi:10.1016/S0006-3223(98)00321-7

Fries, P. (2005). A mechanism for cognitive dynamics: neuronal communication through neuronal coherence. *Trends in Cognitive Sciences, 9(10),* 474-480. doi:10.1016/j.tics.2005.08.011

Friston, K.J. (1998). The disconnection hypothesis. *Schizophrenia Research, 30(2),* 115-125. doi:10.1016/S0920-9964(97)00140-0

Friston, K.J., Holmes, A.P., Worsley, K.J., Poline, J.-P., Frith, C.D., & Frackowiak, R.S.J. (1994). Statistical parametric maps in function imaging: A general linear approach. *Human Brain Mapping, 2(4),* 189-210. doi:10.1002/hmb.460020402

Frith, C.D. (1979). Consciousness, information processing and schizophrenia. *The British Journal of Psychiatry, 134,* 225-235. doi:10.1192/bjp.134.3.225

Fuerst, D.R., Gallinat, J., & Boutros, N.N. (2007). Range of sensory gating values and test-retest reliability in normal subjects. *Psychophysiology, 44,* 620-626. doi:10.1111/j.1469-8986.2007.00524.x

Furnham, A., & Bachtiar, V. (2008). Personality and intelligence as predictors of creativity. *Personality and Individual Differences, 45,* 613-617. doi:10.1016/j.paid.2008.06.023

Furnham, A., Batey, M., Anand, K., & Manfield, J. (2008). Personality, hypomania, intelligence and creativity. *Personality and Individual Differences, 44,* 1060-1069. doi:10.1016/j.paid.2007.10.035

Fusar-Poli, P., & Politi, P. (2008). Images in Psychiatry: Paul Eugen Bleuler and the Birth of Schizophrenia (1908). *The American Journal of Psychiatry, 165(11),* 1407. doi:10.1176/appi.ajp.2008.08050714

García-Martí, G., Aguilar, E.J., Lull, J.J., Martí-Bonmatí, L., Escartí, M.J., Manjón, J.V., . . . Sanjuán, J. (2008). Schizophrenia with auditory hallucinations: A voxel-based morphometry study. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 32(1),* 72-80. doi:10.1016/j.pnpbp.2007.07.014

Gaser, C., Nenadic, I., Buchsbaum, B.R., Hazlett, E.A., & Buchsbaum, M.S. (2004). Ventricular Enlargement in Schizophrenia Related to Volume Reduction of the Thalamus, Striatum, and Superior Temporal Cortex. *The American Journal of Psychiatry, 161(1),* 154-156. doi:10.1176/appi.ajp.161.1.154

Gaser, C., Nenadic, I., Volz, H.-P., Büchel, C., & Sauer, H. (2004). Neuroanatomy of 'Hearing Voices': A Frontotemporal Brain Structural Abnormality Associated with Auditory Hallucinations in Schizophrenia. *Cerebral Cortex, 14(1),* 91-96. doi:10.1093/cercor/bhg107

Giakoumaki, S.G. (2012). Cognitive and Prepulse Inhibition Deficits in Psychometrically High Schizotypal Subjects in the General Population: Relevance to Schizophrenia Research. *Journal of the International Neuropsychological Society, 18,* 643-656. doi:10.1017/S135561771200029X

Gibson, C., Folley, B.S., & Park, S. (2009). Enhanced divergent thinking and creativity in musicians: A behavioral and near-infrared spectroscopy study. *Brain and Cognition, 69,* 162-169. doi:10.1016/j.bandc.2008.07.009

Gilboa, A., Ramirez, J., Köhler, S., Westmacott, R., Black, S.E., & Moscovitch, M. (2005). Retrieval of autobiographical memory in Alzheimer's disease: Relation to volumes of medial temporal lobe and other structures. *Hippocampus, 15(4),* 535-550. doi:10.1002/hipo.20090

Glahn, D.C., Laird, A.R., Ellison-Wright, I., Thelen, S.M., Robinson, J.L., Lancaster, J.L., . . . Fox, P.T. (2008). Meta-Analysis of Gray Matter Anomalies in Schizophrenia: Application of Anatomic Likelihood Estimation and Network Analysis. *Biological Psychiatry, 64,* 774-781. doi:10.1016/j.biopsyh.2008.03.031

Goel, V., & Vartanian, O. (2005). Dissociating the roles of right ventral lateral and dorsal lateral prefrontal cortex in generation and maintenance of hypotheses in set-shift problems. *Cerebral Cortex, 15(8),* 1170-1177. doi:10.1093/cercor/bhh217

Good, C.D., Johnsrude, I., Ashburner, J., Henson, R.N.A., Friston, K.J., & Frackowiak, R.S.J. (2001). Cerebral Asymmetry and the Effects of Sex and Handedness on Brain Structure: A Voxel-Based Morphometric Analysis of 465 Normal Adult Human Brains. *NeuroImage, 14(3),* 685-700. doi:10.1006/nimg.2001.0857

Gooding, D.C., & Braun, J.G. (2004). Visuoconstructive performance, implicit hemispatial inattention, and schizotypy. *Schizophrenia Research, 68,* 261-269. doi:10.1016/S0920-9964(03)00157-9

Gottesman, I.I., & Gould, T.D. (2003). The Endophenotype Conecpt in Psychiatry: Etymology and Strategic Intentions. The American Journal of Psychiatry, 160(4), 636-645. doi:10.1176/appi.ajp.160.4.636

Goulding, A. (2004). Schizotypy models in relation to subjective health and paranormal beliefs and experiences. *Personality and Individual Differences, 37(1),* 157-167. doi:10.1016/j.paid.2003.08.008

Grady, C.L., McIntosh, A.R., Beig, S., Keightley, M.L., Burian, H., & Black, S.E. (2003). Evidence from Functional Neuroimaging of a Compensatory Prefrontal Network in Alzheimer's Disease. *The Journal of Neuroscience, 23(3),* 986-993.

Grady, C.L., Protzner, A.B., Kovacevic, N., Strother, S.C., Afshin-Pour, B., Wojtowicz, M., . . . McIntosh, A.R. (2010). A Multivariate Analysis of Age-Related Differences in Default Mode and Task-Positive Networks across Multiple Cognitive Domains. *Cerebral Cortex, 20(6),* 1432-1447. doi:10.1093/cercor/bhp207

Granger, K.T., Prados, J., & Young, A.M.J. (2012). Disruption of overshadowing and latent inhibition in high schizotypy individuals. *Behavioural Brain Research, 233(1),* 201-208. doi:10.1016/j.bbr.2012.05.003

Grimshaw, G.M., Yelle, S.K., Schoger, J., & Bright, K.S. (2008). Magical ideation is related to questionnaire but not behavioural measures of handedness. *Laterality, 13(1),* 22-33. doi:10.1080/13576500701508539

Gruzelier, J.H. (1996). The factorial structure of schizotypy: Part I. Affinities with syndromes of schizophrenia. *Schizophrenia Bulletin, 22,* 611-620. doi:10.1093/schbul/22.4.611

Gruzelier, J.H., Croft, R.J., Kaiser, J., & Burgess, A. (2000). Personality Syndrome Questionnaire (PSQ): Reliability, validity and experimental evidence. *International Journal of Psychophysiology,* accepted for publication.

Guilford, J.P. (1967). *The nature of human intelligence.* New York, US: McGraw-Hill.

Gupta, C.N., Calhoun, V.D., Rachakonda, S., Chen, J., Patel, V., Liu, J., . . . Turner, J.A. (2014). Patterns of Gray Matter Abnormalities in Schizophrenia Based on an International Mega-analysis. *Schizophrenia Bulletin.* Advance online publication. doi:10.1093/schbul/sbu177

Gur, R.E., & Chin, S. (1999). Laterality in Functional Brain Imaging Studies of Schizophrenia. *Schizophrenia Bulletin, 25(1),* 141-156.

doi:10.1093/oxfordjournals.schbul.a033361

Gur, R.E., McGrath, C., Chan, R.M., Schroeder, L., Turner, T., Turetsky, B.I., . . . Gur, R.C. (2002). An fMRI Study of Facial Emotion Processing in Patients With Schizophrenia. *American Journal of Psychiatry, 159,* 1992-1999. doi:10.1176/appi.ajp.159.12.1992

Gut-Fayand, A., Dervaux, A., Olié, J.-P., Poirier, M.-F., & Krebs, M.-O. (2001). Substance abuse and suicidality in schizophrenia: a common risk factor linked to impulsivity. *Psychiatry Research, 102(1),* 65-72. doi:10.1016/S0165-1781(01)00250-5

Ha, T.H., Youn, T., Ha, K.S., Rho, K.S., Lee, J.M., Kim, I.Y., . . . Kwon, J.S. (2004). Gray matter abnormalities in paranoid schizophrenia and their clinical correlations. *Psychiatry Research: Neuroimaging, 132,* 251-260. doi:10.1016/j.pscychresns.2004.05.001

Haier, R.J., Siegel, B.V., Nuechterlein, K.H., Hazlett, E., Wu, J.C., Paek, J., . . . Buchsbaum, M.S. (1988). Cortical glucose metabolic rate correlates of abstract reasoning and attention studies with positron emission tomography. *Intelligence, 12,* 199-217. doi:10.1016/0160-2896(88)90016-5

Haijma, S.V., Van Haren, N., Cahn, W., Koolschijn, P.C.M.P., Hulshoff Pol, H.E., & Kahn, R.S. (2013). Brain Volumes in Schizophrenia: A Meta-Analysis in Over 18 000 Subjects. *Schizophrenia Bulletin, 39(5),* 1129-1138. doi:10.1093/schbul/sbs118

Hale, T.S., Zaidel, E., McGough, J.J., Phillips, J.M., & McCracken, J.T. (2006). Atypical brain laterality in adults with ADHD during dichotic listening for emotional intonation and words. *Neuropsychologia, 44(6),* 896-904. doi:10.1016/j.neuropsychologia.2005.08.014

Hall, M.H., Schulze, K., Rijsdijk, F., Picchioni, M., Ettinger, U., Bramon, E., . . . Sham, P. (2006). Heritability and Reliability of P300, P50 and Duration Mismatch Negativity. *Behavior Genetics, 36,* 845-857. doi:10.1007/s10519-006-9091-6

Hall, M.H., Taylor, G., Salisbury, D.F., & Levy, D.L. (2011). Sensory Gating Event-Related Potentials and Oscillations in Schizophrenia Patients and Their Unaffected Relatives. *Schizophrenia Bulletin, 37(6),* 1187-1199. doi:10.1093/schbul/sbq027

Ham, T., Leff, A., de Boissezon, X., Joffe, A., & Sharp, D.J. (2013). Cognitive Control and the Salience Network: An Investigation of Error Processing and Effective Connectivity. *The Journal of Neuroscience, 33(16),* 7091-7098. doi:10.1523/jneurosci.4692-12.2013

Hampshire, A., & Owen, A.M. (2006). Fractionating Attentional Control Using Event-Related fMRI. *Cerebral Cortex, 16,* 1679-1689. doi:10.1093/cercor/bhj116

Hanlon, F.M., Houck, J.M., Klimaj, S.D., Caprihan, A., Mayer, A.R., Welsend, M.P., . . . Tesche, C.D. (2012). Frontotemporal anatomical connectivity and working-relational memory performance predict everyday functioning in schizophrenia. *Psychophysiology, 49(10),* 1340-1352. doi:10.1111/j.1469-8986.2012.01448.x

Hazlett, E.A., Buchsbaum, M.S., Byne, W., Wei, T.-C., Spiegel-Cohen, J., Geneve, C., . . . Siever, L.J. (1999). Three-Dimensional Analysis With MRI and PET of the Size, Shape, and Function of the Thalamus in the Schizophrenia Spectrum. *The American Journal of Psychiatry, 156(8),* 1190-1199.

Hazlett, E.A., Buchsbaum, M.S., Haznedar, M.M., Newmark, R., Goldstein, K.E., Zelmanova, Y., . . . Siever, L.J. (2008). Cortical gray and white matter volume in unmedicated schizotypal and schizophrenia patients. *Schizophrenia Research, 101(1-3),* 111-123. doi:10.1016/j.schres.2007.12.472

Hazlett, E.A., Goldstein, K.E., & Kolaitis, J.C. (2012). A Review of Structural MRI and Diffusion Tensor Imaging in Schizotypal Personality Disorder. *Current Psychiatry Reports, 14(1),* 70-78. doi:10.1007/s11920-011-0241-z

Hazlett, E.A., Rothstein, E.G., Rerreira, R., Silverman, J.M., Siever, L.J., & Olincy, A. (2015). Sensory gating disturbances in the spectrum: Similarities and differences in schizotypal personality disorder and schizophrenia. *Schizophrenia Research, 161(2-3),* 283-290. doi:10.1016/j.schres.2014.11.020

Heilman, K.M., Nadeau, S.E., & Beversdorf, D.O. (2003). Creative innovation: possible brain mechanisms. *Neurocase, 9,* 369-379. doi:10.1076/neur.9.5.369.16553

Heishman, S., Taylor, R., & Henningfield, J. (1994). Nicotine and smoking: a review of effects on human performance. *Experimental Clinical Psychopharmacology, 2,* 345-395. doi:10.1037/1064-1297.2.4.345

Herzig, D.A., Sullivan, S., Lewis, G., Corcoran, R., Drake, R., Evans, J., . . . Mohr, C. (2015). Hemispheric Language Asymmetry in First Episode Psychosis and Schizotypy: The Role of Cannabis Consumption and Cognitive Disorganization. *Schizophrenia Bulletin, 42(S2),* S455-S464. doi:10.1093/schbul/sbu179

Herzig, D.A., Tracy, J., Munafò, M., & Mohr, C. (2010). The influence of tobacco consumption on the relationship between schizotypy and hemispheric asymmetry. *Journal of Behavior Therapy and Experimental Psychiatry, 41,* 397-408. doi:10.1016/j.btep.2010.04.003

Heston, L.L. (1966). Psychiatric Disorders in Foster Home Reared Children of Schizophrenic Mothers. *The British Journal of Psychiatry, 112,* 819-825. doi:10.1192/bjp.112.489.819

Hillyard, S.A., & Anllo-Vento, L. (1998). Event-related brain potential in the study of visual selective attention. *Proceedings of the National Academy of Sciences of the United States of America, 95(3),* 781-787. doi:10.1073/pnas.95.3.781

Hirayasu, Y., Shenton, M.E., Salisbury, D.F., Dickey, C.C., Fischer, I.A., Mazzoni, P., . . . McCarley, R.W. (1998). Lower Left Temporal Lobe MRI Volumes in Patients With

First-Episode Schizophrenia Compared With Psychotic Patients With First-Episode Affective Disorder and Normal Subjects. *The American Journal of Psychiatry, 155(10),* 1384-1391. doi:10.1176/ajp.155.10.1384

Hirnstein, M., & Hugdahl, K. (2014). Excess of non-right-handedness in schizophrenia: meta-analysis of gender effects and potential biases in handedness assessment. *The British Journal of Psychiatry, 205,* 260-267. doi:10.1192/bjp.bp.113.137349

Ho, B.-C., Andreasen, N.C., Ziebell, S., Pierson, R., & Magnotta, V. (2011). Long-term Antipsychotic Treatment and Brain Volumes: A Longitudinal Study of First-Episode Schizophrenia. *Archives of General Psychiatry, 68(2),* 128-137. doi:10.1001/archgenpsychiatry.2010.199

Hoffman, R.E., Rapaport, J., Mazure, C.M., & Quinlan, D.M. (1999). Selective Speech Perception Alterations in Schizophrenic Patients Reporting Hallucinated "Voices". *American Journal of Psychiatry, 156,* 393-399.

Holt, N.J., Simmonds-Moore, C.A., & Moore, S.L. (2008). Benign schizotypy: Investigating differences between clusters of schizotypy on paranormal belief, creativity, intelligence and mental health. *The Parapsychological Association 51st Annual Convention, Proceedings of Presented Papers* (pp.82-96), August 13-17, 2008, Winchester.

Honea, R., Crow, T.J., Passingham, D., & Mackay, C.E. (2005). Regional Deficits in Brain Volume in Schizophrenia: A Meta-Analysis of Voxel-Based Morphometry Studies. *The American Journal of Psychiatry, 162(12),* 2233-2245. doi:10.1176/appi.ajp.162.12.2233

Honig, A., Romme, M.A.J., Ensink, B.J., Escher, S., Pennings, M.H.A., & Devries, M.W. (1998). Auditory Hallucinations: A Comparison between Patients and Nonpatients.

Journal of Nervous and Mental Disease, 186(10), 646-651. doi:10.1097/00005053-199810000-00009

Hoptman, M.J., Ardekani, B.A., Butler, P.D., Nierenburg, J., Javitt, D.C., & Lim, K.O. (2004). DTI and impulsivity in schizophrenia: a first voxelwise correlational analysis. *NeuroReport, 15(16),* 2467-2470. doi:10.1097/00001756-200411150-00007

Hori, H., Nagamine, M., Soshi, T., Okabe, S., Kim, Y., & Kunugi, H. (2008). Schizotypal Traits in Healthy Women Predict Prefrontal Activation Patterns during a Verbal Fluency Task: A Near-Infrared Spectroscopy Study. *Neuropsychobiology, 57,* 61-69. doi:10.1159/000129669

Hori, H., Ozeki, Y., Terada, S., & Kunugi, H. (2008). Functional near-infrared spectroscopy reveals altered hemispheric laterality in relation to schizotypy during verbal fluency task. *Progress in Neuro-Psychopharmacology & Biological Psychiatry, 32,* 1944-1951. doi:10.1016/j.pnpbp.2008.09.019

Hori, H., Teraishi, T., Sasayama, D., Matsuo, J., Kinoshita, Y., Ota, M., . . . Kunugi, H. (2014). A latent profile analysis of schizotypy, temperament and character in a nonclinical population: Association with neurocognition. *Journal of Psychiatric Research, 48,* 56-64. doi:10.1016/j.jpsychires.2013.10.006

Horrobin, D. (2001). The Madness of Adam and Eve: How Schizophrenia Shaped Humanity. London: Transworld Publishers.

Houston, R.J., & Stanford, M.S. (2001). Mid-latency evoked potentials in self-reported impulsive aggression. *International Journal of Psychophysiology, 40,* 1-15. doi:10.1016/S0167-8760(00)00120-3

Howard-Jones, P.A., Blakemore, S.J., Samuel, E.A., Summers, I.R., & Claxton, G. (2005). Semantic divergence and creative story generation: an fMRI investigation. *Cognitive Brain Research, 25(1),* 240-250. doi:10.1016/j.cogbrainres.2005.05.013

Huettel, S.A., Song, A.W., & McCarthy, G. (2009). *Function Magnetic Resonance Imaging*, (2nd Ed.). Massachusetts: Sinauer Associates.

Hugdahl, K. (2011). Fifty years of dichotic listening research – Still going and going and. . . *Brain and Cognition, 76,* 211-213. doi:10.1016/j.bandc.2011.03.006

Hugdahl, K., Løberg, E.-M., Falkenberg, L.E., Johnsen, E., Kompus, K., Kroken, R.A., . . . Özgören, M. (2012). Auditory verbal hallucinations in schizophrenia as aberrant lateralized speech perception: Evidence from dichotic listening. *Schizophrenia Research, 140(1-3),* 59-64. doi:10.1016/j.schres.2012.06.019

Hughes, D.J., Furnham, A., & Batey, M. (2013). The structure and personality predictors of self-rated creativity. *Thinking Skills and Creativity, 9,* 76-84. doi:10.1016/j.tsc.2012.10.001

Hulshoff Pol, H.E., & Kahn, R.S. (2008). What Happens After the First Episode? A Review of Progressive Brain Changes in Chronically Ill Patients With Schizophrenia. *Schizophrenia Bulletin, 34(2),* 354-366. doi:10.1093/schbul/sbm168

Humphrey, M.K., Bryson, F.M., & Grimshaw, G.M. (2010). Metaphor processing in high and low schizotypal individuals. *Psychiatry Research, 178,* 290-294. doi:10.1016/j.psychres.2009.06.002

Hurst, R.M., Mitchell, J.T., Kimbrel, N.A., Kwapil, T.K., & Nelson-Gray, R.O. (2007). Examination of the reliability and factor structure of the Autism Spectrum Quotient (AQ) in a non-clinical sample. Personality and Individual Differences, 43(7), 1938-1949. doi:10.1016/j.paid.2007.06.012

Huxley, J., Mayr, E., Osmond, H., & Hoffer, A. (1964). Schizophrenia as a genetic morphism. *Nature, 204,* 220-221. doi:10.1038/204220a0

Israel, S.L., Seibert, T.M., Black, M.L., & Brewer, J.B. (2010). Going Their Separate Ways: Dissociation of Hippocampal and Dorsolateral Prefrontal Activation during Episodic

Retrieval and Post-retrieval Processing. *Journal of Cognitive Neuroscience, 22(3),* 513-525. doi:10.1162/jocn.2009.21198

Jahanshahi, M., Profice, P., Brown, R.G., Ridding, M.C., Dirnberger, G., & Rothwell, J.C. (1998). The effects of transcranial magnetic stimulation over the dorsolateral prefrontal cortex on suppression of habitual counting during random number generation. *Brain: A Journal of Neurology, 121(8),* 1533-1544. doi:10.1093/brain/121.8.1533

Jahshan, C.S., & Sergi, M.J. (2007). Theory of mind, neurocognition, and functional status in schizotypy. *Schizophrenia Research, 89,* 278-286. doi:10.1016/j.schres.2006.09.004

Jansma, J.M., Ramsey, N.F., van der Wee, N.J.A., & Kahn, R.S. (2004). Working memory capacity in schizophrenia: a parametric fMRI study. *Schizophrenia Research, 68,* 159-171. doi:10.1016/S0920-9964(03)00127-0

Jarvick, L.F., & Chadwick, S.B. (1972). Schizophrenia and survival. In S.B. Hammer, K. Salzinger & A. Sutton (Eds.), *Psychopathology.* New York: Wiley.

Jauk, E., Benedek, M., Dunst, B., & Neubauer, A.C. (2013). The relationship between intelligence and creativity: New support for the threshold hypothesis by means of empirical breakpoint detection. *Intelligence, 41(4),* 212-221. doi:10.1016/j.intell.2013.03.003

Javitt, D.C., & Freedman, R. (2015). Sensory Processing Dysfunction in the Personal Experience and Neuronal Machinery of Schizophrenia. *The American Journal of Psychiatry, 172(1),* 17-31. doi:10.1176/appi.ajp.2014.13121691

Jervis, B.W., Nichols, M.J., Allen, E.M., Hudson, N.R., & Johnson, T.E. (1985). The assessment of two methods for removing eye movement artefact from the EEG. *Electroencephalography and Clinical Neurophysiology, 61(5),* 444-452. doi:10.1016/0013-4694(85)91037-5

Jessen, F., Kucharski, C., Fries, T., Papassotiropoulos, A., Hoenig, K., Maier, W., & Heun, R. (2001). Sensory Gating Deficit Expressed by a Disturbed Suppression of the P50 Event-Related Potential in Patients With Alzheimer's Disease. *American Journal of Psychiatry, 158,* 1319-1321. doi:10.1176/appi.ajp.158.8.1319

Jin, Y., Potkin, S.G., Patterson, J.V., Sandman, C.A., Hetrick, W.P., & Bunney, Jr., W.E. (1997). Effects of P50 temporal variability on sensory gating in schizophrenia. *Psychiatry Research, 70,* 71-81. doi:10.1016/S0165-1781(97)03091-6

John, O.P., Donahue, E.M., & Kentle, R.L. (1991). *The Big-Five Inventory: Versions 4a and 54.* Berkley; University of California, Institute of Personality and Social Research.

Jones, T., Caulfield, L., Wilkinson, D., & Weller, L. (2011). The Relationship Between Nonclinical Schizotypy and Handedness on Divergent and Convergent Creative Problem-Solving Tasks. *Creativity Research Journal, 23(3),* 222-228. doi:10.1080/10400419.2011.595964

Jung, R.E., Grazioplene, R., Caprihan, A., Chavez, R.S., & Haier, R.J. (2010). White matter integrity, creativity, and psychopathology: disentangling constructs with diffusion tensor imaging. *PLoS ONE 5(3),* e9818. doi:10.1371/journal.pone.0009818

Jung, R.E., Segall, J.M., Bockholt, H.J., Flore, R.A., Smith, S.M., Chavez, R.S., & Haier, R.J. (2010). Neuroanatomy of Creativity. *Human Brain Mapping, 31,* 398-409. doi:10.1002/hbm.20874

Kantrowitz, J.T., Butler, P.D., Schecter, I., Silipo, G., & Javitt, D.C. (2009). Seeing the World Dimly: The Impact of Early Visual Deficits on Visual Experience in Schizophrenia. *Schizophrenia Bulletin, 35*(6), 1085-1094. doi:10.1093/schbul/sbp100

Karlsson, J.L. (1970). Genetic association of giftedness and creativity with schizophrenia. *Hereditas, 66,* 177-182. doi:10.1111/j.1601-5223.1970.tb02343.x

Kawasaki, Y., Suzuki, M., Nohara, S., Hagino, H., Takahashi, T., Matsui, M., . . . Kurachi, M. (2004). Structural brain differences in patients with schizophrenia and schizotypal disorder demonstrated by voxel-based morphometry. *European Archives of Psychiatry and Clinical Neuroscience, 254(6),* 406-414. doi:10.1007/s00406-004-0522-1

Kawasaki, Y., Suzuki, M., Takahashi, T., Nohara, S., McGuire, P.K., Seto, H., . . . Kurachi, M. (2008). Anomalous Cerebral Asymmetry in Patients with Schizophrenia Demonstrated by Voxel-Based Morphometry. *Biological Psychiatry, 63(8),* 793-800. doi:10.1016/j.biopsych.2007.08.008

Kay, S.R., Fiszbein, A., & Opler, L.A. (1987). The Positive and Negative Syndrome Scale (PANSS) for schizophrenia. *Schizophrenia Bulletin, 13,* 261-276. doi:10.1093/schbul/13.2.261

Keefe, J.A., & Magaro, P.A. (1980). Creativity and schizophrenia: An equivalence of cognitive processes. *Journal of Abnormal Psychology, 89,* 390-398. doi:10.1037/0021-843X.89.3.390

Keightley, M.L., Winocur, G., Graham, S.J., Mayberg, H.S., Hevenor, S.J., & Grady, C.L. (2003). An fMRI study investigating cognitive modulation of brain regions associated with emotional processing of visual stimuli. *Neuropsychologia, 41(5),* 585-596. doi:10.1016/S0028-3932(02)00199-9

Keller, S.S., & Roberts, N. (2008). Voxel-based morphometry of temporal lobe epilepsy: An introduction and review of the literature. *Epilepsia, 49(5),* 741-757. doi:10.1111/j.1528-1167.2007.01485.x

Kendler, K.S. (1985). Diagnostic approaches to schizotypal personality disorder: A historical perspective. *Schizophrenia Bulletin, 11,* 538-553. doi:10.1093/schbul/11.4.538

Kendler, K.S., Thacker, L., & Walsh, D. (1996). Self-report measures of schizotypy as indices of familial vulnerability to schizophrenia. *Schizophrenia Bulletin, 22(3),* 511-521. doi:10.1093/schbul/22.3.511

Kennedy, J.E., & Kanthamani, H. (1995a). An Exploratory Study of the Effects of Paranormal and Spiritual Experiences on Peoples' Lives and Well-Being. *The Journal of the American Society for Psychical Research, 89,* 249-265.

Kennedy, J.E., & Kanthamani, H. (1995b). Association Between Anomalous Experiences and Artistic Creativity and Spirituality. *The Journal of the American Society for Psychical Research, 89,* 333-343.

Khedr, E.M., Hamed, E., Said, A., & Basahi, J. (2002). Handedness and language cerebral lateralization. *European Journal of Applied Physiology, 87(4-5),* 469-473. doi:10.1007/s00421-002-0652-y

Kiang, M., & Kutas, M. (2006). Abnormal typicality of responses on a category fluency task in schizotypy. *Psychiatry Research, 145,* 119-126. doi:10.1016/j.psychres.2005.12.010

Kim, K.H. (2006a). Can We Trust Creativity Tests? A Review of the Torrance Tests of Creative Thinking (TTCT). *Creativity Research Journal, 18(1),* 3-14. doi:10.1207/s15326934crj1801_2

Kim, K.H. (2006b). Is Creativity Unidimensional or Multidimensional? Analyses of the Torrance Tests of Creative Thinking. *Creativity Research Journal 18(3),* 251-259. doi:10.1207/s15326934crj1803_2

Kim, K.H. (2008). Meta-analyses of the relationship of creative achievement to both IQ and divergent thinking test scores. *Journal of Creative Behavior, 42(2),* 106-130. doi:10.1002/j.2162-6057.2008.tb01290.x

Kim, M.A., Tura, E., Potkin, S.G., Fallon, J.H., Manoach, D.S., Calhoun, V.D., & Turner, J.A. (2010). Working memory circuitry in schizophrenia shows widespread cortical inefficiency and compensation. *Schizophrenia Research, 117(1),* 42-51. doi:10.1016/j.schres.2009.12.014

Kimura, D. (1961). Cerebral dominance and the perception of verbal stimuli. *Canadian Journal of Psychology, 15,* 166-170. doi:10.1037/h0083219

Kinney, D.K., Richards, R., Lowing, P.A., LeBlanc, D., Zimbalist, M.E., & Harlan, P. (2001). Creativity in offspring of schizophrenic and control parents: an adoption study. *Creativity Research Journal, 22,* 347-360. doi:10.1207/S15326934CRJ1301_3

Kinsbourne, M., & Cook, J. (1971). Generalized and lateralized effects of concurrent verbalization on a unimanual skill. *Quarterly Journal of Experimental Psychology, 23(3),* 341-345. doi:10.1080/14640746908401828

Kleinhans, N.M., Müller, R.-A., Cohen, D.N., & Courchesne, E. (2008). Atypical functional lateralization for language in autism spectrum disorders. *Brain Research, 1221,* 115-125. doi:10.1016/j.brainres.2008.04.080

Knecht, S., Dräger, B., Deppe, M., Bobe, L., Lohmann, H., Flöel, A., . . . Henningsen, H. (2000). Handedness and hemispheric language dominance in healthy humans. *Brain, 123,* 2512-2518. doi:10.1093/brain/123.12.2512

Koch, K., Schultz, C.C., Wagner, G., Schachtzabel, C., Reichenbach, J.R., Sauer, H., & Schlösser, R.G.M. (2013). Disrupted white matter connectivity is associated with reduced cortical thickness in the cingulated cortex in schizophrenia. *Cortex, 49(3),* 722-729. doi:10.1016/j.cortex.2012.02.001

Korzyukov, O., Pflieger, M.E., Wagner, M., Bowyer, S.M., Rosburg, T., Sundaresan, K., . . . Boutros, N.N. (2007). Generators of the intracranial P50 response in auditory sensory gating. *NeuroImage, 35(2),* 811-826. doi:10.1016/j.neuroimage.2006.12.011

Kosslyn, S.M., Ganis, G., & Thompson, W.L. (2001). Neural foundations of imagery. *Nature Reviews Neuroscience, 2,* 635-642. doi:10.1038/35090055

Kostova, M., de Loye, C., & Blanchet, A. (2011). Left but not right hemisphere semantic processing abnormalities in language comprehension in subjects with schizotypy traits. *Psychiatry Research, 185,* 84-91. doi:10.1016/j.psychres.2010.05.006

Koutsouleris, N., Gaser, C., Jäger, M., Bottlender, R., Frodl, T., Holzinger, S., . . . Meisenzahl, E.M. (2008). Structural correlates of psychopathological symptom dimensions in schizophrenia: A voxel-based morphometric study. *NeuroImage, 39,* 1600-1612. doi:10.1016/j.neuroimage.2007.10.029

Kowatari, Y., Lee, S.H., Yamamura, H., Nagamori, Y., Levy, P., Yamane, S., & Yamamoto, M. (2009). Neural networks involved in artistic creativity. *Human Brain Mapping, 30(5),* 1678-1690. doi:10.1002/hbm.20633

Koychev, I., Deakin, J.F.W., Haenschel, C., & El-Deredy, W. (2011). Abnormal neural oscillations in schizotypy during a visual working memory task: Support for a deficient top-down network? *Neuropsychologia, 49,* 2866-2873. doi:10.1016/j.neuropsychologia.2011.06.012

Koychev, I., El-Deredy, W., Haenschel, C., & Deakin, J.F.W. (2010). Visual information processing deficits as biomarkers of vulnerability to schizophrenia: An event-related potential study in schizotypy. *Neuropsychologia, 48,* 2205-2214. doi:10.1016/j.neuropsychologia.2010.04.014

Kraepelin, E. (1971). *Dementia praecox and paraphrenia.* (R. M. Barclay, Trans.). In G.M. Robertson (Ed.). New York: Krieger. (Original work published 1909-1913).

Kravetz, S., Faust, M., & Edelman, A. (1998). Dimensions of schizotypy and lexical decision in the two hemispheres. *Personality and Individual Differences, 25,* 857-871. doi:10.1016/S0191-8869(98)00066-X

Kring, A.M., & Moran, E.K. (2008). Emotional Response Deficits in Schizophrenia: Insights From Affective Science. *Schizophrenia Bulletin, 34(5),* 819-834. doi:10.1093/schbul/sbn071

Krishnan, A., Williams, L.J., McIntosh, A.R., & Abdi, H. (2011). Partial Least Squares (PLS) methods for neuroimaging: A tutorial and review. *NeuroImage, 56(2),* 455-475. doi:10.1016/j.neuroimage.2010.07.034

Kubicki, M., Shenton, M.E., Salisbury, D.F., Hirayasu, Y., Kasai, K., Kikinis, R., . . . McCarley, R.W. (2002). Voxel-Based Morphometric Analysis of Gray Matter in First Episode Schizophrenia. *NeuroImage, 17(4),* 1711-1719. doi:10.1006/nimg.2002.1296

Kubicki, M., Westin, C.F., McCarley, R.W., & Shenton, M.E. (2005). The application of DTI to investigate white matter abnormalities in schizophrenia. *Annals of the New York Academy of Sciences, 1064,* 134-148. doi:10.1196/annals.1340.024

Kühn, S., Schubert, F., & Gallinat, J. (2012). Higher prefrontal cortical thickness in high schizotypal personality trait. *Journal of Psychiatric Research, 46,* 960-965. doi:10.1016/j.jpsychires.2012.04.007

Kumari, V., Antonova, E., & Geyer, M.A. (2008). Prepulse inhibition and "psychosis-proneness" in healthy individuals: an fMRI study. *European Psychiatry, 23,* 274-280. doi:10.1016/j.eurpsy.2007.11.006

Kumari, V., Toone, B., & Gray, J.A. (1997). Habituation and prepulse inhibition of the acoustic startle reflex: effects of smoking status and psychosis-proneness. *Personality and Individual Differences, 23(2),* 183-191. doi:10.1016/S0191-8869(97)00045-7

Kutas, M., & Federmeier, K.D. (2011). Thirty years and counting: Finding meaning in the N400 component of the event related brain potential (ERP). *Annual Review of Psychology, 62,* 621-647. doi:10.1146/annurev.psych.093008.131123

Kwapil, T.R., & Barrantes-Vidal, N. (2014). Schizotypy: Looking Back and Moving Forward. *Schizophrenia Bulletin.* Advance online publication. doi:10.1093/schbul/sbu186

Kyaga, S., Lichtenstein, P., Bornan, M., Hultman, C., Långström, N., & Landén, M. (2011). Creativity and mental disorder: family study of 300 000 people with severe mental disorder. *The British Journal of Psychiatry, 199,* 373-379. doi:10.1192/bjp.bp.110.085316

LaFrance, E.B. (1995). Creative thinking differences in three groups of exceptional children as expressed through completion of figural forms. *Roeper Review, 17(4),* 248-252. doi:10.1080/02783199509553675

Lawrie, S.M., McIntosh, A.M., Hall, J., Owens, D.G.C., & Johnstone, E.C. (2008). Brain Structure and Function Changes During the Development of Schizophrenia: The Evidence From Studies of Subjects at Increased Genetic Risk. *Schizophrenia Bulletin, 34(2),* 330-340. doi:10.1093/schbul/sbm158

Lawrie, S.M., Whalley, H.C., Abukmeil, S.S., Kestelman, J.N., Donnelly, L., Miller, P., . . . Johnstone, E.C. (2001). Brain structure, genetic liability, and psychotic symptoms in subjects at high risk of developing schizophrenia. *Biological Psychiatry, 49(10),* 811-823. doi:10.1016/S0006-3223(00)01117-3

Lee, S.-H., Kubicki, M., Asami, T., Seidman, L.J., Goldstein, J.M., Mesholam-Gately, R.I., . . . Shenton, M.E. (2013). Extensive white matter abnormalities in patients with first-episode schizophrenia: A diffusion tensor imaging (DTI) study. *Schizophrenia Research, 143(2-3),* 231-238. doi:10.1016/j.schres.2012.11.029

Lenzenweger, M.F. (2006). Schizotaxia, Schizotypy, and Schizophrenia: Paul E. Meehl's Blueprint for the Experimental Psychopathology and Genetics of Schizophrenia.

Journal of Abnormal Psychology, 115(2), 195-200. doi:10.1037/0021-843X.115.2.195

Lenzenweger, M.F. (1998). Schizotypy and Schizotypic Psychopathology: Mapping an Alternative Expression of Schizophrenia Liability. In M.F. Lenzenweger & R.H. Dworkin (Eds.), *Origins and development of schizophrenia: Advances in experimental psychopathology.* Washington: American Psychological Association. doi:10.1037/10305-004

Lenzenweger, M.F., & Korfine, L. (1992). Confirming the latent structure and base rate of schizotypy: A taxometric analysis. *Journal of Abnormal Psychology, 101(3),* 567-571. doi:10.1037/0021-843X.101.3.567

Leonhard, D., & Brugger, P. (1998). Creative, Paranormal, and Delusional Thought: A Consequence of Right Hemisphere Semantic Activation? *Neuropsychiatry, Neuropsychology, & Behavioral Neurology, 11(4),* 177-183.

Leung, A., & Chue, P. (2000). Sex differences in schizophrenia, a review of the literature. *Acta Psychiatrica Scandinavica, Supplement, 101(401),* 3-38. doi:10.1111/j.0065-1591.2000.0ap25.x

Levine, B., Kovacevic, N., Nica, E.I., Cheung, G., Gao, F., Schwartz, M.L., & Black, S.E. (2008). The Toronto traumatic brain injury study: Injury severity and quantified MRI. *Neurology, 70(10),* 771-778. doi:10.1212/01.wnl.0000304108.32283.aa

Levitan, C., Ward, P.B., & Catts, S.V. (1999). Superior temporal gyral volumes and laterality correlates of auditory hallucinations in schizophrenia. *Biological Psychiatry, 46,* 955-962. doi:10.1016/S0006-3223(98)00373-4

Levy, J. (1977). The mammalian brain and the adaptive advantage of cerebral asymmetry. *Annals of the New York Academy of Sciences, 299,* 264-272. doi:10.1111/j.1749-6632.1977.tb41913.x

Lewis, D.A., Fish, K.N., Arion, D., & Gonzalez-Burgos, G. (2011). Perisomatic inhibition and cortical circuit dysfunction in schizophrenia. *Current Opinion in Neurobiology, 21(6),* 866-872. doi:10.1016/j.conb.2011.05.013

Li, X., Branch, C.A., & DeLisi, L.E. (2009). Language pathway abnormalities in schizophrenia: a review of fMRI and other imaging studies. *Current Opinion in Psychiatry, 22,* 131-139. doi:10.1097/YCO.0b013e328324bc43

Li, X., Branch, C.A., Ardekani, B.A., Bertisch, H., Hicks, C., & DeLisi, L.E. (2007). fMRI study of language activation in schizophrenia, schizoaffective disorder and in individuals genetically at high risk. *Schizophrenia Research, 96,* 14-24. doi:10.1016/j.schres.2007.07.013

Lijffijt, M., Cox, B., Acas, M.D., Lane, S.D., Moeller, F.G., & Swann, A.C. (2012). Differential relationships of impulsivity of antisocial symptoms on P50, N100, or P200 auditory sensory gating in controls and antisocial personality disorder. *Journal of Psychiatric Research, 46,* 743-750. doi:10.1016/j.jpsychires.2012.03.001

Limb, C.J., & Braun, A.R. (2008). Neural Substartes of Spontaneous Musical Performance: An fMRI Study of Jazz Improvisation. *PLoS ONE, 3(2),* e1679. doi:10.1371/journal.pone.0001679

Lindell, A.K. (2011). Lateral thinkers are not so laterally minded: Hemispheric asymmetry, interaction, and creativity. *Laterality, 16(4),* 479-498. doi:10.1080/1357650X.2010.497813

Lindell, A.K., Notice, K., & Withers, K. (2009). Reduced language processing asymmetry in non-autistic individuals with high levels of autism traits. *Laterality, 14(5),* 457-472. doi:10.1080/13576500802507752

Lindquist, M.A. (2008). The Statistical Analysis of fMRI Data. *Statistical Science, 23(4),* 439-464. doi:10.1214/09-STS282

Linscott, R.J. (2013). The taxonicity of schizotypy: Does the same taxonic class structure emerge from analyses of different attributes of schizotypy and from fundamentally different statistical methods? *Psychiatry Research, 210(2),* 414-421. doi:10.1016/j.psychres.2013.07.029

Liouta, E., Smith, A.D., & Mohr, C. (2008). Schizotypy and pseudoneglect: A critical update on theories of hemispheric asymmetries. *Cognitive Neuropsychiatry, 13(2),* 112-134. doi:10.1080/13546800801936698

Lipp, O.V., & Vaitl, D. (1992). Latent inhibition in human Pavlovian differential conditioning: effects of additional stimulation after preexposure and relation to schizotypal traits. *Personality and Individual Differences, 13,* 1003-1012. doi:10.1016/0191-8869(92)90133-A

Liu, S.K., Chiu, C.-H., Chang, C.-J., Hwang, T.-J., Hwu, H.-G., & Chen, W.J. (2002). Deficits in Sustained Attention in Schizophrenia and Affective Disorders: Stable Versus State-Dependent Markers. *The American Journal of Psychiatry, 159(6),* 975-982. doi:10.1176/appi.ajp.159.6.975

Løberg, E.-M., Hugdahl, K., & Green, M.F. (1999). Hemispheric asymmetry in schizophrenia: a "dual deficits" model. *Biological Psychiatry, 45(1),* 76-81. doi:10.1016/S0006-3223(98)0021904

Lohr, J.B., Hellige, J.B., Cherry, B.J., Lulow, L., Kwok, W., & Caligiuri, M.P. (2006). Impaired hemispheric communication in schizophrenia: A study using the consonant-vowel-consonant task. *Schizophrenia Research, 87,* 279-288. doi:10.1016/j.schres.2006.05.018

Lubow, R.E., & Moore, A.U. (1959). Latent inhibition: the effect of non-reinforced pre-exposure to conditional stimulus. *Journal of Comparative and Physiological Psychology, 52,* 416-419. doi:10.1037/h0046700

Lubow, R.E., Kaplan, O., Abramovich, P., Rudnick, A., & Laor, N. (2000). Visual search in schizophrenia: latent inhibition and novel pop-out effects. *Schizophrenia Research, 45*, 145-156. doi:10.1016/S0920-9964(99)00188-7

Ludwig, A.M. (1995). The price of greatness: Resolving the creativity and madness controversy. New York: Guildford Press.

Lv, M., Liu, Y., Du, Y., Chen, X., Fan, J., Qian, Y., & Xu, T. (2014). Study on P50 Sensory Gating in Children with Autism Spectrum Disorders in Shanghai. *North American Journal of Medicine and Science, 7(3),* 103-106. doi:10.7156/najms.2014.0703103

Malaspina, D., Bruder, G., Furman, V., Gorman, J.M., Berman, A., & Van Heertum, R. (2000). Schizophrenia Subgroups Differing in Dichotic Listening Laterality Also Differ in Neurometabolism and Symptomatology. *The Journal of Neuropsychiatry and Clinical Neurosciences, 12,* 485-492. doi:10.1176/jnp.12.4.485

Marini, A., Spoletini, I., Rubino, I.A., Ciuffa, M., Bria, P., Martinotti, G., . . . Spalletta, G. (2008). The language of schizophrenia: An analysis of micro and macrolinguistic abilities and their neuropsychological correlates. *Schizophrenia Research, 105(1-3),* 144-155. doi:10.1016/j.schres.2008.07.011

Martins-de-Souza, D., Maccarrone, G., Wobrock, T., Zerr, I., Gormanns, P., Reckow, S., . . . Turck, C.W. (2010). Proteome analysis of the thalamus and cerebrospinal fluid reveals glycolysis dysfunction and potential biomarkers candidates for schizophrenia. *Journal of Psychiatric Research, 44(16),* 1176-1189. doi:10.1016/j.jpsychires.2010.04.014

Mashal, N., Faust, M., Hendler, T., & Jung-Beeman, M. (2007). An fMRI investigation of the neural correlates underlying the processing of novel metaphoric expressions. *Brain and Language, 100(2),* 115-126. doi:10.1016/j.bandl.2005.10.005

Mason, O., & Claridge, G. (1999). Individual Differences in Schizotypy and Reduced Asymmetry Using the Chimeric Faces Task. *Cognitive Neuropsychiatry, 4(4),* 289-301. doi:10.1080/135468099395846

Mason, O., & Claridge, G. (2006). The Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE): Further description and extended norms. *Schizophrenia Research, 82(2-3),* 203-211. doi:10.1016/j.schres.2005.12.845

Mason O., Claridge, G., & Jackson, M. (1995). New scales for the assessment of schizotypy. *Personality and Individual Differences, 18(1),* 7-13. doi:10.1016/0191-8869(94)00132-C

Mason, O., Claridge, G., & Williams, L. (1997). Questionnaire measurement. In G. Claridge (Ed.), *Schizotypy: Implications for illness and health.* Oxford: Oxford University Press.

Mason, O., Linney, Y., & Claridge, G. (2005). Short scales for measuring schizotypy. *Schizophrenia Research, 78,* 293-296. doi:10.1016/j.schres.2005.06.020

Mason, M.F., Norton, M.I., Van Horn, J.D., Wegner, D.M., Grafton, S.T., & Macrae, C.N. (2007). Wandering Minds: The Default Network and Stimulus-Independent Thought. *Science, 315,* 393-395. doi:10.1126/science.1131295

Masters, A. (1997). Schizophrenia: the illness. In P.M. Ellis & S.C.D. Collings (Eds.), *Mental Health in New Zealand from a Public Health Perspective* (pp. 354-374). Wellington: Public Health Group, Ministry of Health.

Mata, I., Gilvarry, C.M., Jones, P.B., Lewis, S.W., Murray, R.M., & Sham, P.C. (2003). Relatives Are Associated With Positive Symptoms in Psychotic Probands. *Schizophrenia Bulletin, 29(2),* 273-283. doi:10.1093/oxfordjournals.schbul.a007004

Mata, I., Sham, P.C., Gilvarry, C.M., Jones, P.B., Lewis, S.W., & Murray, R.M. (2000). Childhood schizotypy and positive symptoms in schizophrenic patients predict

schizotypy in relatives. *Schizophrenia Research, 44,* 129-136. doi:10.1016/S0920-9964(99)00222-41

Matheson, S., & Langdon, R. (2008). Schizotypal traits impact upon executive working memory and aspects of IQ. *Psychiatry Research, 159,* 207-214. doi:10.1016/j.psychres.2007.04.006

McCreery, C., & Claridge, G. (2002). Healthy schizotypy: the case of out-of-the-body experiences. *Personality and Individual Differences, 32(1),* 141-154. doi:10.1016/S0191-8869(01)00013-7

McGrath, J., Saha, S., Chant, D., & Welham, J. (2008). Schizophrenia: A Concise Overview of Incidence, Prevalence, and Mortality. *Epidemiologic Reviews, 30*(1), 67-76. doi:10.1093/epirev/mxn001

McGuffin, P., Owen, M.J., & Farmer, A.E. (1995). Genetic basis of schizophrenia. *Lancet, 346,* 678-682. doi:10.1016/S0140-6736(95)92285-7

McIntosh, A.R., & Lobaugh, N.J. (2004). Partial least squares analysis of neuroimaging data: applications and advances. *NeuroImage, 23,* S250-S263. doi:10.1016/j.neuroimage.2004.07.020

McIntosh, A.R., Bookstein, F.L., Haxby, J.V., & Grady, C.L. (1996). Spatial Pattern Analysis of Functional Brain Images Using Partial Least Squares. *NeuroImage, 3,* 143-157. doi:10.1006/nimg.1996.0016

McKiernan, K.A., D'Angelo, B.R., Kaufman, J.N., & Binder, J.R. (2006). Interrupting the "stream of consciousness": An fMRI investigation. *NeuroImage, 29(4),* 1185-1191. doi:10.1016/j.neuroimage.2005.09.030

Mechelli, A., Allen, P., Amaro Jr., E., Fu, C.H.Y., Williams, S.C.R., Brammer, M.J., . . . McGuire, P.K. (2007). Misattribution of speech and impaired connectivity in patients

with auditory verbal hallucinations. *Human Brain Mapping, 28(11),* 1213-1222. doi:10.1002/hbm.20341

Mechri, A., Gassab, L., Slama, H., Gaha, L., Saoud, M., & Krebs, M.O. (2010). Neurological soft signs and schizotypal dimensions in unaffected siblings of patients with schizophrenia. *Psychiatry Research, 175(1-2),* 22-26. doi:10.1016/j.psychres.2008.10.013

Meehl, P.E. (1962). Schizotaxia, schizotypy, schizophrenia. *American Psychologist, 17(12),* 827-838. doi:10.1037/h0041029

Meehl, P.E. (1990). Toward an Integrated Theory of Schizotaxia, Schizotypy, and Schizophrenia. *Journal of Personality Disorders, 4(1),* 1-99. doi:10.1521/pedi.1990.4.1.1Mendez, M.F. (2004). Dementia as a window to the neurology of art. *Medical Hypotheses, 63,* 1-7. doi:10.1016/j.mehy.2004.03.002

Mendrek, A., Kiehl, K.A., Smith, A.M., Irwin, D., Forster, B.B., & Liddle, P.F. (2005). Dysfunction of a distributed neural circuitry in schizophrenia patients during a working-memory performance. *Psychological Medicine, 35,* 187-196. doi:10.1017/S0033291704003228

Menon, V., & Uddin, L.Q. (2010). Saliency, switching, attention and control: a network model of insula function. *Brain Structure and Function, 214,* 655-667. doi:10.1007/s00429-010-0262-0

Menzies, L., Achard, S., Chamberlain, S.R., Fineberg N., Chen, C.-H., del Campo, N., . . . Bullmore, E. (2007). Neurocognitive endophenotypes of obsessive-compulsive disorder. *Brain, 130,* 3223-3236. doi:10.1093/brain/awm205

Merten, T., & Fischer, I. (1999). Creativity, personality and word association responses: associative behaviour in forty supposedly creative persons. *Personality and Individual Differences, 27,* 933-942. doi:10.1016/S0191-8869(99)00042-2

Meyer-Lindenberg, A., Poline, J.-B., Kohn, P.D., Holt, J.L., Egan, M.F., Weinberger, D.R., & Berman, K.F. (2001). Evidence for Abnormal Cortical Functional Connectivity During Working Memory in Schizophrenia. *The American Journal of Psychiatry, 158(11),* 1809-1817. doi:10.1176/appi.ajp.158.11.1809

Miller, E.N., & Chapman, L.J. (1983). Continued word association in hypothetically psychosis-prone college students. *Journal of Abnormal Psychology, 92,* 468-478. doi:10.1037/0021-843X.92.4.468

Miller, L.S., & Burns, S.A. (1995). Gender Differences in Schizotypic Features in a Large Sample of Young Adults. The Journal of Nervous and Mental Disease, 183(10), 657-661. doi:10.1097/00005053-199510000-00007

Milne, R.D., Syngeniotis, A., Jackson, G., & Corballis, M.C. (2002). Mixed Lateralization of Phonological Assembly in Developmental Dyslexia. *Neurocase, 8,* 205-209. doi:10.1093/neucas/8.3.205

Milner, B. (1984). Behavioural effects of frontal-lobe lesions in man. *Trends in Neurosciences, 7,* 403-407. doi:10.1016/S0166-2236(84)80143-5

Miran, M., & Miran, E. (1984). Cerebral asymmetries: neuropsychological measurement and theoretical issues. *Biological Psychology, 19,* 295-304. doi:10.1016/0301-0511(84)90044-9

Modinos, G., Mechelli, A., Ormel, J., Groenewold, N.A., Aleman, A., & McGuire, P.K. (2010). Schizotypy and brain structure: a voxel-based morphometry study. *Psychological Medicine, 40,* 1423-1431. doi:10.1017/S0033291709991875

Modinos, G., Ormel, J., & Aleman, A. (2010). Altered activation and functional connectivity of neural systems supporting cognitive control of emotion in psychosis proneness. *Schizophrenia Research, 118,* 88-97. doi:10.1016/j.schres.2010.01.030

Modinos, G., Renken, R., Ormel, J., & Aleman, A. (2011). Self-reflection and the psychosis-prone brain: An fMRI study. *Neuropsychology, 25(3),* 295-305. doi:10.1037/a0021747

Moes, P.E., Brown, W.S., & Minnema, M.T. (2007). Individual differences in interhemispheric transfer time (IHTT) as measured by event related potentials. *Neuropsychologia, 45(11),* 2626-2630. doi:10.1016/j.neuropsychologia.2007.03.017

Mohanty, A., Herrington, J.D., Koven, N.S., Fisher, J.E., Wenzel, E.A., Webb, A.G., . . . Miller, G.A. (2005). Neural Mechanisms of Affective Interference in Schizotypy. *Journal of Abnormal Psychology, 114(1),* 16-27. doi:10.1037/0021-843X.114.1.16

Mohanty, A., Heller, W., Koven, N.S., Fisher, J.E., Herrington, J.D., & Miller, G.A. (2008). Specificity of emotion-related effects on attentional processing in schizotypy. *Schizophrenia Research, 103(1-3),* 129-137. doi:10.1016/j.schres.2008.03.003

Mohr, C., Krummenacher, P., Landis, T., Sandor, P.S., Fathi, M., & Brugger, P. (2005). Psychometric schizotypy modulates levodopa effects on lateralized lexical decision performance. *Journal of Psychiatric Research, 39(3),* 241-250. doi:10.1016/j.jpsychires.2004.08.006

Monti, M.M. (2011). Statistical analysis of fMRI time-series: a critical review of the GLM approach. *Frontiers in Human Neuroscience, 5(28),* 1-13. doi:10.3389/fnhum.2011.00028

Moore, D.W., Bhadelia, R.A., Billings, R.L., Fulwiler, C., Heilman, K.M., Rood, K.M.J., & Gansler, D.A. (2009). Hemispheric connectivity and the visual-spatial divergent-thinking component of creativity. *Brain and Cognition, 70(3),* 267-272. doi:10.1016/j.bandc.2009.02.011

Moritz, S.H., Mass, R., & Junk, U. (1998). Further evidence of reduced negative priming in positive schizotypy. *Personality and Individual Differences, 9,* 257-268. doi:10.1016/S0191-8869(97)00205-5

Mumford, M.D., & Gustafson, S.B. (1988). Creativity syndrome: integration, application, and innovation. *Psychological Bulletin, 103,* 27-43. doi:10.1037/0033-2909.103.1.27

Näätänen, R., & Picton, T. (1987). The N1 Wave of the Human Electric and Magnetic Response to Sound: A Review and an Analysis of the Component Structure. *Psychophysiology, 24(4),* 375-425. doi:10.1111/j.1469-8986.1987.tb00311.x

Nagamoto, H.T., Adler, L.E., Waldo, M., & Freedman, R. (1989). Sensory Gating in Schizophrenics and Normal Controls: Effects of Changing Stimulation Interval. *Biological Psychiatry, 25,* 549-561. doi:10.1016/0006-3223(89)90215-1

Nagamoto, H.T., Adler, L.E., Waldo, M.C., Griffith, J., & Freedman, R. (1991). Gating of auditory response in schizophrenics and normal controls: effects of recording sites and stimulation interval on the P50 wave. *Schizophrenia Research, 4,* 31-40. doi:10.1016/0920-9964(91)90007-E

Najt, P., Bayer, U., & Hausmann, M. (2012). Atypical lateralisation in emotional prosody in men with schizotypy. *Laterality, 17(5),* 533-548. doi:10.1080/1357650X.2011.586702

Najt, P., Perez, J., Sanches, M., Peluso, M.A.M., Glahn, D., & Soares, J.C. (2007). Impulsivity and bipolar disoder. *European Neuropsychopharmacology, 17(5),* 313-320. doi:10.1016/j.euroneuro.2006.10.002

Natsubori, T., Hashimoto, R.-I., Yahata, N., Inoue, H., Takano, Y., Iwashiro, N., . . . Yamasue, H. (2014). An fMRI study of visual lexical decision in patients with schizophrenia and clinical high-risk individuals. *Schizophrenia Research, 157(1-3),* 218-224. doi:10.1016/j.schres.2014.05.027

Neckelmann, G., Specht, K., Lund, A., Ersland, L., Smievoll, A.I., Neckelmann, D., & Hugdahl, K. (2006). MR morphometry analysis of grey matter volume reduction in schizophrenia: association with hallucinations. *International Journal of Neuroscience, 116(1),* 9-23. doi:10.1080/00207450690962244

Nelson, B., & Rawlings, D. (2010). Relating Schizotypy and Personality to the Phenomenology of Creativity. *Schizophrenia Bulletin, 36(2),* 388-399. doi:10.1093/schbul/sbn098

Nelson, M.T., Seal, M.L., Pantelis, C., & Phillips, L.J. (2013). Evidence of a dimensional relationship between schizotypy and schizophrenia: A systematic review. *Neuroscience and Biobehavioral Reviews, 37,* 317-327. doi:10.1016/j.neubiorev.2013.01.004

Nestor, P.G., O'Donnell, B.F., McCarley, R.W., Niznikiewicz, M., Barnard, J., Shen, Z.J., . . . Shenton, M.E. (2002). A new statistical method for testing hypotheses of neuropsychological/MRI relationships in schizophrenia: partial least squares analysis. *Schizophrenia Research, 53(1-2),* 57-66. doi:10.1016/S0920-9964(00)00171-7

Nettle, D. (2001). Strong imagination: madness, creativity and human nature. Oxford: Oxford University Press.

Nettle, D. (2006). Schizotypy and mental health amongst poets, visual artists, and mathematicians. *Journal of Research in Personality, 40,* 876-890. doi:10.1016/j.jrp.2005.09.004

Neubauer, A.C., & Fink, A. (2009). Intelligence and neural efficiency. *Neuroscience & Biobehavioral Reviews, 33,* 1004-1023. doi:10.1016/j.neubiorev.2009.04.001

Ng, V.W.K., Bullmore, E.T., de Zubicaray, G.I., Cooper, A., Suckling, J., & Williams, S.C.R. (2001). Identifying Rate-Limiting Nodes in Large-Scale Cortical Networks for

Visuospatial Processing: An Illustration using fMRI. *Journal of Cognitive Neuroscience, 13(4),* 537-545. doi:10.1162/08989290152001943

Nitschke, J.B., & Heller, W. (2002). The neuropsychology of anxiety disorders: Affect, cognition, and neural circuitry. In H. D'Haenen, J.A. Den Boer, & P. Willner (Eds.), *Biological psychiatry* (pp. 975–988). Chichester, UK: John Wiley & Sons.

Niznikiewicz, M., Singh Mittal, M., Nestor, P.G., & McCarley, R.W. (2010). Abnormal inhibitory processes in semantic networks in schizophrenia. *International Journal of Psychophysiology, 75(2),* 133-140. doi:10.1016/j.ijpsycho.2009.10.006

Nunn, J., & Peters, E. (2001). Schizotypy and patterns of lateral asymmetry on hemispheric-specific language tasks. *Psychiatry Research, 103,* 179-192. doi:10.1016/S0165-1781(01)00273-6

O'Reilly, T., Dunbar, R., & Bentall, R. (2001). Schizotypy and creativity: an evolutionary connection? *Personality and Individual Differences, 31,* 1067-1078. doi:10.1016/S0191-8869(00)00204-X

Oertel-Knöchel, V., & Linden, D.E.J. (2011). Cerebral Asymmetry in Schizophrenia. *The Neuroscientist, 17(5),* 456-467. doi:10.1177/1073858410386493

Ogawa, S., Lee, T.M., Kay, A.R., & Tank, D.W. (1990). Brain magnetic resonance imaging with contrast dependant on blood oxygenation. *Proceedings of the National Academy of Sciences of the United States of America, 87(24),* 9868-9872. doi:10.1073/pnas.87.24.9868

Olabi, B., Ellison-Wright, I., McIntosh, A.M., Wood, S.J., Bullmore, E., & Lawrie, S.M. (2011). Are There Progressive Brain Changes in Schizophrenia? A Meta-Analysis of Structural Magnetic Resonance Imaging Studies. *Biological Psychiatry, 70(1),* 88-96. doi:10.1016/j.biopsych.2011.01.032

Oldfield, R.C. (1971). The assessment and analysis of handedness: The Edinburgh inventory. *Neuropsychologia, 9(1),* 97-113. doi:10.1016/0028-3932(71)90067-4

Olincy, A., & Martin, L. (2005). Diminished Suppression of the P50 Auditory Evoked Potential in Bipolar Disorder Subjects With a History of Psychosis. *American Journal of Psychiatry, 162,* 43-49. doi:10.1176/appi.ajp.162.1.43

Ottemiller, D.D., Elliott, C.S., & Giovannetti, T. (2014). Creativity, Overinclusion, and Everyday Tasks. *Creativity Research Journal, 26(3),* 289-296. doi:10.1080/10400419.2014.929407

Otten, L.J., & Rugg, M.D. (2005). Interpreting event-related brain potentials. In T.C. Handy (Ed.), *Event-related potentials: A methods handbook.* Cambridge, Massachusetts: The MIT Press.

Park, H.R.P., Badzakova-Trajkov, G., & Waldie, K.E. (2012). Language lateralisation in late proficient bilinguals: A lexical decision fMRI study. *Neuropsychologia, 50,* 688-695. doi:10.1016/j.neuropsychologia.2012.01.005

Park, S., & McTigue, K. (1997). Working memory and the syndromes of schizotypal personality. *Schizophrenia Research, 26,* 213-220. doi:10.1016/S0920-9964(97)00051-0

Park, S., Lenzenweger, M.F., Püschel, J., & Holzman, P.S. (1996). Attentional Inhibition in Schizophrenia and Schizotypy: A Spatial Negative Priming Study. *Cognitive Neuropsychiatry, 1(2),* 125-149. doi:10.1080/135468096396596

Patterson, J.V., Hetrick, W.P., Boutros, N.N., Jin, Y., Sandman, C., Stern, H., . . . Bunney Jr., W.E. (2008). P50 sensory gating ratios in schizophrenics and controls: A review and data analysis. *Psychiatry Research, 158,* 226-247. doi:10.1016/j.psychres.2007.02.009

Peralta, V., & Cuesta, M.J. (1999). Dimensional structure of psychotic symptoms: an item-level analysis of SAPS and SANS symptoms in psychotic disorders. *Schizophrenia Research, 38,* 13-26. doi:10.1016/S0920-9964(99)00003-1

Pfefferbaum, A., Sullivan, E.V., & Carmelli, D. (2001). Genetic regulation of regional microstructure of the corpus callosum in late life. *Neuroreport, 12,* 1677-1681. doi:10.1097/00001756-200106130-00032

Pizzagalli, D., Lehmann, D., & Brugger, P. (2001). Lateralized direct and indirect semantic priming effects in subjects with paranormal experiences and beliefs. *Psychopathology, 34,* 75-80. doi:10.1159/000049284

Plucker, J.A. (1999). Is the proof in the pudding? Reanalyses of Torrance's (1958 to Present) longitudinal data. *Creativity Research Journal, 12,* 103-114. doi:10.1207/s15326934crj1202_3

Plucker, J.A., & Renzulli, J.S. (1999). Psychometric approaches to the study of human creativity. In R.J. Sternberg (Ed.), *Handbook of creativity* (pp. 35-61). Cambridge, UK: Cambridge University Press.

Polich, J. (2007). Updating P300: An integrative theory of P3a and P3b. *Clinical Neurophysiology, 118(10),* 2128-2148. doi:10.1016/j.clinph.2007.04.019

Post, F. (1994). Creativity and psychopathology. A study of 291 world-famous men. *British Journal of Psychiatry, 165,* 22-34. doi:10.1192/bjp.165.1.22

Potter, D., Summerfelt, A., Gold, J., & Buchanan, R.W. (2006). Review of Clinical Correlates of P50 Sensory Gating Abnormalities in Patients with Schizophrenia. *Schizophrenia Bulletin, 32(4),* 692-700. doi:10.1093/schbul/sbj050

Premkumar, P., Ettinger, U., Inchley-Mort, S., Sumich, A., Williams, S.C., Kuipers, E., & Kumari, V. (2012). Neural processing of social rejection: the role of schizotypal personality traits. *Human Brain Mapping, 33(3),* 695-706. doi:10.1002/hbm.21243

Prévost, M., Rodier, M., Renoult, L., Kwann, Y., Dionne-Dostie, E., Chapleau, I., . . . Debruille, J.B. (2010). Schizotypal traits and N400 in healthy subjects. *Psychophysiology, 47(6),* 1047-1056. doi:10.1111/j.1469-8986.2010.01016.x

Psychological Corporation. (1999). *Wechsler Abbreviated Scale of Intelligence manual.* San Antonia, TX: Harcourt Assessment, Inc.

Radek, R.J., Miner, H.M., Bratcher, N.A., Decker, M.W., Gopalakrishnan, M., & Bitner, R.S. (2006). $\alpha_4\beta_2$ Nicotinic receptor stimulation contributes to the effects of nicotine in the DBA/2 mouse model of sensory gating. *Psychopharmacology, 187,* 47-55. doi:10.1007/s00213-006-0394-3

Radel, R., Davranche, K., Fournier, M., & Dietrich, A. (2015). The role of (dis)inhibition in creativity: Decreased inhibition improves idea generation. *Cognition, 134,* 110-120. doi:10.1016/j.cognition.2014.09.001

Rado, S. (1953). Dynamics and classification of disordered behaviour. *American Journal of Psychiatry, 110,*406-416. doi:10.1176/ajp.110.6.406

Radua, J., Borgwardt, S., Crescini, A., Mataix-Cols, D., Meyer-Lindenberg, A., McGuire, P.K., & Fusar-Poli, P. (2012). Multimodel meta-analysis of structural and functional brain changes in first episode psychosis and the effects of antipsychotic medication. *Neuroscience & Biobehavioral Reviews, 36(10),* 2325-2333. doi:10.1016/j.neubiorev.2012.07.012

Raichle, M.E., & Snyder, A.Z. (2007). A default mode of brain function: A brief history of an evolving idea. *NeuroImage, 37,* 1083-1090. doi:10.1016/j.neuroimage.2007.02.041

Raine, A. (1991). The SPQ: a scale for the assessment of schizotypal personality based on DSM-III-R criteria. *Schizophrenia Bulletin, 17(4),* 555-564. doi:10.1093/schbul/17.4.555

Raine, A. (2006). Schizotypal Personality: Neurodevelopmental and Psychosocial Trajectories. *Annual Review of Clinical Psychology, 2,* 291-326. doi:10.1146/annurev.clinpsy.2.022305.095318

Raine, A., Lencz, T., & Mednick, S.A. (1995). *Schizotypal Personality Disorder.* Cambridge: Cambridge University Press. doi:10.1017/CBO9780511759031

Raine, A., Reynolds, C., Lencz, T., Scerbo, A., Triphon, N., & Kim, D. (1994). Cognitive-perceptual, interpersonal, and disorganized features of schizotypal personality. *Schizophrenia Bulletin, 20,* 191-201. doi:10.1093/schbul/20.1.191

Raine, A., Sheard, C., Reynolds, G.P., & Lencz, T. (1992). Pre-frontal structural and functional deficits associated with individual differences in schizotypal personality. *Schizophrenia Research, 7,* 237-247. doi:10.1016/0920-9964(92)90018-Z

Rapp, A.M., Mutschler, D.E., Wild, B., Erb, M., Lengsfeld, I., Saur, R., & Grodd, W. (2010). Neural correlates of irony comprehension: The role of schizotypal personality traits. *Brain and Language, 113(1),* 1-12. doi:10.1016/j.bandl.2009.11.007

Rawlings, D., & Borge, A. (1987). Personality and hemisphere functions: Two experiments using the dichotic shadowing technique. *Personality and Individual Differences, 8,* 438-488. doi:10.1016/0191-8869(87)90210-8

Rawlings, D., & Claridge, G.S. (1984). Schizotypy and hemisphere function – III. Performance asymmetries on tasks of letter recognition and local/global processing. *Personality and Individual Differences, 5,* 657-664. doi:10.1016/0191-8869(84)90113-2

Rawlings, D., & Locarnini, A. (2008). Dimensional schizotypy, autism, and unusual word associations in artists and scientists. *Journal of Research in Personality, 42(2),* 465-471. doi:10.1016/j.jrp.2007.06.005

Raz, J., Zheng, H., Ombao, H., & Turetsky, B. (2003). Statistical tests for fMRI based on experimental randomization. *NeuroImage, 19,* 226-232. doi:10.1016/S1053-8119(03)00115-0

Reichsman, F. (1981). Life experiences and creativity of great composers: a psychosomatist's view. *Psychosomatic Medicine, 43,* 291-300. doi:10.1097/00006842-198108000-00001

Rentzsch, J., Jockers-Scherübl, M.C., Boutros, N.N., & Gallinat, J. (2008). Test-retest reliability of P50, N100 and P200 auditory sensory gating in healthy subjects. *International Journal of Psychophysiology, 67,* 81-90. doi:10.1016/j.ijpsycho.2007.10.006

Repovs, G., Csernansky, J.G., & Barch, D.M. (2011). Brain Network Connectivity in Individuals with Schizophrenia and Their Siblings. *Biological Psychiatry, 69,* 967-973. doi:10.1016/j.biopsych.2010.11.009

Reynolds, C.A., Raine, A., Mellingen, K., Venables, P.H., & Mednick, S.A. (2000). Three-Factor Model of Schizotypal Personality. *Schizophrenia Bulletin, 26(3),* 603-618. doi:10.1093/oxfordjournals.schbul.a033481

Richards, R., Kinney, D.K., Lunde, I., Benet, M., & Merzel, A.P.C. (1988). Creativity in manic-depressives, cyclothmes, their normal relatives, and control subjects. *Journal of Abnormal Psychology, 97,* 281-288. doi:10.1037/0021-843X.97.3.281

Richardson, A.J., Mason, O., & Claridge, G. (1997). Schizotypy and cerebral lateralization. In G. Claridge (Ed.), *Schizotypy: Implications for illness and health.* Oxford University Press.

Riding, R., & Cheema, I. (1991). Cognitive Styles – an overview and integration. *Educational Psychology, 11(3-4),* 193-215. doi:10.1080/0144341910110301

Rolfe, M.H.S., Kirk, I.J., & Waldie, K.E. (2007). Interhemispheric callosal transfer in adults with attention-deficit/hyperactivity disorder: an event-related potential study. *Neuroreport, 18(3),* 255-259. doi:10.1097/WNR.0b013e328011e6f9

Runco, M.A. (1991). *Divergent thinking.* Norwood, NJ: Ablex Publishing Corporation.

Runco, M.A. (2004). Creativity. *Annual Review of Psychology, 55,* 657-687. doi:10.1146/annurev.psych.55.090902.141502

Runco, M.A., & Acar, S. (2012). Divergent Thinking as an Indicator of Creative Potential. *Creativity Research Journal, 24(1),* 66-75. doi:10.1080/10400419.2012.652929

Russ, S.W., Robins, A.L., & Christiano, B.A. (1999). Pretend play: Longitudinal prediction of creativity and affect in fantasy in children. *Creativity Research Journal, 12,* 129-139. doi:10.1207/s15326934crj1202_5

Rust, J. (1988). The Rust Inventory of Schizotypal Cognitions (RISC). *Schizophrenia Bulletin, 14(2),* 317-322. doi:10.1093/schbul/14.2.317

Sabri, O., Erkwoh, R., Schreckenberger, M., Owega, A., Sass, H., & Buell, U. (1997). Correlation of positive symptoms exclusively to hyperperfusion or hypoperfusion of cerebral cortex in never-treated schizophrenics. *The Lancet, 349(9067),* 1735-1739. doi:10.1016/S0140-6736(96)08380-8

Salgado-Pineda, P., Fakra, E., Delaveau, P., McKenna, P.J., Pomarol-Clotet, E., & Blin, O. (2011). Correlated structural and functional brain abnormalities in the default mode network in schizophrenia patients. *Schizophrenia Research, 125(2-3),* 101-109. doi:10.1016/j.schres.2010.10.027

Sánchez-Ruiz, M.J., Hernández-Torrano, D., Pérez-González, J.C., Batey, M., & Petrides, K.V. (2011). The relationship between trait emotional intelligence and creativity across subject domains. *Motivation and Emotion, 35,* 461-473. doi:10.1007/s11031-011-9227-8

Santosa, C.M., Strong, C.M., Nowakowska, C., Wang, P.W., Rennicke, C.M., & Ketter, T.A. (2007). Enhanced creativity in bipolar disorder patients: A controlled study. *Journal of Affective Disorders, 100,* 31-39. doi:10.1016/j.jad.2006.10.013

Sayo, A., Jennings, R.G., & Van Horn, J.D. (2012). Study factors influencing ventricular enlargement in schizophrenia: A 20 year follow-up meta-analysis. *NeuroImage, 59(1),* 154-167. doi:10.1016/j.neuroimage.2011.07.011

Schlösser, R., Hutchinson, M., Joseffer, S., Rusinek, H., Saarimaki, A., Stevenson, J., . . . Brodie, J.D. (1998). Functional magnetic resonance imaging of human brain activity in a verbal fluency task. *Journal of Neurology, Neurosurgery & Psychiatry, 64,* 492-498. doi:10.1136/jnnp.64.4.492

Schlösser, R.G.M., Nenadic, I., Wagner, G., Güllmar, D., von Consbruch, K., Köhler, S., . . . Sauer, H. (2007). White matter abnormalities and brain activation in schizophrenia: A combined DTI and fMRI study. *Schizophrenia Research, 89(1-3),* 1-11. doi:10.1016/j.schres.2006.09.007

Schmechtig, A., Lees, J., Grayson, L., Craig, K.J., Dadhiwala, R., Dawson, G.R., . . . Ettinger, U. (2013). Effects of risperidone, amisulpride and nicotine on eye movement control and their modulation by schizotypy. *Psychopharmacology, 227(2),* 331-345. doi:10.1007/s00213-013-2973-4

Schmitt, A., Hasan, A., Gruber, O., & Falkai, P. (2011). Schizophrenia as a disorder of disconnectivity. *European Archives of Psychiatry and Clinical Neuroscience, 261(Supplement 2),* S150-S154. doi:10.1007/s00406-011-0242-2

Schofield, K., & Mohr, C. (2014). Schizotypy and hemispheric asymmetry: Results from two Chapman scales, the O-LIFE questionnaire, and two laterality measures. *Laterality, 19(2),* 178-200. doi:10.1080/1357650X.2013.789883

Schuldberg, D. (1990). Schizotypal and hypomanic traits, creativity, and psychological health. *Creativity Research Journal, 3(3),* 218-230. doi:10.1080/10400419009534354

Schuldberg, D. (2001). Six Subclinical Spectrum Traits in Normal Creativity. *Creativity Research Journal, 13(1),* 5-16. doi:10.1207/S15326934CRJ1301_2

Schultz, S.K., & Andreasen, N.C. (1999). Schizophrenia. *Lancet, 353,* 1425-1430. doi:10.1016/S0140-6736(98)07549-7

Schultze-Lutter, F., Klosterkötter, J., & Ruhrmann, S. (2014). Improving the clinical prediction of psychosis by combining ultra-high risk criteria and cognitive basic symptoms. *Schizophrenia Research, 154(1-3),* 100-106. doi:10.1016/j.schres.2014.02.010

Scott, J., Welham, J., Martin, G., Bor, W., Najman, J., O'Callaghan, M., . . . McGrath, J. (2008). Demographic correlates of psychotic-like experiences in young Australian adults. *Acta Psychiatrica Scandinavica, 118(3),* 230-237. doi:10.1111/j.1600-0447.2008.01214.x

Seeber, K., & Cadenhead, K.S. (2005). How does studying schizotypal personality disorder inform us about the prodrome of schizophrenia? *Current Psychiatry Reports, 7,* 41-50. doi:10.1007/s11920-005-0024-5

Shan, J.-C., Liu, C.-M., Chiu, M.-J., Liu, C.-C., Chien, Y.-L., Hwang, T.-J., . . . Hwu, H.-G. (2013). A Diagnostic Model Incorporating P50 Sensory Gating and Neuropsychological Tests for Schizophrenia. *PLoS ONE, 8(2),* e57197. doi:10.1371/journal.pone.0057197

Shepherd, A.M., Laurens, K.R., Matheson, S.L., Carr, V.J., & Green, M.J. (2012). Systematic meta-review and quality assessment of the structural brain alterations in schizophrenia. Neuroscience & Biobehavioral Reviews, 36(4), 1342-1356. doi:10.1016/j.neubiorev.2011.12.015

Shergill, S.S., Brammer, M.J., Amaro, E., Williams, S.C.R., Murray, R.M., & McGuire, P.K. (2004). Temporal course of auditory hallucinations. *British Journal of Psychiatry, 185,* 516-517. doi:10.1192/bjp.185.6.516

Siever, L.J., Koenigsberg, H.W., Harvey, P., Mitropoulou, V., Laruelle, M., Abi-Dargham, A., . . . Buchsbaum, M. (2002). Cognitive and brain function in schizotypal personality disorder. *Schizophrenia Research, 54(1-2),* 157-167. doi:10.1016/S0920-9964(01)00363-2

Sigi Hale, T., McCracken, J.T., McGough, J.J., Smalley, S.L., Phillips, J.M., & Zaidel, E. (2005). Impaired linguistic processing and atypical brain laterality in adults with ADHD. *Clinical Neuroscience Research, 5(5-6),* 255-263. doi:10.1016/j.cnr.2005.09.006

Silvia, P.J. (2008). Creativity and intelligence revisited: A latent variable analysis of Wallach and Kogan (1965). *Creativity Research Journal, 20,* 34-39. doi:10.1080/10400410701841807

Skudlarski, P., Jagannathan, K., Anderson, K., Stevens, M.C., Calhoun, V.D., Skudlarska, B.A., & Pearlson, G. (2010). Brain Connectivity Is Not Only Lower but Different in Schizophrenia: A Combined Anatomical and Functional Approach. *Biological Psychiatry, 68(1),* 61-69. doi:10.1016/j.biopsych.2010.03.035

Smith, E.E., & Jonides, J. (1999). Storage and Executive Processes in the Frontal Lobes.*Science, 283(5408),* 1657-1661. doi:10.1126/science.283.5408.1657

Snitz, B.E., MacDonald III, A.W., & Carter, C.S. (2006). Cognitive deficits in unaffected first-degree relatives of schizophrenia patients: A meta-analytic review of putative endophenotypes. *Schizophrenia Bulletin, 32(1),* 179-194. doi:10.1093/schbul/sbi048

Somers, M., Sommer, I.E., Boks, M.P., & Kahn, R.S. (2009). Hand-preferences and population schizotypy: A meta-analysis. *Schizophrenia Research, 108(1-3),* 25-32. doi:10.1016/j.schres.2008.11.010

Sommer, I., Ramsey, N., Kahn, R., Aleman, A., & Bouma, A. (2001). Handedness, language lateralisation and anatomical asymmetry in schizophrenia: Meta-analysis. *The British Journal of Psychiatry, 178,* 344-351. doi:10.1192/bjp.178.4.344

Sommer, I.E.C., Ramsey, N.F., & Kahn, R.S. (2001). Language lateralization in schizophrenia, an fMRI study. *Schizophrenia Research, 52(1-2),* 57-67. doi:10.1016/S0920-9964(00)00180-8

Spitzer, M. (1997). A Cognitive Neuroscience View of Schizophrenic Thought Disorder. *Schizophrenia Bulletin, 23(1),* 29-50. doi:10.1093/schbul/23.1.29

Spreen, O., & Strauss, E. (1998). *A compendium of neuropsychological tests* (2nd Ed.). New York: Oxford University Press.

Stanos, J.F. (2004). Test review: Wechsler abbreviated scale of intelligence. *Rehabilitation Counseling Bulletin, 48,* 56-57. doi:10.1177/00343552040480010801

Stefanis, N.C., Hanssen, M., Smirnis, N.K., Avramopoulos, D.A., Evdokimidis, I.K., Stefanis, C.N., . . . Van Os, J. (2002). Evidence that three dimensions of psychosis have a distribution in the general population. *Psychological Medicine, 32,* 347-358. doi:10.1017/S0033291701005141

Steinmann, S., Leicht, G., & Mulert, C. (2014). Interhemispheric auditory connectivity: structure and function related to auditory verbal hallucinations. *Frontiers in Human Neuroscience, 8(55),* 1-10. doi:10.3389/fnhum.2014.00055

Sternberg, R., & O'Hara, L.A. (2000). Intelligence and creativity. In R. Sternberg (Ed.), *Handbook of intelligence.* Cambridge: Cambridge University Press. doi:10.1017/CBO9780511807947.028

Sterzer, P., & Kleinschmidt, A. (2010). Anterior insula activations in perceptual paradigms: often observed but barely understood. *Brain Structure and Function, 214,* 611-622. doi:10.1007/s00429-010-0252-2

Strauss, G.P., Jetha, S.S., Ross, S.A., Duke, L.A., & Allen, D.N. (2010). Impaired facial affect labelling and discrimination in patients with deficit syndrome schizophrenia. *Schizophrenia Research, 118,* 146-153. doi:10.1016/j.schres.2010.01.016

Strauss, M.E. (1993). Relations of Symptoms to Cognitive Deficits in Schizophrenia. *Schizophrenia Bulletin, 19(2),* 215-231. doi:10.1093/schbul/19.2.215

Sullivan, P.F., Kendler, K.S., & Neale, M.C. (2003). Schizophrenia as a Complex Trait: Evidence From a Meta-analysis of Twin Studies. *Archives of General Psychiatry, 60,* 1187-1192. doi:10.1001/archpsyc.60.12.1187

Sun, L., Castellanos, N., Grützner, C., Koethe, D., Rivolta, D., Wibral, M., . . . Uhlhaas, P.J. (2013). Evidence for dysregulated high-frequency oscillations during sensory processing in medication-naïve, first episode schizophrenia. *Schizophrenia Research, 150(2-3),* 519-525. doi:10.1016/j.schres.2013.08.023

Sun, S., & Sinha, V.K. (2009). Event-related potential: An overview. *Industrial Psychiatry Journal, 18(1),* 70-73. doi:10.4103/0972-6748.57865

Sussman, J.E., Lymer, G.K.S., McKirdy, J., Moorhead, T.W.J., Maniega, S.M., Job, D., . . . McIntosh, A.M. (2009). White matter abnormalities in bipolar disorder and schizophrenia detected using diffusion tensor magnetic resonance imaging. *Bipolar Disorders, 11(1),* 11-18. doi:10.1111/j.1399-5618.2008.00646.x

Suzuki, A., & Usher, M. (2009). Individual differences in language lateralisation, schizotypy and the remote-associate task. *Personality and Individual Differences, 46,* 622-626. doi:10.1016/j.paid.2009.01.006

Suzuki, M., Nohara, S., Hagino, H., Kurokawa, K., Yotsutsuji, T., Kawasaki, Y., . . . Kurachi, M. (2002). Regional changes in brain gray and white matter in patients with schizophrenia demonstrated with voxel-based analysis of MRI. *Schizophrenia Research, 55(1-2),* 41-54. doi:10.1016/S0920-9964(01)00224-9

Swann, A.C., Lijffijt, M., Lane, S.D., Steinberg, J.L., & Moeller, F.G. (2009). Trait impulsivity and response inhibition in antisocial personality disorder. *Journal of Psychiatric Research, 43(12),* 1057-1063. doi:10.1016/j.jpsychires.2009.03.003

Symms, M., Jäger, H.R., Schmierer, K., & Yousry, T.A. (2004). A review of structural magnetic resonance neuroimaging. *Journal of Neurology, Neurosurgery, and Psychiatry, 75,* 1235-1244. doi:10.1136/jnnp.2003.032714

Tabak, N.T., & Weisman de Mamani, A.G. (2013). Latent profile analysis of healthy schizotypy within the extended psychosis phenotype. *Psychiatry Research, 210(3),* 1008-1013. doi:10.1016/j.psychres.2013.08.006

Takahashi, H., Iwase, M., Canuet, L., Yasuda, Y., Ohi, K., Fukumoto, M., . . . Takeda, M. (2010). Relationship between prepulse inhibition of acoustic startle response and schizotypy in healthy Japanese subjects. *Psychophysiology, 47(5),* 831-837. doi:10.1111/j.1469-8986.2010.010000.x

Takeuchi, H., Taki, Y., Sassa, Y., Hashizume, H., Sekiguchi, A., Fukushima, A., & Kawashima, R. (2010). White matter structures associated with creativity: Evidence from diffusion tensor imaging. *NeuroImage, 51,* 11-18. doi:10.1016/j.neuroimage.2010.02.035

Takeuchi, H., Taki, Y., Hashizume, H., Sassa, Y., Nagase, T., Nouchi, R., & Kawashima, R. (2011). Failing to deactivate: The association between brain activity during a working memory task and creativity. *NeuroImage, 55(2),* 681-687. doi:10.1016/j.neuroimage.2010.11.052

Tandon, R., Kesahvan, M.S., & Nasrallah, H.A. (2008). Schizophrenia, "Just the Facts": What we know in 2008. Part 1: Overview. *Schizophrenia Research, 100,* 4-19. doi:10.1016/j.schres.2008.01.022

Taylor, S.F., Kornblum, S., & Tandon, R. (1996). Facilitation and interference of selective attention in schizophrenia. *Journal of Psychiatric Research, 30,* 251-259. doi:10.1016/0022-3956(95)00046-1

Teplan, M. (2002). Fundamentals of EEG Measurement. *Measurement Science Review, 2(2),* 1-11.

Thirion, B., Pinel, P., Mériaux, S., Roche, A., Dehaene, S., & Poline, J.-B. (2007). Analysis of a large fMRI cohort: Statistical and methodological issues for group analyses. *NeuroImage, 35(1),* 105-120. doi:10.1016/j.neuroimage.2006.11.054

Thoma, R.J., Hanlon, F.M., Moses, S.N., Edgar, J.C., Huang, M., Weisend, M.P., . . . Cañive, J.M. (2003). Lateralization of Auditory Sensory Gating and Neuropsychological Dysfunction in Schizophrenia. *The American Journal of Psychiatry, 160(9),* 1595-1605. doi:10.1176/appi.ajp.160.9.1595

Thys, E., Sabbe, B., & De Hert, M. (2014). The assessment of creativity in creativity/psychopathology research – a systematic review. *Cognitive Neuropsychiatry, 19(4),* 359-377. doi:10.1080/13546805.2013.877384

Toga, A.W., & Thompson, P.M. (2003). Mapping brain asymmetry. *Nature Reviews Neuroscience, 4(1),* 37-48. doi:10.1038/nrn1009

Torrance, E.P. (1966). *Torrance Tests of Creative Thinking.* Bensenville, IL: Scholastic Testing Service.

Torrance, E.P. (2008a). *Torrance Tests of Creative Thinking.* Bensenville, IL: Scholastic Testing Service.

Torrance, E.P. (2008b). Torrance Tests of Creative Thinking: Manual for Scoring and Interpreting Results Verbal Forms A and B. Bensenville, IL: Scholastic Testing Service, Inc.

Torrance, E.P., Ball, O.E., & Safter, H.T. (2008). *Torrance Tests of Creative Thinking: Streamlined Scoring Guide for Figural Forms A and B.* Bensenville, IL: Scholastic Testing Service, Inc.

Tsakanikos, E., & Claridge, G. (2005). More words, less words: Verbal fluency as a function of 'positive' and 'negative' schizotypy. *Personality and Individual Differences, 39(4),* 705-713. doi:10.1016/j.paid.2005.02.019

Tsuang, M.T. (1993). Genotypes, phenotypes, and the brain: A search for connections in schizophrenia. *British Journal of Psychiatry, 163,* 299-307. doi:10.1192/bjp.163.3.299

Tucker, D.M. (1993). Spatial sampling of head electrical fields: the geodesic sensor net. *Electroencephalography & Clinical Neurophysiology, 87*(3), 154-163. doi:10.1016/0013-4694(93)90121-B

Uc, E.Y., Skinner, R.D., Rodnitzky, R.L., & Garcia-Rill, E. (2003). The midlatency auditory evoked potential P50 is abnormal in Huntington's disease. *Journal of Neurological Sciences, 212,* 1-5. doi:10.1016/S0022-510X(03)00082-0

Upmanyu, V.V., Bhardwaj, S., & Singh, S. (1996). Word-association emotional indicators: Associations with anxiety, psychoticism, neuroticism, extraversion, and creativity. *The Journal of Social Psychology, 136,* 521-529. doi:10.1080/00224545.1996.9714034

van Haren, N.E.M., Hulshoff Pol, H.E., Schnack, H.G., Cahn, W., Mandl, R.C.W., Collins, D.L., . . . Kahn, R.S. (2007). Focal Gray Matter Changes in Schizophrenia across the

Course of the Illness: A 5-Year Follow-Up Study. *Neuropsychopharmacology, 32,* 2057-2066. doi:10.1038/sj.npp.1301347

Van Strien, J.W., & Van Kampen, D. (2009). Positive schizotypy scores correlate with left visual field interference for negatively valenced emotional words: A lateralized .emotional Stroop study. *Psychiatry Research, 169(3),* 229-234. doi:10.1016/j.psychres.2008.06.019

Vartanian, O. (2012). Dissociable neural systems for analogy and metaphor: Implications for the neuroscience of creativity. *British Journal of Psychology, 103,* 302-316. doi:10.1111/j.2044-8295.2011.02073.x

Verdoux, H., & van Os, J. (2002). Psychotic symptoms in non-clinical populations and the continuum of psychosis. *Schizophrenia Research, 54,* 59-65. doi:10.1016/S0920-9964(01)00352-8

Vigneau, M., Beaucousin, V., Hervé, P.-Y., Jobard, G., Petit, L., Crivello, F., . . . Tzourio-Mazoyer, N. (2011). What is right-hemisphere contribution to phonological, lexico-semantic, and sentence processing?: Insights from a meta-analysis. *NeuroImage, 54(1),* 577-593. doi:10.1016/j.neuroimage.2010.07.036

Villarreal, M.F., Cerquetti, D., Caruso, S., Schwarcz López Aranguren, V., Gerschcovich, E.R., . . . Leiguarda, R.C. (2013). Neural Correlates of Musical Creativity: Differences between High and Low Creative Subjects. *PLoS ONE 8(9),* e75427. doi:10.1371/journal.pone.0075427

Vink, M., Ramsey, N.F., Raemaekers, M., & Kahn, R.S. (2005). Negative priming in schizophrenia revisited. *Schizophrenia Research, 79,* 211-216. doi:10.1016/j.schres.2005.05.004

Vollema, M.G., & van den Bosch, R.J. (1995). The Multidimensionality of Schizotypy. *Schizophrenia Bulletin, 21(1),* 19-31. doi:10.1093/schbul/21.1.19

Waldie, K.E., Haigh, C.E., Badzakova-Trajkov, G., Buckley, J., & Kirk, I.J. (2013). Reading the Wrong Way with the Right Hemisphere. *Brain Sciences, 3(3),* 1060-1075. doi:10.3390/brainsci3031060

Waldie, K.E., & Mosley, J.L. (2000). Hemispheric Specialization for Reading. *Brain and Language, 75(1),* 108-122. doi:10.1006/brin.2000.2346

Wan, L., Crawfod, H., & Boutros, N. (2006). P50 sensory gating: Impact of high vs. low schizotypal personality and smoking status. *International Journal of Psychophysiology, 60,* 1-9. doi:10.1016/j.ijpsycho.2005.03.024

Wang, J., Miyazato, H., Hokama, H., Hiramatsu, K.-I., & Kondo, T. (2004). Correlation between P50 suppression and psychometric schizotypy among non-clinical Japanese subjects. *International Journal of Psychophysiology, 52,* 147-157. doi:10.1016/j.ijpsycho.2003.06.001

Wang, Y., Yan, C., Yin, D.-Z., Fan, M.-X., Cheung, E.F.C., Pantelis, C., & Chan, R.C.K. (2014a). Neurobiological Changes in Schizotypy: Evidence From Both Volume-Based Morphometric Analysis and Resting-State Functional Connectivity. *Schizophrenia Bulletin.* Advance online publication. doi:10.1093/schbul/sbu178

Wang, Y., Yan, T.-X., Su, L., Yan, C., Wang, Y., Huang, J., . . . Raymond, C.K. (2014b). Neural correlates of prospective memory in individuals with schizotypal personality features. *Neuropsychology, 28(3),* 373-381. doi:10.1037/neu0000035

Waters, F., Woodward, T., Allen, P., Aleman, A., & Sommer, I. (2012). Self-recognition Deficits in Schizophrenia Patients With Auditory Hallucinations: A Meta-analysis of the Literature. *Schizophrenia Bulletin, 38(4),* 741-750. doi:10.1093/schbul/sbq144

Waters, F.A.V., Badcock, J.C., & Maybery, M.T. (2007). Hearing Voices: What Are They Telling Us? In J.E. Pletson (Ed.), *Psychology and Schizophrenia,* pp. 201-224. New York: Nova Science Publishers, Inc.

Waters, F.A.V., Badcock, J.C., Maybery, M.T., & Michie, P.T. (2003). Inhibition in schizophrenia: association with auditory hallucinations. *Schizophrenia Research, 62,* 275-280. doi:10.1016/S0920-9964(02)00358-4

Watis, L., Chen, S.H., Chua, H.C., Chong, S.A., & Sim, K. (2008). Glutamatergic abnormalities of the thalamus in schizophrenia: a systematic review. *Journal of Neural Transmission, 115(3),* 493-511. doi:10.1007/s00702-007-0859-5

Wechsler D. (1999). *Wechsler Abbreviated Scale of Intelligence (WASI).* San Antonio, Texas: The Psychological Corporation.

Wechsler, S. (2006). Validity of the Torrance Tests of Creative Thinking to the Brazilian Culture. *Creativity Research Journal, 18,* 15-25. doi:10.1207/s15326934crj1801_3

Weinstein, S., & Graves, R.E. (2001). Creativity, schizotypy, and laterality. *Cognitive Neuropsychiatry, 6(2),* 131-146. doi:10.1080/13546800042000098

Weiss, E.M., Hofer, A., Golaszewski, S., Siedentopf, C., Felber, S., & Fleischhacker, W.W. (2006). Language lateralization in unmedicated patients during an acute episode of schizophrenia: A functional MRI study. *Psychiatry Research: Neuroimaging, 146(2),* 185-190. doi:10.1016/j.pscychresns.2005.11.003

Welsh, R.C., Chen, A.C., & Taylor, S.F. (2010). Low-Frequency BOLD Fluctuations Demonstrate Altered Thalamocortical Connectivity in Schizophrenia. *Schizophrenia Bulletin, 36(4),* 713-722. doi:10.1093/schbul/sbn145

Whitfield-Gabrieli, S., Thermenos, H.W., Milanovic, S., Tsuang, M.T., Faraone, S.V., McCarley, R.W., . . . Seidman, L.J. (2009). Hyperactivity and hyperconnectivity of the default network in schizophrenia and in first-degree relatives of persons with schizophrenia. *Proceedings of the National Academy of Sciences, 106(4),* 1279-1284. doi:10.1073/pnas.0809141106

Whitford, T.J., Grieve, S.M., Farrow, T.F.D., Gomes, L., Brenna, J., Harris, A.W.F., . . . Williams, L.M. (2006). Progressive grey matter atrophy over the first 2-3 years of illness in first-episode schizophrenia: A tensor-based morphometry study. *NeuroImage, 32(2),* 511-519. doi:10.1016/j.neuroimage.2006.03.041

Widiger, T.A. (2001). What Can Be Learned From Taxometric Analyses? *Clinical Psychology: Science and Practice, 8(4),* 528-533. doi:10.1093/clipsy.8.4.528

Woodruff, P.W.R., Wright, I.C., Bullmore, E.T., Brammer, M., Howard, R.J., Williams, S.C.R., . . . Murray, R.M. (1997). Auditory Hallucinations and the Temporal Cortical Response to Speech in Schizophrenia: A Functional Magnetic Resonance Imaging Study. *The American Journal of Psychiatry, 154(12),* 1676-1682. doi:10.1176/ajp.154.12.1676

Wright, I.C., Ellison, Z.R., Sharma, T., Friston, K.J., Murray, R.M., & McGuire, P.K. (1999). Mapping of grey matter changes in schizophrenia. *Schizophrenia Research, 35(1),* 1-14. doi:10.1016/S0920-9964(98)00094-2

Youn, T., Park, H.-J., Kim, J.-J., Kim, M.S., & Kwon, J.S. (2003). Altered hemispheric asymmetry and positive symptoms in schizophrenia: equivalent current dipole of auditory mismatch negativity. *Schizophrenia Research, 59(2-3),* 253-260. doi:10.1016/S0920-9964(02)00154-8

Yuan, W., Szaflarski, J.P., Schmithorst, V.J., Schapiro, M., Byars, A.W., Strawsburg, R.H., & Holland, S.K. (2006). fMRI Shows Atypical Language Lateralization in Pediatric Epilepsy Patients. *Epilepsia, 47(3),* 593-600. doi:10.1111/j.1528-1167.2006.00474.x

Yung, A.R., Phillips, L.J., Yuen, H.P., & McGorry, P.D. (2004). Risk factors for psychosis in an ultra high-risk group: psychopathology and clinical features. *Schizophrenia Research, 67(2-3),* 131-142. doi:10.1016/S0920-9964(03)00192-0

Zanes, J., Hatfield, R., Houtler, B., & Whitman, D. (1998). The relationship between creativity and psychosis-proneness. *Personality and Individual Differences, 24,* 879-881. doi:10.1016/S0191-8869(97)00199-2

Zhou, S.Y., Suzuki, M., Takahashi, T., Hagino, H., Kawasaki, Y., Matsui, M., . . . Kurachi, M. (2007). Parietal lobe volume deficits in schizophrenia spectrum disorders. *Schizophrenia Research, 89,* 35-38. doi:10.1016/j.schres.2006.08.032

Ziegler, G., Dahnke, R., Winkler, A.D., & Gaser, C. (2013). Partial least squares correlation of multivariate cognitive abilities and local brain structure in children and adolescents. *NeuroImage, 82,* 284-294. doi:10.1016/j.neuroimage.2013.05.088

Zipursky, R.B., Marsh, L., Lim, K.O., DeMent, S., Shear, P.K., Sullivan, E.V., . . . Pfefferbaum, A. (1994). Volumetric MRI assessment of temporal lobe structures in schizophrenia. *Biological Psychiatry, 35(8),* 501-516. doi:10.1016/0006-3223(94)90097-3

Appendix A: Participant Information Sheet

SCHOOL OF PSYCHOLOGY
Faculty of Science
The University of Auckland
Private Bag 92019,
Auckland 1142, New Zealand

THE UNIVERSITY OF AUCKLAND
NEW ZEALAND
Te Whare Wānanga o Tāmaki Makaurau

PARTICIPANT INFORMATION SHEET

Project Title
Laterality and creativity in adults with and without schizotypal personality traits.

About the Researcher
My name is Haeme Park and I am working towards a PhD in Psychology at the University of Auckland under the supervision of Associate Professor Karen Waldie. I would like to invite you to participate in my research project at the University of Auckland. It is important to read this document carefully so that you can make an informed decision about whether you would like to participate.

Research Background
The general aim of this research is to examine the relationship between personality and brain activity. In particular, I am interested in the concept of schizotypy, which is defined as a cluster of personality traits that may lead to a predisposition to schizophrenia and schizophrenia-related disorders within a healthy population. Studies have shown that individuals who score high on schizotypy show an increased right hemispheric involvement when performing language tasks (most people mainly use just their left hemisphere for language). This pattern of greater spread of brain activation in the brain is also thought to be an important factor in creative thinking. Research has confirmed a positive correlation between the levels of schizotypy and creativity (i.e., people who score high on schizotypy scales also rate higher on measures of creativity).

The overall aim of this study is to provide a more comprehensive understanding of the neural bases of schizotypy by utilising cognitive, behavioural, and brain scanning techniques. By completing this research, I hope to further determine the relationship between schizotypy and the brain, and particularly the potential effects these traits have on brain hemispheric differences as well as the level of creativity.

What is Involved?
This project will be divided into three separate sessions. The first session will consist of various questionnaires which will determine your eligibility for the next two sessions. These will consist of two neuroimaging experiments, using electroencephalogram (EEG) and functional magnetic resonance imaging (fMRI).

For the first session, you will be asked to fill out five questionnaires. These will be:
1. A demographic questionnaire, which will include questions about your background (including questions about any family history of mental illness);
2. The Wechsler Abbreviated Scale of Intelligence (WASI), which will test your IQ;
3. The Edinburgh Handedness Inventory, which will determine your handedness;
4. The Oxford-Liverpool Inventory of Feelings and Experiences (O-LIFE), which will measure your level of schizotypy;

5. The Torrence Tests for Creative Thinking (TTCT), which will measure your level of creativity.

You will also be asked to do a quick dual-task on a computer which involves reading a paragraph on the computer screen while tapping the keyboard at the same time. These will be conducted on Level 3 of the Human Sciences Building, City Campus, and will take up to three hours. As compensation for your time, you will receive a Countdown voucher worth $20.

There are two potentially emotionally distressing items in the demographic questionnaire which ask for personal and family histories of mental illness. In addition, you will also be informed of your level of schizotypy. In the event that you find these (or any other questions) upsetting, you can choose to immediately stop participation. Contact details of the study supervisors and the Head of Department of Psychology have been provided at the end of this information sheet should you choose to discuss the cause of the distress.

If you are selected to take part in the next two sessions, you will be notified by email where you can agree or disagree to further participate in the research. The next part of the study will involve EEG which will measure brain function. Recoding EEG involves placing electrodes on the surface of the scalp by means of an elastic 'cap'. The electrodes are encased in sponges, which are soaked in an electrolyte solution (consisting of shampoo, salt, and water) prior to being placed on your head. This part of the study will take up to an hour, and involves no pain or discomfort. This will also take place on Level 3 of the HSB building in the EEG laboratory.

Finally, we will also measure brain activity using functional magnetic resonance imaging (fMRI) which detects magnetic fields generated by the flow of blood to active areas of the brain. MRI is routinely used for clinical purposes and has no known harmful effects on the human body. It is painless, and involves no radiation exposure, needles or injections. However, since it is associated with a strong magnetic field, some people may not be eligible to volunteer because of the presence of the following:

- Pacemakers/defibrillators
- Hearing aids
- Metal clips in the brain (aneurysm clips)
- Metal fragments in or near the eyes

At the MRI unit, all volunteers will first be checked for these and any other reasons a magnetic resonance scan should not be performed. There is also a possibility of some people feeling claustrophobic in the MRI scanner. There will be an emergency buzzer placed in the scanner prior to the experiment, and you can press it to stop the experiment immediately at any time and choose to leave if you feel any level of discomfort. The research will be conducted at CAMRI, Medical School, Grafton Campus. This part of the experiment will take no longer than 2 hours.

There is a possibility that a clinical abnormality is detected through performing a scan on you. If this occurs, you will be informed of this and will be referred back to your general practitioner. Because the images are not routinely reviewed by a radiologist, we are unable to perform diagnostic scans of areas where you have known abnormalities for medical purposes.

Participation Incentive

For your time, you will be paid $20 in vouchers after the first session, and a further $40 in Countdown vouchers upon the completion of both EEG and fMRI experiments. You will also

receive an electronic copy of the anatomical image of your brain. You can also request a copy of the final published report of this study.

Confidentiality and Anonymity

Participation in this study is entirely voluntary, and if you choose to participate, you can change your mind at any time without giving a reason and without any negative consequences. After your participation is completed, you will still have the right to request that your data be withdrawn from the study for up to three months. You will be given a copy of this document to keep. The anonymity of the data you provide will be preserved and any information that identifies you as a participant will be used confidentially. Your name will only appear on the attached Consent Form, which will be coded with an identification number that will be used throughout the study. If the information you provide is reported or published, this will be done in a way that does not identify you as its source.

Access to consent forms and data will be restricted to the researchers directly involved in this project and will be stored in a locked cabinet on university premises. All data will be kept for a minimum period of six years to allow for publication and future re-analysis, after which time it will be securely and confidentially disposed of.

If you would like to participate in this research project, please contact me (Haeme Park) via email. If you any have questions or concerns about the project, please contact one of the following:

Principal Investigator:
Associate Professor Karen Waldie PhD
Department of Psychology
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Student:
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The MRI Centre Director is:

Dr Brett Cowan
Centre for Advanced MRI
University of Auckland
FHMS, 85 Park Road
Grafton.
Ph: (09) 373 7599 Ext. 89513
Email: b.cowan@auckland.ac.nz

For any queries regarding ethical concerns you may contact the Chair, The University of Auckland Human Participants Ethics Committee, The University of Auckland, Office of the Vice Chancellor, Private Bag 92019, Auckland 1142. Telephone 09 373-7599 extn. 83711.

Appendix B: Participant Consent Form

SCHOOL OF PSYCHOLOGY
Faculty of Science
The University of Auckland
Private Bag 92019,
Auckland 1142, New Zealand

THE UNIVERSITY OF AUCKLAND
NEW ZEALAND
Te Whare Wānanga o Tāmaki Makaurau

CONSENT FORM

THIS CONSENT FORM WILL BE HELD FOR A PERIOD OF SIX YEARS

Project title: Laterality and creativity in adults with and without schizotypal personality traits.

Researchers: Haeme Park, Professor Ian Kirk, Associate Professor Karen Waldie.

I have read and understood the accompanying Participant Information Sheet, which explains this research project and my role as a participant. I have had an opportunity to ask questions and have had them answered satisfactorily.

In particular I understand that:

- I will be asked to complete various questionnaires which will determine my eligibility for further neuroimaging experiments. This will take up to three hours.
- I may be asked to participate in the EEG and fMRI experiments, which will take place at the City Campus and the Grafton Campus, the University of Auckland, respectively.
- In the unlikely event that a clinically significant abnormality is accidentally found in my brain during the MRI scan, the researchers will be obliged to inform me.
- I have the right to stop participation at any time without having to give a reason.
- Whether or not I participate will not affect my relationship with the researchers.
- For three months after my participation I will still have the right to request that my data be withdrawn from the study.
- My name will appear only on this form. The data from this research will be stored anonymously, coded by number.
- Research publications and presentations from this study will not contain any information that could identify me.
- I will receive $20 in compensation for the first part of the research, and $40 for the EEG and fMRI sessions as well as an electronic copy of the anatomical scan of my brain.

I voluntarily agree to take part in this research.

Signed: _____

Name: _____

(please print)

Date: _____

(Researcher use only)
Participant Number:

Approved By The University of Auckland Human Participants Ethics Committee On For (3) Years Until 01/07/2014 Reference Number 2011 / 323

Appendix C: Edinburgh Handedness Inventory

EDINBURGH HANDEDNESS INVENTORY

Last name: _____

First names: _____

Date of birth: _____ Gender: _____

Please indicate your preference for the use of the left or right hand in the following tasks by placing a "+" in the appropriate column. If you have such a strong preference for one hand that you would never try to use the other unless forced to, place a "++" in the column. If you would perform the task with either hand place a "+" in both columns.

Some of the tasks require both hands. In these cases the part of the task, or object, for which hand preference is wanted is indicated in the brackets.

Please try to answer all of the questions. Only leave a blank if you have no experience of the task or object.

		LEFT	RIGHT
1	Writing		
2	Drawing		
3	Throwing		
4	Scissors		
5	Toothbrush		
6	Knife (without fork)		
7	Spoon		
8	Broom (upper hand)		
9	Striking match (match)		
10	Opening box (lid)		
I	Which foot do you prefer to kick with?		
II	Which eye do you use when only using one?		

Appendix D: The Oxford-Liverpool Inventory of Feelings and Experiences

Do you believe in telepathy?	Yes	No
Do you ever feel sure that something is about to happen, even though there does not seem to be any reason for you thinking that?	Yes	No
Do you ever suddenly feel distracted by distant sounds that you are not normally aware of?	Yes	No
Do you often have days when indoor lights seem so bright that they bother your eyes?	Yes	No
Does your sense of smell sometimes become unusually strong?	Yes	No
Have you felt as though your head or limbs were somehow not your own?	Yes	No
Have you sometimes sensed an evil presence around you, even though you could not see it?	Yes	No
Have you wondered whether the spirits of the dead can influence the living?	Yes	No
On occasions, have you seen a person's face in front of you when no one was there?	Yes	No
When in the dark do you often see shapes and forms even though there's nothing there?	Yes	No
When you look in the mirror does your face sometimes seem quite different from usual?	Yes	No
Are your thoughts sometimes so strong that you can almost hear them?	Yes	No
Can some people make you aware of them just by thinking about you?	Yes	No
Do ideas and insights sometimes come to you so fast that you cannot express them all?	Yes	No
Do the people in your daydreams seem so true to life that you sometimes think they are real?	Yes	No
Do you sometimes feel that your accidents are caused by mysterious forces?	Yes	No
Do you think you could learn to read other's minds if you wanted to?	Yes	No
Does it often happen that nearly every thought immediately and automatically suggests an enormous number of ideas?	Yes	No
Does a passing thought ever seem so real it frightens you?	Yes	No

Does your voice ever seem distant or faraway?	Yes	No
Have you ever felt that you have special, almost magical powers?	Yes	No
Is your hearing sometimes so sensitive that ordinary sounds become uncomfortable?	Yes	No
Do you ever have a sense of vague danger or sudden dread for reasons that you do not understand?	Yes	No
Do you feel so good at controlling others that it sometimes scares you?	Yes	No
Have you ever thought you heard people talking only to discover that it was in fact some nondescript noise?	Yes	No
Have you felt that you might cause something to happen just by thinking too much about it?	Yes	No
Have you occasionally felt as though your body did not exist?	Yes	No
Have you sometimes had the feeling of gaining or losing energy when certain people look at you or touch you?	Yes	No
Are the sounds you hear in your daydreams really clear and distinct?	Yes	No
Do your thoughts sometimes seem as real as actual events in your life?	Yes	No
Are you easily distracted when you read or talk to someone?	Yes	No
Do you ever feel that your speech is difficult to understand because the words are all mixed up and don't make sense?	Yes	No
Do you often experience an overwhelming sense of emptiness?	Yes	No
Do you often feel lonely?	Yes	No
Is it hard for you to make decisions?	Yes	No
Are you a person whose mood goes up and down easily?	Yes	No
Are you easily hurt when people find fault with you or the work you do?	Yes	No
Are you sometimes so nervous that you are 'blocked'?	Yes	No
Do you dread going into a room by yourself where other people have already gathered and are talking?	Yes	No
Do you easily lose your courage when criticised or failing in something?	Yes	No
Do you find it difficult to keep interested in the same thing for a long time?	Yes	No

Do you frequently have difficulty in starting to do things?	Yes	No
Do you often feel that there is no purpose to life?	Yes	No
Do you often have difficulties in controlling your thoughts?	Yes	No
Do you often worry about things you should not have done or said?	Yes	No
Do you worry about awful things that might happen?	Yes	No
No matter how hard you try to concentrate do unrelated thoughts creep into your mind?	Yes	No
When in a crowded room, do you often have difficulty in following a conversation?	Yes	No
Are you easily confused if too much happens at the same time?	Yes	No
Are you easily distracted from work by daydreams?	Yes	No
Do you often feel ‘fed up’?	Yes	No
Do you worry too long after an embarrassing experience?	Yes	No
Would you call yourself a nervous person?	Yes	No
Do you often hesitate when you are going to say something in a group of people whom you more or less know?	Yes	No
Can you usually let yourself go and enjoy yourself at a lively party?	Yes	No
Do people who try to get to know you better usually give up after a while?	Yes	No
Do you feel that making new friends isn’t worth the energy it takes?	Yes	No
Do you find the bright lights of a city exciting to look at?	Yes	No
Do you like going out a lot?	Yes	No
Do you prefer watching television to going out with other people?	Yes	No
Do you usually have very little desire to buy new kinds of food?	Yes	No
Is it fun to sing with other people?	Yes	No
Are people usually better off if they stay aloof from emotional involvements with people?	Yes	No
Are there very few things that you have ever really enjoyed doing?	Yes	No

Are you much too independent to really get involved with other people?	Yes	No
Are you rather lively?	Yes	No
Can just being with friends make you feel really good?	Yes	No
Do you have many friends?	Yes	No
Do you like mixing with people?	Yes	No
Do you thinking having close friends is not as important as some people say?	Yes	No
Does it often feel good to massage your muscles when they are tired or sore?	Yes	No
Has dancing or the idea of it always seemed dull to you?	Yes	No
Have you often felt uncomfortable when your friends touch you?	Yes	No
Is trying new foods something you have always enjoyed?	Yes	No
On seeing a soft thick carpet have you sometimes had the impulse to take off your shoes and walk barefoot in it?	Yes	No
When things are bothering you do you like to talk to other people about it?	Yes	No
Do you feel very close to your friends?	Yes	No
Do you love having your back massaged?	Yes	No
Have you had very little fun from physical activities like walking, swimming, or sports?	Yes	No
Do you enjoy many different kinds of play and recreation?	Yes	No
Is it true that your relationships with other people never get very intense?	Yes	No
Do people who drive carefully annoy you?	Yes	No
Do you often feel like doing the opposite of what other people suggest, even though you know they are right?	Yes	No
Do you often feel the impulse to spend money which you know you can't afford?	Yes	No
Do you often have an urge to hit someone?	Yes	No
Do you sometimes talk about things you know nothing about?	Yes	No
Are you usually in an average sort of mood, not too high and not too low?	Yes	No
Do you at times have an urge to do something harmful or shocking?	Yes	No

Do you ever have the urge to break or smash things?	Yes	No
Do you often change between intense liking and disliking of the same person?	Yes	No
Do you stop to think things over before doing anything?	Yes	No
Do you think people spend too much time safeguarding their future with savings and insurance?	Yes	No
Have you ever blamed someone for doing something you know was really your fault?	Yes	No
Have you ever cheated at a game?	Yes	No
Have you ever felt the urge to injure yourself?	Yes	No
When in a group of people do you usually prefer to let someone else be the centre of attention?	Yes	No
When you catch a train do you often arrive at the last minute?	Yes	No
Would being in debt worry you?	Yes	No
Would you take drugs which may have strange or dangerous effects?	Yes	No
Do you consider yourself to be pretty much an average kind of person?	Yes	No
Have you ever taken advantage of someone?	Yes	No
Would you like other people to be afraid of you?	Yes	No
Do you often overindulge in alcohol or food?	Yes	No
Would it make you nervous to play the clown in front of other people?	Yes	No

Appendix E: Demographic Questionnaire

Demographic Questionnaire

Please complete the questionnaire by answering all questions. This is entirely voluntary and the information will be treated confidentially.

---

1. Date of Birth _____

2. Gender (circle one) Male Female

3. Ethnicity (circle one)

Australian	British	Chinese	Cook Island Maori
German	Indian	Japanese	Middle Eastern
NZ European	NZ Maori	Other Asian	Other European
Other Pacific Island	Tongan	Other _____	

4. How many languages do you speak? _____

5. Are you currently studying/have you ever undertaken studies at a tertiary level?

Yes No

6. If yes, what is/was the course of study? (E.g., engineering, law, photography.)

_____

7. What are your interests/hobbies?

_____

8. Do you have any history of mental illness? Yes No

9. If yes, please elaborate.

_____

_____

10. Are you currently on medication for your illness? Yes No

11. Do you have any history of mental illness in your family? Yes No

12. If yes, please elaborate.

_____

_____

13. Please give a rating from 1 to 7 regarding the level of creativity in your professional life (i.e., at work or at tertiary education).

No significant creativity						Extreme creativity
1	2	3	4	5	6	7

14. Please give a rating from 1 to 7 regarding the level of creativity in your extra-curricular life (i.e., hobbies, interests).

No significant creativity						Extreme creativity
1	2	3	4	5	6	7

15. Considering both your professional and personal life, please give a rating from 1 to 7 regarding how creative you see yourself to be.

Not creative						Extremely creative
1	2	3	4	5	6	7

Thank you.