

Dissociating Variations in Attention with Schizotypy and Anxiety

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Abstract

Establishing how cognitive abnormalities result in the signs and symptoms that define schizophrenia and anxiety disorders (and their co-morbidity) has become a prominent question in clinically, and sub-clinically, applied research. Abnormal performance in schizophrenia, schizotypy and anxiety has been observed in comparison to healthy individuals on a range of cognitive and behavioural tasks. For example, abnormal attention to irrelevant information has long been recognised by clinicians, which has since encouraged researchers to elucidate the nature of the relationship between schizophrenia, and anxiety more recently, with allocation of attention to stimuli in laboratory studies providing empirical evidence for an attentional view of these disorders.

The pre-exposure effect (slower learning to a stimulus that has been rendered familiar by preexposure, relative to a novel cue), hereafter referred to as latent inhibition, has been shown to be inversely correlated with schizotypy, and abnormal in people with schizophrenia, but findings are inconsistent. One potential contributing factor to this inconsistency is that many tasks that purport to measure latent inhibition are confounded by alternative effects that also retard learning and co-vary with schizotypy, such as learned irrelevance (experience of a cue as irrelevant to the occurrence of an outcome due to inconsistent/uncorrelated presentations of a cue and a target). The general aim of this thesis is to address, or begin to address, some of the key questions and limitations with existing research that evaluate latent inhibition and learned irrelevance as potentially useful cognitive endophenotypes for schizophrenia and anxiety disorders. The current experiments separate out the effects of latent inhibition and learned irrelevance to assess the independent effects of these phenomena on schizotypy (and by extension schizophrenia) and anxiety. By teasing apart, the effects of latent inhibition and

learned irrelevance the attempt is to disentangle, and improve understanding of attentional abnormalities observed in these sub-clinical traits and by extension, their related pathologies.

Across Experiments 1-4, the purpose was two-fold. The first was to address the limitations of existing latent inhibition tasks by designing a paradigm that examines a purer effect of latent inhibition, by minimising the contribution of learned irrelevance, and assessing how this latent inhibition task co-varies with schizotypy and anxiety (Chapter 2: Experiments 1 and 2). The second was to examine the alternative, potentially less equivocal, learned attentional paradigm (learned irrelevance) and assess the relationship between this task with both schizotypy and anxiety (Chapter 3: Experiments 3 and 4). Based on the assumption that latent inhibition and learned irrelevance share similar psychological underpinnings (in this case, attentional), we anticipated the effect of schizotypy and anxiety to be comparable in the two types of attention tasks here. The results however indicate a double dissociation; an abnormally persistent latent inhibition effect in high positive schizotypy individuals (Experiments 1 and 2) and a reduced learned irrelevance effect in high state anxious individuals (Experiments 3 and 4). The possibility that latent inhibition is non-attentional and the implications of these findings for associative models of attention and learning are explored.

The aim of Experiments 5 and 6 were to explore the causal relationship between induced variations in anxiety (stress, relaxation or neutral mood) and learned variations in attention, using a less ambiguous measure of attention (compared to latent inhibition): learned irrelevance. Based on the findings from Experiments 3 and 4, a reduced attentional bias towards previously established predictive cues was expected in individuals induced with an acute state of anxiousness, relative to individuals induced with either a relaxed or neutral mood state. This pattern of results was observed but to a weaker extent than the previous experiments,

suggesting that induced variations in anxiety do not have the same relationship with learning as naturally occurring variations in anxiety, as observed in Experiments 3 and 4. Further analyses revealed that the relationship between reduced learned irrelevance and anxiety was mediated by individuals who were also characterised by high levels of schizotypy, and by extension vulnerability to schizophrenia. Given the potential common underlying cognitive processes to both anxiety and schizophrenia, it seems likely that therapies which target the symptoms of anxiety (e.g., Attentional Bias Modification Treatment; ABMT) would be beneficial to individuals who have also been diagnosed with a psychotic disorder.

This work represents the first attempt to investigate the independent effects of latent inhibition and learned irrelevance on schizotypy and anxiety, using refined tasks that minimised the contribution of either learning phenomenon on each other. How these learning tasks co-vary in patients with schizophrenia and clinically diagnosed anxiety however remains for future research to determine¹. At this juncture, the current findings lend support to the potential cognitive endophenotype status of learned irrelevance (considering its status as a less ambiguous measure of attention) and its continued use to provide a base for the development of relevant attentional bias modification treatments.

¹ This work in clinically diagnosed populations (including preparation for publication: Granger et al.) is currently on-going in our lab.

Publications

The data contained in this thesis have been published as follows:

Chapter 2

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Chapter 1: General Introduction

1. Introduction

It has been proposed that schizophrenia is associated with a breakdown of an attentional filter; reflecting an inability to reduce attention to (or ignore) irrelevant stimuli (McGhie & Chapman, 1961; Hemsley, 1987), and such conclusions have prompted studies to elucidate the nature of this relationship in the laboratory. Many of these studies have translated designs from animal conditioning experiments (i.e., latent inhibition, learned irrelevance and blocking), in an attempt to understand the interaction of attention and associative learning, and how this might relate to schizophrenia and its associated pathologies, such as anxiety.

Psychotic disorders such as schizophrenia exist on a continuum, ranging from typical imaginative states (low schizotypy), to features related to schizophrenic symptoms (high schizotypy), suggesting that natural variations in these schizotypal characteristics can serve as a proxy for the full blown condition (Claridge, 1997). This has been supported by studies indicating that attentional mechanisms are similarly disrupted in high psychometrically-defined schizotypal individuals and people with schizophrenia (e.g. Baruch, Hemsley & Gray, 1988a,b; Gray et al., 2002; Evans, Gray & Snowden, 2007; Schmidt-Hansen, Killcross & Honey, 2009; Le Pelley, Schmidt-Hansen, Harris, Lunter & Morris, 2010a; Granger, Prados & Young, 2012). However, within a ‘fully dimensional’ framework, this continuum is extended to represent the highest point ending, not only in clinical diagnoses of schizophrenia but also in pathological spectra comorbid with schizophrenia, such as anxiety (Rossi et al., 2000; Rossi & Daneluzzo, 2002). In line with this proposition, measures of anxiety have been shown to co-vary with schizotypal traits that also appear to modulate attentional effects that have been translated from animal conditioning studies (Braunstein-Bercovitz, 2002).

The experiments reported in this thesis investigate the attentional mechanisms underlying the sub-dimensions of schizotypy (and by extension schizophrenia) to assess whether attentional abnormalities are specific to the symptoms of schizophrenia, or whether they are non-specific effects, related to the high levels of anxiety that accompany these states.

A. Overview of Schizophrenia, Schizotypy and Anxiety

1.1 Schizophrenia: Symptoms, Classification & Causes

1.1.1 Schizophrenia at the symptom level

Schizophrenia is a severe form of mental illness affecting around 1% of the global population with direct costs of treating the disorder estimated to be around £2.6 billion per year in the UK alone (Tajima-Pozo et al., 2015). The general incidence of schizophrenia is reported to be slightly lower in females with a later age of onset in the late-20's, relative to the early- to mid-20's for males. Earlier age of onset in males has been linked to worse premorbid adjustment, lower educational achievement and a worse overall prognosis (Diagnostic and Statistical Manual of Mental Disorders [DSM-V], American Psychiatric Association, 2013). Lifetime prevalence also varies by race/ethnicity, across countries and by geographic origin for immigrants and children of immigrants (DSM-V). Schizophrenia is defined by 3 groups of symptoms. Positive symptoms reflect marked departures from ordinary cognition, which include; delusions; hallucinations; disorganized speech (e.g. frequent derailment or incoherence); grossly disorganized or catatonic behaviours. Negative symptoms reflect the absence or diminution of normal daily functions, which is characterized by affective flattening, alogia (poverty of speech), or avolition (lack of motivation). Cognitive symptoms are subtle and may only be recognised when tests are performed; cognitive symptoms include: poor

executive functioning, trouble focusing or paying attention, and problems with working memory (DSM-V, 2013).

1.1.2 Classification of symptoms

The DSM is the handbook used by mental health care professionals worldwide to guide diagnosis of mental disorders. In line with the development of new research and knowledge, the DSM has been periodically reviewed since it was first published in 1952. The latest revision is DSM-V and the classification for schizophrenia based on this revision can be found in Appendix 1. The DSM-V states that in order for schizophrenia to be diagnosed, symptoms must have been present for six months and include at least one month of active symptoms (i.e., delusions, hallucination or disorganised speech). The diagnostic criteria no longer identify sub-types of schizophrenia (previously identified as Paranoid; Disorganised; Catatonic; Undifferentiated and Residual sub-types in the DSM-IV, 1994), due to overlapping sub-type symptoms and symptoms changing from one sub-type to another. The sub-types are now used to provide further detail in diagnosis. For example, paranoid schizophrenia (marked by delusions and auditory hallucinations) is now used to specify schizophrenia and other psychotic conditions such as schizoaffective disorder (see also section 1.2.1). This specifier can also be used to diagnose other disorder areas such as bipolar disorder and major depressive disorder (DSM-V, 2013).

This latest revision of the DSM-V, whilst not changing significantly from DSM-IV, has made an important shift towards a dimensional approach rather than a categorical approach to diagnosis. Previous classification systems based on a categorical approach, defined the presence or absence of a disorder to be clear cut; for instance in DSM-III and DSM-IV, a schizophrenia diagnosis could only be given if present symptoms were clearly not due to another Axis I disorder, such as an anxiety, mood or substance abuse disorder. However, the

newly-adopted dimensional approach characterises the relationship between schizophrenia, and other disorders such as schizoaffective disorder, bipolar disorder and major depression (See also section 1.1.4). This current consensus also supports schizophrenia forming a continuum with normal behaviour. For example several epidemiologic and clinical studies have demonstrated a symptomatic continuum of psychotic like experiences ranging from self-reported infrequent psychotic symptoms in the general population to schizotypal traits, to schizotypal personality disorder, and finally to full-blown psychosis resulting in a diagnosable primary psychotic disorder (for a review see Esterberg & Compton, 2009).

1.1.3 Causes of schizophrenia

The degree of heterogeneity regarding the symptomatology of schizophrenia is one reason for the difficulty in its classification and the confusion surrounding its aetiology. Despite the vast amount of research dedicated to the topic, the exact causes of schizophrenia remain unclear. It has been proposed there are multiple causes of schizophrenia and it is the result of a complex interplay between a number of different environmental (e.g., stress and major trauma; Morgan & Fisher, 2007), neurological (neurotransmitter abnormalities; Vallone, Picetti & Borrelli, 2000) and genetic factors (see Sanders et al., 2008 for the reviewed role of 14 candidate genes).

1.1.3.1 Key Neurological factors

(1) Dopamine hypothesis of schizophrenia

The hypothesis that dopamine (DA) and dopaminergic mechanisms are central to schizophrenia has been one of the most enduring theories in psychiatric research. Dopamine (as well as adrenaline and noradrenaline) is an abundant neurotransmitter that is part of the catecholamine group. Dopaminergic projections predominantly give rise to nigrostriatal,

mesolimbic and mesocortical pathways and impairments in the dopamine system result from dopamine dysfunctions in these brain areas (Birsch, 2014). The first formulation of the hypothesis (version I) emphasised the role of hyperactive dopamine transmission in the etiology of schizophrenia. This emerged from the discovery of anti-psychotic drugs and the influential research by Carlsson and Lindqvist (1963) who demonstrated that these drugs augmented the metabolism of dopamine in animals. Additionally, reserpine, an effective drug for treating psychosis, was found to block the reuptake of dopamine and other monoamines, leading to their dissipation; whilst amphetamine, which increases synaptic monoamine levels, was found to induce psychotic symptoms (Carlsson, Lindqvist & Magnusson, 1957). These observations provided further evidence for the dopamine hypothesis of schizophrenia and much emphasis in research then focused on excess transmission at dopamine receptors and blockade of these receptors to treat psychosis (Matthysse, 1973; Snyder, 1976). However, whilst this original version of the hypothesis could explain hyperactivity of dopamine in schizophrenia, little consideration was given to how it might relate to the co-existence of positive and negative symptoms.

The dopamine hypothesis was later reformulated (version II) due to increasing awareness of the chronicity of negative and cognitive symptoms and their resistance to dopamine D2 receptor antagonism (the main receptor for antipsychotic drugs). The advancement of imaging data suggested that these symptoms were possibly the result of reduced dopamine D1 receptor activation in the prefrontal cortex (PFC) and subsequent findings emerged suggesting the importance of prefrontal dopamine transmission at D1 receptors (the main DA receptor in the neocortex) for optimal PFC performance (see Knable & Weinberger, 1997). Such observations led to the hypothesis that the effects of abnormalities in dopamine function could vary by brain region, and that whilst hyperactive dopamine

transmission in the mesolimbic areas was found to be implicated in the positive symptoms; hypoactive dopamine transmission in the prefrontal cortex was found to be implicated in the cognitive and negative symptoms of schizophrenia (Howes & Kapur, 2009).

However, a major shortcoming of both the original hypothesis (version I) and the revised hypothesis (version II) was in their lack of explanation detailing how dopaminergic abnormalities actually led to the clinical expression of the disease. This omission gave way to a third conceptualisation of the theory which suggested that multiple ‘hits’ act together to cause a dysregulation of dopamine, drawing upon evidence from environmental, animal, genetic, family and imaging studies schizophrenia (Howes & Kapur, 2009). Version III of the theory implicates the development in the neuroscience literature of increasing evidence for the role of dopamine in motivational salience and reward prediction (e.g., Robbins & Everitt, 1982, 1996; Schultz, Dayan & Montague, 1997), which provided a framework to link dopamine dysregulation to the symptoms of schizophrenia using salience and reward. Such developments of the hypothesis (see: Kapur, 2003; Kapur, Mizrahi & Li, 2005) have suggested that dysregulated dopamine transmission disrupts the normal process of contextually driven salience attribution and leads to an aberrant assignment of salience to stimuli, independent of and out of synchrony with the context. Such inappropriately distributed salience represents an ‘altered experience of the world’ and it is argued that psychotic (positive) symptoms, such as hallucinations and delusion, emerge over time as the individual’s own experience of aberrant salience. Hallucinations and delusions are thus constructed by the individual and represent the individual’s existing cognitive and cultural background; allowing the same dopaminergic abnormality to have different clinical expressions across different individuals. Negative symptoms are proposed to be downstream from this: dopamine dysregulation leading to aberrant salience in turn causes a ‘drowning out’ of stimuli indicating reward (i.e., stimuli in

synchrony with the context); the result being social withdrawal and neglect of interests. In support of this explanation, schizophrenia has been associated with reduced ventral striatal activation to reward, and greater reduction correlates with increased negative symptoms (Juckel, Schlagenhauf & Koslowski, 2006).

(2) Glutamate hypothesis of schizophrenia

Whilst the dopamine hypothesis of schizophrenia has been the most influential in terms of explanatory power for symptoms of the illness, theories involving other neurotransmitters have also been proposed. Glutamatergic hypofunction has also been implicated in the pathophysiology of schizophrenia, since the observation that phencyclidine, ketamine and other *N*-methyl-D-aspartate (NMDA) receptor blockers induced positive symptoms in healthy volunteers or exacerbated the positive, negative and cognitive dysfunction in patients with schizophrenia (Javitt & Zukin, 1991; Krystal et al., 1994; Lahti et al., 1995). NMDA receptors are a major subtype of glutamate receptors which are important for complex behaviours such as associative learning, attention and, executive function, each of which are dysfunctional in schizophrenia (e.g., Robbins & Murphy, 2006).

Imaging studies also support the role of glutamate in schizophrenia by demonstrating reduced NMDA receptor binding in the hippocampus for patients free from anti-psychotic medication (Pilowsky et al., 2006). Additionally, post-mortem studies indicate increased expression of glutamate receptors in frontal and parieto-temporal brain areas in patients with schizophrenia. It has been suggested that this increase in glutamate receptors is likely to reflect post-synaptic up-regulation in response to lowered glutamatergic neuronal activity (Law & Deakin, 2001). These clinical observations suggest that symptoms of schizophrenia might be improved by increasing glutamatergic neural transmission and have provided a salient driving

force behind the glutamatergic hypothesis regarding the pathophysiology and treatment of schizophrenia. As such, clinical trial evidence has shown that four weeks of treatment with an agonist for the metabotropic glutamate 2/3 receptor (mGlu2/3R) has similar efficacy to olanzapine (D2 antagonist) in ameliorating both positive and negative symptoms of schizophrenia (Patil et al., 2007). On this basis of such evidence, the NMDA model is now considered to be one of the most useful models for both etiological conceptualisation of schizophrenia and novel treatment development (Tamminga, 1998; see Javitt., 2010 for a review).

1.1.3.2 Genetic and environmental factors

It is well-established that schizophrenia (and schizophrenia spectrum disorders) has a hereditary component and the risk of developing schizophrenia for relatives of schizophrenic probands correlates with the degree of shared genes (Brown, 2011). For example, compared to the general population lifetime prevalence of 1%; the risk of developing schizophrenia increases to 10-15% for dizygotic twins who share 50% of their genes and, to 48% for monozygotic twins who share 100% of their genes (see Tsuang, 2000; Riley et al., 2005; Brown, 2011). However, if the development of schizophrenia was based on genetic equivalence alone then concordance rates of 100% would be expected; the most plausible explanation is for a role of environmental factors which act on a complex set of susceptibility genes (Brown, 2011; see also DSM-V, 2013). Numerous environmental influences have been proposed to interact with genetic liability in the development of schizophrenia that may act right from the period of conception, through to the onset of the illness (e.g., Dean & Murray, 2005). For example, risk factors during early life include: prenatal/postnatal exposure to infection (e.g., rubella, influenza), maternal malnutrition (e.g., famine, folic acid, iron, and vitamin D), fetal/neonatal hypoxic and other obstetric complications, and maternal stress. Other

developmental determinants include socioeconomic status; child abuse and cannabis/drug abuse (see Brown, 2011 for a comprehensive review).

1.1.4 Psychiatric Co-morbidities and Schizophrenia

Psychiatric co-morbidities are common among individuals diagnosed with schizophrenia. Co-morbidity with anxiety and depressive symptoms in particular are high, with an estimated prevalence of 15% for panic disorder, 29% for posttraumatic stress disorder, and 23% for obsessive-compulsive disorder (Buckley, Miller, Lehrer & Castle, 2009). Approximately 50% of patients with schizophrenia have a co-morbid diagnosis with depression (Buckley et al.). Psychiatric co-morbidities complicate the clinical picture of schizophrenia, causing an increase in schizophrenic symptoms. For example, negative symptoms are worsened by depression, panic attacks can drive paranoia and cannabis abuse can worsen positive and disorganisation symptoms (Green, Canuso, Brenner & Wjck, 2003; Harrison et al., 2008). In order to deal with complex sets of symptoms, diagnostic symptoms have previously embraced a hierarchy, where the management of psychotic symptoms have been considered more important than the management of depression, anxiety or substance abuse (Hausmann & Fleischhacker, 2002). However, the evolution of the diagnostic criteria in the different editions of DSM is contributing to an increased awareness of these co-morbidities (Achim et al., 2011). The following section focuses on the co-morbidity of anxiety in schizophrenia in particular.

1.1.4.1 Co-morbid anxiety in schizophrenia

The presence of anxiety disorders in individuals diagnosed with schizophrenia is gaining increased attention. Approximately, 38.3% of individuals with schizophrenia spectrum disorders present at least one anxiety disorder (compared to around 18.2% of the general population with a diagnosed anxiety disorder), with a large amount of data suggesting this co-

morbidity is associated with more severe clinical characteristics and a profound effect on prognosis (Buckley et al., 2009; Hausmann & Fleischacker, 2002). One study has shown that in a group of 128 individuals diagnosed with schizophrenia, higher scores on psychometric measures of anxiety were positively correlated with more ostensible symptoms of psychosis, such as, hallucinations, and also with more prominent symptoms of depression, withdrawal and poorer functioning (Lysaker & Salvers, 2007). Moreover, a group of individuals with a high risk of developing schizophrenia showed that increased levels of social anxiety were associated with later progression to schizophrenia (Johnstone et al., 2005). These data clearly emphasise the importance of understanding the relationship between schizophrenia and anxiety.

1.2 Schizotypy

1.2.1 Overview of schizotypy

Meehl (1962) introduced the term ‘schizotaxia’ to describe the genetic predisposition to schizophrenia that could be manifested, even without full manifestations of schizophrenia. The schizophrenia spectrum disorders include schizotypal personality disorder, delusional disorder, brief psychotic disorder, schizophreniform disorder, schizoaffective disorder, substance/medication-induced psychotic disorder and psychotic disorder due to another medical condition, as defined in the diagnostic schema (DSM-V, 2013). These personality disorders reflect the phenotypic expression of a liability for schizophrenia, as evidenced from familial studies but are not associated with the profound psychosocial disturbance characteristic of schizophrenia (Battaglia et al., 1995). Advocates of this quasi-dimensional approach consider ‘schizotypy’ to derive from the term ‘schizophrenic genotype’ which states personality traits exist on a dimension but their presence is indicative of a greater disposition towards (future) schizophrenia (Eckblad & Chapman, 1983; Claridge, 1997). However, within a fully dimensional approach to schizophrenia (McCreery & Claridge, 1995), schizotypy is

viewed as a personality continuum upon which all people vary, and may never reach a level where diagnosis of a mental health condition is necessary. From this view, schizotypy is neutral in terms of mental health but interacts with environmental risk (e.g., stress) and protective factors (e.g., supportive social networks), leading to healthy outcomes such as creativity, or unhealthy outcomes such as psychosis (Nettle, 2006).

That schizotypal traits may exist on a continuum with schizophrenia has, in many ways, revolutionised schizophrenia research. As there is capacity to study individuals without clinical diagnosis of schizophrenia but who should have similar cognitive and behavioural profiles as patient groups. Psychometrically identified schizotypy is adopted in order to avoid confounds that can often accompany research in patients with schizophrenia, such as medication state, disease chronicity, and symptom nature and severity (Fonseca-Pedero et al., 2008). Also, as those with higher levels of schizotypy are at a greater risk of later development of schizophrenia spectrum disorders, there is opportunity to study what leads to manifestation of the illness (Tyrka et al., 1995). The reliability and validity of schizotypy scales are discussed in the following section.

1.2.2 Measures of schizotypy

The dimensions of schizotypy are most commonly measured using self-report scales that can be broadly split into two categories based on their theoretical origin (Bentall, 1989; Mason, Claridge & Williams, 1997): symptom-oriented or personality-oriented. The assumption held by these different approaches however, remains the same; that symptoms of schizophrenia and schizotypal traits exist on a continuum.

Symptom-oriented scales for schizotypy are based on the relationship between psychosis proneness and DSM-IV specified conditions for schizotypal personality disorder; the focus of items in these scales is based on psychotic perceptual-deviations and traits reflective of schizophrenic symptomology. A group of scales that belong to this category are those developed by Chapman and his colleagues (Chapman et al., 1978; Eckblad et al., 1982; Eckblad & Chapman, 1983). Included in the Chapman scales are: The Physical Anhedonia Scale (Chapman et al., 1976) and the Revised Social Anhedonia Scale (Mishlove & Chapman, 1985), assessing anhedonic tendencies, particularly indexing social withdrawal due to a lack of interest in intimacy and interaction. The Perceptual Aberration Scale (Chapman et al., 1978) assesses perceptual distortions, especially those related to body image; and the Magical Ideation Scale (Eckblad & Chapman, 1983) which measures magical beliefs and ideas of reference. Such clinical scales are advantageous as they use diagnostic criteria as reference points in the development of these dimensional scales, providing a clear link between schizophrenia and schizotypy.

The second category of self-report measures, personality-oriented scales; aim to address the key issue that many schizotypy scales (such as those outlined above), are not acceptable to the non-patients that typically complete them. For example, many healthy individuals feel uncomfortable recording positive responses to questions that clearly relate to psychiatric illness, due to the stigma surrounding mental health illnesses. As an alternative approach, other scales were constructed in order to be more applicable to the normal population. The Launay-Slade Hallucination Scale (LSHS; Launay and Slade, 1981) was developed to assess predisposition to hallucinations in healthy individuals, and was developed under the premise that experience of hallucinations occurs on a continuum with normal mental states. The Rust Inventory for Schizotypal Cognitions (RISC; Rust, 1987) was developed to

measure schizotypal cognitions in relation to positive schizophrenic symptoms; which could not be considered extreme, but once responses are collated can indicate those with high levels of schizotypal traits. Other personality-oriented scales include; the Schizotypal Personality Scale (STA; Claridge & Broks, 1984) and the Schizotypal Personality Questionnaire (SPQ; Raine, 1991), designed to reflect the DSM-III descriptions of schizotypal traits. Eysenck and Eysenck (1975) developed the Eysenck Personality Questionnaire (EPQ) with one factor relating to a general dimension of psychoticism; developed on the assumption of a continuum of normal personality differences. Eysenck's P scale is aimed at assessing psychotic tendencies and thus a predisposition towards psychosis. This scale however has been criticised in terms of its validity in relation to reflecting psychosis, and it has instead been suggested that P more accurately reflects traits of hostility and impulsivity, as opposed to the most prominent psychotic like factors, such as unusual experiences and magical thinking (Zuckerman, Kuhlman & Camac et al., 1988).

A major criticism of the scales described in the previous paragraphs is based on their psychometric properties predominantly measuring positive symptom-like traits, categorizing schizotypy as a single dimension. This weakens their applicability to non-clinical populations, and furthermore fails to represent the heterogeneity of schizotypy as negative symptomology is not accounted for in the majority of the scales. Newer scales have attempted to overcome this shortcoming, whilst at the same time encapsulate elements of both symptom-oriented and personality-oriented scales. They have aimed for increased reliability and a clear distinction of subcomponents of schizotypy via large-scale factor analysis studies. The consensus emerging from such factor analysis studies suggest that schizotypy is a multi-dimensional construct which has three main components: 'positive schizotypy', 'negative schizotypy' and 'cognitive disorganisation' (see Bentall et al., 1989; Vollema & van den Bosch, 1995; Mason et al., 1997).

These are consistent with the three-factor model of schizophrenia symptoms (Vollema & Hoijsink, 2000), which suggests a close similarity between traits and symptoms, providing evidence for an uninterrupted continuum between normality and clinical diagnoses of schizophrenia (Bentall et al., 1989). On the basis of these findings Mason, Claridge and Jackson (1995) developed the Oxford-Liverpool inventory of feelings and experiences (O-LIFE) to measure these schizotypy factors in a single questionnaire. The development of this questionnaire was based on a factor analysis of fifteen existing psychosis-proneness questionnaires in over 1000 subjects (Bentall et al.), which was later replicated to reveal the same factor structure (Claridge et al., 1996). In addition to the three schizotypy factors, these studies identified a fourth component which has more generally been labelled 'anti-social behaviour,' loading on to the Eysenck P-scale (Eysenck and Eysenck, 1975), the Hypomania scale (Eckblad and Chapman, 1986), and the Borderline Personality scale (STB; Claridge and Broks (1984). On the basis of these findings, which to date, includes the most extensive study of schizotypy carried out; the 159 item O-LIFE questionnaire was developed to include four scales, comprising; unusual experiences (positive schizotypy), introverted anhedonia (negative schizotypy), cognitive disorganization and impulsive nonconformity (anti-social behaviour).

The unusual experiences subscale contains hallucinatory, magical thinking and perceptual aberration items which reflect positive schizotypy, consistent with positive symptoms of schizophrenia and include items such as 'Are your thoughts sometimes so strong that you can almost hear them?' The cognitive-disorganisation subscale assesses disruptions in attention, concentration and decision making, along with feelings of purposelessness, moodiness and social anxiety. This subscale reflects the disorganised aspects of psychosis (such as disorganised speech and inappropriate affect), and includes items 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?' The introvertive anhedonia subscale reflects anhedonia (inability to experience pleasure) and describes a dislike for emotional and physical intimacy. It also places emphasis on independence and solitude and is consistent with negative symptoms of schizophrenia, termed negative schizotypy. This subscale includes items such as 'Are people usually better off if they stay aloof from emotional involvements with other people?' Impulsive nonconformity measures recklessness, impulsive, self-abusive and antisocial behaviours and includes items such as 'Do you ever have the urge to break or smash things?' However, this subscale has not been found in any of the schizophrenic symptom validation studies; it has been suggested that this scale is more likely to represent a measure of psychopathy and criminality than symptoms observed in schizophrenia (Zuckerman et al., 1988)².

The reliability and consistency of the O-LIFE is well-established with all four scales demonstrating high test-retest reliability of greater than 0.70 (Burch et al., 1988), and high internal consistency: Unusual Experiences $\alpha = 0.89$; Cognitive Disorganisation $\alpha = 0.87$; Introvertive Anhedonia $\alpha = 0.82$; and Impulsive Nonconformity $\alpha = 0.77$ (Mason et al., 1995; see also Haselgrove et al., 2015). These results have since been replicated to a similar degree by Rawlings and Freeman (1997: 0.77, 0.81, 0.85 and 0.72). Extensive laboratory investigations have also established the construct validity of the O-LIFE as a measure of schizotypal traits by demonstrating predictable effects in relation to neuropsychological function; particularly on measures of latent inhibition (see Lubow & Weiner, 2010 for a review)

² The adequacy of Impulsive Nonconformity as a valid schizophrenia-like construct has been challenged. It has instead been suggested that this scale is likely to represent a measure of psychopathy and criminality than symptoms observed in schizophrenia. It has also been argued that IntrovAv and the CogDis dimensions are not analogous to the Scale for the Assessment of Negative Symptoms (SANS) in patients with schizophrenia. The UnEx dimension as a measure of positive schizotypy has however been reported to significantly correlate with the Scale for the Assessment of Positive Symptoms (SAPS) in patients with schizophrenia (Cochrane, Petch & Pickering, 2010).

and on several other attentional, perceptual and reasoning paradigms (Jolley et al., 1999; Steel et al., 2002; Tsakanikos and Reed, 2003; Mason et al., 2004; Sellen et al., 2005). Based on the psychometric properties of the O-LIFE questionnaire and its ability to reflect the heterogeneity of schizotypy, it is increasingly being utilised in current schizotypy/schizophrenia research, and furthermore in relation to attention and associative learning (see section 1.5).

1.3 Clinical Anxiety: Symptoms, Classification & Causes

1.3.1 Clinical Anxiety at the symptom level

Both ‘anxiety’ and ‘fear’ are constructs that underlie the symptoms of anxiety disorders. Anxiety is defined as a future-oriented mood state associated with preparation for possible, upcoming negative events, and fear is an alarm response to real/perceived present or imminent threat (Barlow, 2002). Whilst these two states overlap, they also differ as anxiety is more often associated with worry, muscle tension and cautious or avoidant behaviours in preparation for future danger. Whereas fear is more often associated with thoughts of imminent threat, escape behaviours and increased autonomic arousal ready for fight or flight, including sweating, trembling, heart palpitations, and nausea (Lang, 1968; see Craske et al., 2009 for a review). Panic attacks are a particular type of fear response which feature prominently as an anxiety disorder, but also in other mental disorders as well (DSM-V, 2013), discussed more in the following section (1.3.2).

Clinical anxiety disorders can be separated from normative levels of transient fear or anxiety (often stress-induced) by being excessive and persistent (e.g., at least 6 months), however, the duration is more flexible for children and often shorter (typically for separation anxiety disorder and selective mutism). Cultural and contextual factors are taken into account by the clinician to decide whether the symptoms of fear and anxiety are excessive or out of

proportion to the situation. An anxiety disorder will only be diagnosed when the symptoms are not the consequential physiological effects of medication or a substance, or to another mental disorder/condition (DSM-V, 2013).

1.3.2 Classification of symptoms

The DSM-V includes 9 anxiety disorders, sequenced according to the typical age of onset. Separation anxiety disorder (excessive fear and anxiety about being separated from attachment figures to the degree that it is inappropriate) and selective mutism (consistent reluctance to speak in social situations where speech is expected, e.g., at school) are now classified as anxiety disorders; rather than disorders of early onset as classified in DSM-IV. The remaining disorders include; specific phobia (fearful or anxious of certain objects or situations which can relate to animals; natural environment; blood-injection-injury; situational); panic disorder (recurrent, unexpected panic attacks in response to a typically feared object or situation); agoraphobia (fearful or anxious about certain situations e.g., being in open/enclosed spaces, using public transportation). Substance/medication-induced anxiety disorder involves anxiety due to substance intoxication or withdrawal. The last anxiety disorder, generalised anxiety disorder (GAD), is the most common amongst adults and is characterised by persistent and excessive anxiety and worry about various situations which the individual finds difficult to control, such as performance at work or school. GAD also includes physical symptoms such as restlessness, fatigue, difficulty with concentration or mind going blank, irritability, muscle tension and sleep disturbance. The diagnostic criteria for anxiety disorders no longer include obsessive-compulsive disorder (characterised by the presence of repetitive behaviours that the individual feels driven to perform in response to unwanted obsessive thoughts and urges) or trauma- and stressor-related disorders (e.g., posttraumatic

stress disorder; anxiety, nightmares and flashbacks caused by traumatic events). These disorders now have their own respective chapters in the DSM-V.

The following sections focus on the causes of anxiety disorders, in general (GAD) as the focus of the experiments reported in this thesis focus on subclinical levels of general, everyday anxiety. The DSM-V classification for GAD can be found in Appendix 2.

1.3.3 Causes of anxiety

Comparable to other forms of mental illness (see section 1.1.3 for a discussion on schizophrenia), the exact cause of anxiety disorders is unknown, but are proposed to be the result of a combination of factors, including a constellation of brain regions, neurochemical mechanisms (Rauch, Shin & Phelps, 2006) and environmental stress (see Craske et al., 2009).

1.3.3.1 Functional neuroanatomy and neurochemical correlates

Autonomic activation, such as tachycardia (heart rate which exceeds the normal resting rate) and increased arousal are among the most immediate psychophysiological responses observed when experiencing a state of anxiety. As such, the ascending noradrenergic system, which originates from the locus coeruleus (LC), has been proposed as the core system around which feelings of anxiety are organised. The LC is highly responsive to alerting/stressful stimuli and contains a large portion of noradrenaline (NA) cell bodies found in the brain. Some LC neurons project to the paraventricular nucleus (PVN) in the hypothalamus and activate the hypothalamopituitary-adrenocortical (HPA) axis, which triggers/facilitates the stress response associated with increased anxiety. Noradrenergic LC neurons also project to other brain areas involved in the fear/anxiety response, i.e., the amygdala, prefrontal cortex, hippocampus, hypothalamus and the thalamus. The LC is also innervated by brain areas such as the amygdala

which is involved in the assessment of threat and in forming associations with danger in the environment. The LC is considered a key brain stem region involved in anxiety and is in a key position to influence anxiety-related neuroanatomical structures, including cortical areas (Sullivan, Coplan, Kent & Gorman, 1999).

It has been suggested that observed limbic abnormalities in patients with anxiety may result from the dysregulation of neurotransmitters, including increased release of noradrenaline (see Tanaka et al., 1982, 1983; Limori et al., 1982), serotonin (see Bagdy, 1998; Murphy et al., 2001) and dopamine (Nutt et al., 1998), particularly in the hypothalamus and amygdala regions. Gamma-Aminobutyric acid (GABA) is the main inhibitory neurotransmitter in the brain and the GABA_A benzodiazepine receptor is also thought to play an important role in anxiety-related disorders and is an important target for several anxiolytic drugs, i.e., diazepam and lithium. For example, the diazepam-sensitive $\alpha 2$ -GABA_A subtype appears to be specifically involved in reducing anxiety (Mohler, Crestani & Rudolf, 2002) and is largely expressed in the hippocampus, the amygdala, and the striatum.

1.3.3.2. Familial, genetic and environmental causes

The importance of the role of genetic factors in the familial clustering of anxiety has been demonstrated by numerous twin studies of anxiety symptoms and disorders (Kendler, Eaves & Walters, 1996). The evidence for GAD specifically however comes from a limited amount of studies. The familial odds ratio for developing GAD has been reported to be approximately 5 (Noyes, Clarkson & Crowe, 1987) and heritability is reported to be 0.32 among female pair twins (Kendler, Neale & Kessler, 1992). There is also a 3.5% increased risk of anxiety symptoms and disorders among offspring of parents with anxiety disorders, compared to controls. Children at risk for developing an anxiety disorder have been

characterised by behavioural inhibition (behavioural withdrawal in the face of novel and challenging situations), increased autonomic reactivity (Biedel, 1988), somatic symptom (Reichler, Sylvester & Hyde, 1988), social fears (Turner, Beidel & Costello, 1987), enhanced startle reflex (Merikangas, Avenevoli, Dierker, 1999) and respiratory sensitivity (Pine, Klein & Coplan, 2000), relative to controls (for a review see; Merikangas & Pine, 2002).

Anxiety sensitivity is another potential trait marker for the development of anxiety disorders, which is characterised by beliefs that feelings of anxiety are predictive of harmful physiological or psychological consequences such as fainting or having a heart attack. Therefore, the fear alone of benign arousal/anxiety sensations and feelings produces an active state of anxiety which can in turn increase the amount and intensity of the anxiousness/arousal experienced. Anxiety sensitivity is thus considered a risk factor for the development of anxiety disorders and is also reported to be a potential premorbid marker for the development of anxiety disorders in high-risk but not low-risk youth (Pollock, Carter, & Dierker et al., 2002). Other environmental risk factors include family disruption, poor parental monitoring/low social class of rearing, stressful life events in childhood and adulthood and mental health problems (see Gandy et al., 2012; Moreno-Peral, 2014; Newman et al., 2016). Thus the role of environmental influences in the etiology of anxiety is well established and the relatively moderate magnitude of heritability strongly implicates an important role for environmental influences in the development of anxiety symptoms and disorder onset.

1.4 Sub-clinical Anxiety

1.4.1 Overview of sub-clinical anxiety

Catell (1966) first introduced the distinction between state and trait anxiety, which was later elaborated by Spielberger (1966, 1972, 1976). Much research has since suggested that

anxiety is best understood by conceptually and empirically distinguishing between these state and trait facets (e.g. Endler and Kocovski, 2001; Kocovski, Endler, Cox, and Swinson, 2004; Rapee and Medro, 1994; Reiss, 1997; Spielberger, 1985a, b). Spielberger (1983) defines state anxiety as a transient emotion that consists of subjective feelings of tension, apprehension, nervousness and worry in response to stress that varies in intensity and which fluctuates over time. Trait anxiety, on the other hand, is not transient and reflects a stable tendency to experience anxiety on a daily basis. This disposition to experience anxiety has been conceptualized as a personality trait, and the validity of the state-trait anxiety distinction, as investigated through psychometric evaluation, has received extensive support in the literature (Spielberger, 1989; Spielberger, Vagg, Barker, Donham, & Westberry, 1980), see also section 1.4.2.

Even at a sub-clinical level, everyday feelings of stress and worry constitute a burden, and the impact of sub-clinical anxiety is becoming recognized as a major contributor to psychological, social and economic costs. Anxiety can make concentration difficult (Beddington et al., 2008), leading to problems in work environments (work-related anxiety resulted in 15 million working days lost in 2013; Office for National Statistics, 2014) and social environments (including distress, withdrawal; NHS Choices, 2015).

1.4.2 Measures of sub-clinical anxiety

The distinction between state and trait anxiety is embodied in the State-Trait Anxiety Inventory (STAI: Spielberger, 1983), consisting of two 20-item self-report scales. The STAI state scale assesses how respondents feel at the moment of completing the questionnaire and the STAI trait scale assesses how frequently respondents generally experience symptoms of anxiety. Since the development of the STAI, the measure continues to be extremely popular in psychological research, cited in over 400 peer reviewed journal articles. However, despite its

extensive use, the state and trait scales of the STAI have been criticized for their inability to discriminate between symptoms of anxiety and depression (see Gros et al., 2007). Even with a revision of the scales in response to these concerns, critiques of the STAI persist; factor analytic investigation support that the STAI does not provide a pure measure of anxiety, as distinct from depression (Caci et al., 2003).

Ree, MacLeod, French & Locke (2008) developed the State-Trait Inventory for Cognitive and Somatic Anxiety (STICSA) to address the limitations of the STAI. The STICSA was designed to provide a more accurate measure of pure anxiety, by better discriminating between the symptoms of anxiety and depression. Symptoms relatively unique to anxiety were favoured (i.e., physiological arousal and anxious thoughts), whereas symptoms that were non-specific and unique to depression were not favoured. The STICSA replicates the format of the state and trait scales in the STAI; each scale consists of 21 self-report items. The STICSA state scale assess how respondents “feel right now, at this very moment, even if this is not how you usually feel,” whereas, the trait scale assesses “how often, in general, the statement is true of you.” Each item is rated on a 4-point Likert scale, ranging from 1 (*not at all*) to 4 (*very much so*).

In contrast to the STAI, the STICSA separates anxiety into cognitive and somatic symptoms- existing research suggests anxiety may comprise these distinct symptom dimensions and therefore their inclusion in anxiety assessment is important (e.g., Clark and Watson, 1991; Himadi, Boice, and Barlow, 1985; Koksai and Power, 1990; Koksai, Power and Sharp, 1991). The somatic scale includes self-report symptoms such as sweating, trembling, palpitations and muscle tension. Whereas the cognitive scale includes symptoms that are associated with thought processes, including worry, intrusive thoughts, and lack of

concentration. Other self-report scales have been developed to measure the somatic and cognitive dimensions of anxiety, but unlike the STICSA questionnaire (Ree et al., 2008) none have been designed to distinguish these dimensions within both state and trait anxiety. Some of these scales include: The Cognitive Somatic Anxiety Questionnaire (Schwartz et al., 1978); the Endler Multidimensional Anxiety Scales (EMAS: Endler, Parker, Bagby and Cox, 1991) and the Lehrer and Woolfolk Anxiety Questionnaire (Lehrer & Woolfolk, 1982; for a review see Ree et al., 2008). In contrast, the STICSA questionnaire distinguishes state and trait dimensions of both cognitive and somatic anxiety; with research suggesting the questionnaire is a reliable and valid measure of anxiety in both sub-clinical and clinical populations (Ree et al., 2008). Based on the psychometric properties of the STICSA questionnaire and its ability to reflect a purer measure of anxiety, distinct from depression, it is increasingly being utilised in current anxiety research, and furthermore in relation to attention and associative learning (see section 1.6).

B. Cognitive dysfunction in Schizophrenia, Schizotypy and Anxiety

A prominent question in schizophrenia and anxiety research, concerns how a range of neurological abnormalities result in the signs and symptoms that define these disorders. One way to address this question is the study of cognitive endophenotypes. An endophenotype can be described as a link between the genotype (the genetic makeup of an organism) and phenotype (the organism's observable traits and characteristics) of a disorder. A 'cognitive' endophenotype then is defined as a quantifiable trait linking overt clinical symptoms, to the genetic and biological predisposition to the illness (Braff, Greenwood, Swerdlow, Light & Schork, 2008). In relation to schizophrenia, the overt symptom might be psychosis, but an underlying phenotype, for example, may be aberrant salience attribution to environmental

stimuli (as discussed in section 1.1.3.1). For a cognitive deficit to be considered a viable endophenotype for schizophrenia, it must be present when the individual is not suffering from the illness, and there must be evidence to establish it as genetic (i.e., via studies involving first degree relatives, where the deficit is also demonstrated in these individuals). Deficits in selective attention (e.g., latent inhibition: slower learning to a previously-exposed cue, relative to a novel cue) have been reported in first-degree relatives in individuals with schizophrenia (Serra, Joene, Toone & Gray, 2001) and also in healthy ‘schizotypal’ individuals that display symptoms similar to those observed in schizophrenia individuals (Lubow & Weiner, 2010, for a review). These findings suggest latent inhibition deficits are a possible endophenotype for schizophrenia. Similarly, disruptions in selective attention are also observed in individuals with a diagnosis of anxiety and in individuals scoring highly on sub-clinical measures of anxiety (Braunstein-Bercovitz, 2000, 2002); suggesting a deficit in attention that is also a possible endophenotype for anxiety patients. How attentional dysfunction is associated with schizophrenia, schizotypy and anxiety, is reviewed next, before moving on to discuss, in more detail, how these conditions interact in relation to such variations in selective attention.

1.5 Schizophrenia, Schizotypy and Attention Dysfunction

Disturbances in attention are considered to be a fundamental cognitive deficit in patients with schizophrenia (e.g. McGhie & Chapman, 1961; Hemsley, 1987). Various forms of attentional impairment have been reported in schizophrenia, including deficits in sensory-motor gating (Braff, Geyer & Swerdlow, 2001), attentional set shifting (Jazbec et al., 2007), response inhibition (Barch, Carter, Hachten, Usher & Cohen, 1999), spatial cuing (Posner, Early, Reiman, Pardo & Dhawan, 1988; Strauss, Alphas & Boekamp, 1992), and signal detection (Servan-Schreiber, Cohen & Steingard, 1996). These examples represent deficits in how attention determines performance, typically under conditions of instruction where

participants are told which cue is the target or where to attend. However, attention can also determine how much is learned, and vice versa; for example, tests of latent inhibition (Lubow & Moore, 1959) and learned irrelevance (Le Pelley & McLaren, 2003) indicate individuals can learn to ignore irrelevant stimuli (i.e., stimuli which are poor predictors of the events that follow them). However, in contrast to healthy individuals, it has been proposed that schizophrenia is associated with a deficit in the ability to reduce attention to irrelevant stimuli (e.g. McGhie & Chapman; Hemsley). Support for an attentional view of schizophrenia has since been provided by studies investigating the relationship between latent inhibition (for a review see Lubow & Moore, 2010; see section 1.5.1) and learned irrelevance (Le Pelley, Schmidt-Hansen, Harris, Lunter & Morris, 2010a; see section 1.5.2) and schizophrenia. Whilst this thesis explores latent inhibition and learned irrelevance designs, it should be noted that a similar literature exists for blocking; reduced learning about the relationship between stimulus (Y) and an outcome when presented in a compound (stimulus X and stimulus Y) because the outcome has previously been predicted by stimulus X (Shanks, 1985). Critically, studies have found reduced blocking in schizophrenia (Bender, Muller, Oades, & Sartory, 2001; Jones, Hemsley, Ball, & Serra, 1997; Moran, Owen, Crookes, Al-Uzri, & Reveley, 2008) and high schizotypal individuals relative to low schizotypal individuals (Haselgrove & Evans, 2010; Moran, Al-Uzri, Watson, & Reveley, 2003). Thus, in comparison to healthy participants, individuals with schizophrenia and high schizotypy individuals essentially learn as much about the redundant cue (stimulus Y) as they do about the initially trained cue (stimulus X) which has been taken as evidence for an inability to ignore irrelevant stimuli in these individuals (see Morris et al., 2012 for a review). Therefore, there are conditioning procedures: latent inhibition, learned irrelevance and blocking which have been interpreted as the consequence of learning to ignore irrelevant stimuli, and evidence of impairments in each, in patients with schizophrenia and high schizotypal individuals.

1.5.1 Latent inhibition

In a typical latent inhibition task, a stimulus is rendered familiar by mere exposure, before being established as a cue for another stimulus. Latent inhibition is seen where organisms learn more slowly about the preexposed stimulus, relative to a novel stimulus during a subsequent test of learning (Lubow & Moore, 1959). The effect is extremely reliable having been demonstrated across a wide variety of species and learning preparations (for a review see: Hall, 1991; Lubow & Weiner, 2010). There are two explanations for latent inhibition. One class of explanation emphasizes the acquisition of a stimulus- ‘nothing of consequence’ or stimulus- ‘context’ association during pre-exposure which interferes with the expression of the stimulus–outcome association during subsequent conditioning (e.g. Bouton, 1993; Weiner, 2003). Of more influence however, is the class of explanation which suggests that attention decreases to the cue during preexposure, retarding its ability to enter into an association with the outcome during subsequent training (e.g. Lubow, 1989; Mackintosh, 1975; Pearce & Hall, 1980; Wagner, 1978).

The most common procedure used to demonstrate latent inhibition in humans has been a between-participant task that comprises two-phases: preexposure and test (e.g., Baruch, Hemsley & Gray, 1988a; Gray, Fernandez, Williams, Ruddle & Snowden, 2002). During preexposure, participants are allocated to either a preexposed group or a non-preexposed group. The preexposed group are exposed to an irrelevant stimulus which is followed by no further consequence at this time, whereas, the non-preexposed group are not exposed to this stimulus. Throughout the preexposure stage participants are typically engaged in a masking-task. Both preexposed and non-preexposed groups then complete the test phase in which the preexposed stimulus (a novel stimulus for the non-preexposed group) is paired with a target outcome. Latent inhibition is demonstrated when the preexposed group is slower to learn the stimulus-

target association than the non-preexposed group. Attentional analyses of latent inhibition propose that, during preexposure, attention diminishes to the preexposed stimulus so that, subsequently, participants in the preexposed-group take longer to learn the association between the stimulus and the target (Lubow & Gerwitz, 1995; Mackintosh, 1975; Pearce & Hall, 1980).

1.5.1.1 Latent inhibition and schizophrenia

1.5.1.1.1 Attenuated latent inhibition in schizophrenia: Mixed findings

Consistent with the idea that individuals with schizophrenia have a deficit in attention is the observation of an attenuation of latent inhibition in these individuals, which is reflected as the *absence* of slower learning to the preexposed cue, compared to the non-preexposed cue in a between-participants design. During the test-phase, clinical participants with schizophrenia preexposed to the stimulus, show faster learning of the association between the stimulus and the target relative to healthy participants.

Attenuation of latent inhibition is typically seen in individuals with acute schizophrenia, rather than individuals with chronic schizophrenia (e.g. Baruch et al; Gray, Hemsley & Gray, 1992; Rascle et al., 2001; Gray et al., 2002, Vaitl et al., 2002, but see also; Swerdlow et al., 1996, Williams et al., 1998; Cohen et al., 2004). In line with the DA hypothesis of schizophrenia (see section 1.1.3.1), this relationship has been attributed to augmented DA activity in acute patients as administration of the indirect dopamine agonist; amphetamine both attenuates latent inhibition and induces positive symptoms (Abi-Dargham et al., 1998; Breier & Berg, 1999). This relationship has been expanded to account for schizophrenia patients' impaired ability to allocate attention to stimuli - an impairment that can lead to spurious associations being formed between stimuli in the environment from which unusual thought

patterns and positive symptoms (i.e., hallucinations, delusions) are formed (Kapur, 2005; Cassaday & Moran, 2010, Moran et al., 2008). This observed attentional disruption has been proposed to represent the core cognitive deficit underlying the positive symptoms of acute schizophrenia (Gray et al., 1991; Rascle et al., 2001). However, the relationship between attenuated latent inhibition and positive symptomatology has been challenged. Gray et al. (1992) suggested that a reduction of latent inhibition is associated with the acute stage of schizophrenia rather than the positive symptoms per se. When acute and chronic patients with schizophrenia were matched for their level of positive symptoms, an attenuation of latent inhibition was only observed in acute, not chronic patients. Later studies have provided mixed findings: normal latent inhibition has been observed in both acute medicated (Swerdlow et al., 1996) and un-medicated (Williams et al., 1998) patients. More recent studies have shown that acute patients with schizophrenia do show attenuated latent inhibition, but that this was correlated with their negative rather than positive symptoms (Rascle et al., 2001), whereas Cohen et al. (2004) found latent inhibition in schizophrenia patients with high levels of positive symptoms did not differ from that of healthy controls (for a review see: Schmidt-Hansen & Le Pelley, 2012).

1.5.1.1.2 Enhanced latent inhibition in schizophrenia

One possible explanation for the inconsistencies may be because the effect has an additional pole of expression – an enhanced, or abnormally persistent, latent inhibition effect with the chronic stage of schizophrenia (Weiner, 2003). Under certain experimental conditions, abnormally persistent latent inhibition has been attributed to the effects of glutamate antagonists at the N-methyl-D-aspartate (NMDA) receptor, as opposed to attenuated latent inhibition - which has been attributed to over-activity of the DAergic system. In addition to DAergic models of schizophrenia, which predominantly account for the positive symptoms of

the illness, an association between schizophrenia and the glutamatergic system has been related much more to the prevalence of negative and cognitive symptoms (which are typically observed in the chronic phase of the illness; for a review see; Javitt, 2007, 2010). To the best of our knowledge, only three studies have shown that latent inhibition is abnormally persistent in chronic patients. Rascle et al. (2001), Cohen et al. (2004) and Gal et al. (2009) all report enhanced latent inhibition in patients in a chronic stage of their illness. Although enhanced latent inhibition has been tentatively associated with negative symptoms, this effect appears more specific to illness chronicity (Gal et al., 2009). It thus seems accurate to suggest that schizophrenia is associated with an abnormal expression of latent inhibition. Whether an attenuation or enhancement of the effect is observed, depends on the stage of the illness and possibly the patient's medication status.

1.5.1.2 Latent inhibition and schizotypy

As previously stated in section 1.2, comparisons of the cognitive abilities of schizophrenic patients with controls can introduce a number of confounds, notably the medication state of the different groups. To overcome this issue, a dimensional approach can be adopted in which variations in schizotypal personality characteristics are measured in a normal population and correlated with performance on cognitive tasks. A number of studies have now indicated that attentional mechanisms are similarly disrupted in high psychometrically defined schizotypal individuals and people with schizophrenia (e.g., Baruch, Hemsley & Gray, 1988b; Gray et al., 2002; Evans, Gray & Snowden, 2007; Schmidt-Hansen, Killcross & Honey, 2009; Le Pelley, Schmidt-Hansen, Harris, Lunter & Morris, 2010; Granger, Prados & Young, 2012). However, like the schizophrenia literature (e.g., Baruch et al., 1988a; Gray et al., 1992 Rascle et al., 2001), previous studies that have

investigated the relationship between schizotypy and latent inhibition have revealed mixed results.

1.5.1.2.1 Attenuated latent inhibition in schizotypy: Mixed findings

Baruch, Hemsley and Gray (1988b) were the first to report a relationship between latent inhibition and schizotypy in the normal population, reporting reduced latent inhibition in participants who scored high, but not low (as determined by a median split) on the Psychoticism dimension of the Eysenck personality questionnaire (EPQ; Eysenck & Eysenck, 1975 see also; Lubow et al., 1992; Allan et al., 1995). Similarly, Gray et al. (2003) reported measures of schizotypy to be correlated with reduced latent inhibition, but only when using a between-participant latent inhibition task (see also: Braunstein-Bercovitz & Lubow, 1998a; Burch, Hemsley & Joseph, 2004). However, another between-participant latent inhibition task used by Lipp, Siddle & Arnold (1994) reported no significant association of the effect with the EPQ (Eysenck & Eysenck), and an association between latent inhibition and the schizotypal personality questionnaire (Claridge & Broks, 1984) that only approached statistical significance (see also: Lipp & Vaitl, 1992). Furthermore, this trend was due to differences in the non-preexposed control group, with high scorers tending to learn faster than low scorers, rather than the theoretically more interesting, preexposed group. The between-participant tasks used by Baruch et al (1988b) also revealed no association between latent inhibition and scores on the Launay-Slade Hallucination Scale (Launay & Slade, 1981). Other studies have shown that, given sufficient preexposure, individuals high in schizotypy can in fact demonstrate a latent *facilitation* effect³ (De la Casa, Ruiz & Lubow, 1993), but see Burch et al. (2004). Therefore, where some authors report a reduction in latent inhibition with higher levels of

³ An increase in the rate of learning to the preexposed stimulus relative to the non-preexposed stimulus

schizotypy, others do not, and with some authors suggesting a reversal of latent inhibition with higher schizotypy (see also: Lubow & Weiner, 2010; Lubow, Kaplan & De la Casa, 2001; De la Casa & Lubow, 2002; Shira & Kaplan, 2009; Kaplan & Lubow, 2001; Lubow & Kaplan 1997).

More recent studies have tended to employ a within-participant procedure for detecting latent inhibition in which learning about a novel and familiar stimulus is measured in the same participant. Evans et al. (2007), Schmidt-Hansen et al. (2009) and Granger et al. (2012) all showed a deficit in latent inhibition that was related to the positive dimension of the O-LIFE (Mason et al., 1995). However, the attenuated latent inhibition effect with unusual experiences reported by Evans et al and Schmidt-Hansen et al, did not reach the conventional cut-off point for statistical significance. A significant reduction in latent inhibition was attained by Granger et al., but this was a result of an association between the *difference* between the preexposed and non-preexposed stimuli and unusual experiences. This latter observation is problematic, because any correlation between schizotypy and a composite constructed from these two scores does not reveal which of its components is, or is not, contributing to the overall effect. As such it is entirely possible that it is a difference in performance to the *non-preexposed* stimulus, not the *preexposed* stimulus that contributes to the co-variation of the composite measure with schizotypy. In support of this possibility, Granger et al did not see any significant relationship between the unusual experiences dimension and learning about the preexposed stimulus alone.

1.5.1.2.2 Limitations of existing latent inhibition designs

A number of studies of latent inhibition in humans have modified its basic procedure in order to ensure that participants engage with the experiment during pre-exposure. First, the outcome from the second stage of the experiment might be also included in the first stage of

the experiment - unpaired with the cue (e.g. Swerdlow et al., 1996; Cohen et al., 2004; Gal et al., 2009; Lubow & Kaplan, 1997; De la Casa & Lubow, 2001; Lubow & De la Casa, 2002). Second, a secondary, masking, task may be presented concurrently with the pre-exposed cue. For example, a list of nonsense syllables may be presented and participants required to count the number of times one syllable appears during preexposure (e.g. Baruch et al., 1988a; Gray, Hemsley & Gray, 1992). The use of either of these modifications constrains translation between human studies and animal models that do not require such procedures to observe latent inhibition (Lubow, 2005). But, more importantly, they also generate procedures that align themselves with other learning phenomena, rather than latent inhibition. For example, by exposing the target outcome during the pre-exposure stage of the experiment in an uncorrelated (or unpaired) fashion with the pre-exposed cue may result in the establishment of learned irrelevance or conditioned inhibition to the pre-exposed cue; which is known to retard the acquisition of later learning (e.g.: Baker & Mackintosh, 1977; Rescorla, 1969) and known to co-vary with schizotypy (Schmidt-Hansen et al., 2009; Le Pelley et al., 2010; Migo et al., 2006). Evans et al. (2007) have described a within-participant latent inhibition procedure that, they suggest, circumvents the inclusion of a masking task during preexposure. However, this task sets up an expectation of the target stimulus, prior to the preexposure phase through instruction; casting doubt on whether the retardation in learning reflects a genuine latent inhibition effect rather than some other effect whose origin might be quite different (e.g., conditioned inhibition; see Rescorla, 1969). Existing latent inhibition designs are described in more detail in Chapter 2, and the limitations of these designs are described and addressed.

In addition, whilst in the schizophrenia/schizotypy literature it has been explicitly assumed that latent inhibition designs provide a measure of the influence of attentional processes on associative learning (e.g., Bender et al., 2001; Rascle et al., 2001; Moran et al.,

2003), there are other accounts of latent inhibition that make no reference to attention. For example, it has been argued that latent inhibition can result from participants computing conditional probabilities, where the conditional probability of a particular outcome given the presence of a cue will be lower for a cue that has had extensive nonreinforced preexposure than for a cue that has not (Lubow & Weiner, 2010). On this approach, the abnormal expression of latent inhibition in individuals with high schizotypy/schizophrenia might reflect an abnormality in inferential reasoning (cf, Garety et al., 1991; Sellen et al., 2005), rather than attention. However, this does not mean that the attentional view of schizophrenia is incorrect, merely that the currently-available evidence provides equivocal support for it (see Le Pelley et al., 2010a). A paradigm that can provide a less ambiguous measure of the impact of attention on learning is thus desirable to provide support for the attentional dysfunction view of schizophrenia; one potential candidate is the learned irrelevance paradigm which is discussed in the following section.

1.5.2 Learned irrelevance

A related approach to the examination of the abnormalities of attentional control displayed by individuals with schizophrenia makes use of a phenomenon inhibition known as learned irrelevance (Mackintosh, 1973). Learned irrelevance refers to the finding that the experience of a cue as irrelevant to the occurrence of an outcome (i.e., due to inconsistent/uncorrelated presentations of a cue and a target), retards later new learning about that cue. For example, Mackintosh (1973) demonstrated that rats given uncorrelated exposure between a tone and water, showed slower subsequent learning about a contingent tone-water relationship, compared to rats given no preexposure to the tone or water (see also Baker & Mackintosh, 1977; Allen et al., 2002; Linden et al., 1997; Baker et al., 2003; Bonardi & Ong, 2003; Baker, Murphy & Mehta, 2003). A commonly accepted view of learned irrelevance

states that it reflects a reduction in learning rate to a cue as a result of prior experience of that cues irrelevance with respect to an outcome. This reduction in learning is taken to reflect a decrease in attention to the cue (on the assumption that attention is determined by relevance; see Mackintosh, 1975; Kruschke, 2001) and there is experimental evidence to support this view (see: Livesey, Harris & Harris, 2009).

The fact that learned irrelevance involves slower learning about a cue following non-reinforced preexposure makes it similar to latent inhibition. However, the procedure used for generating the two effects is different. The literature reports two different paradigms to generate an effect of learned irrelevance. The first involves exposure to inconsistent/uncorrelated presentations of a cue and a target (rather than the cue presented without a target in tasks of latent inhibition). In the learned irrelevance task reported by Schmidt-Hansen, Killcross & Honey (2009), participants are presented with a series of letters, presented one after the other in the centre of the screen and are instructed to press the spacebar as quickly as possible when the letter X is presented. Amidst filler letters, the letter X is either preceded by either a novel letter (e.g., H) or by a letter that has been preexposed (e.g., S) in conjunction with uncorrelated presentations of X. Therefore, the preexposed letter (e.g., S) is presented without consequence on some trials, and precedes the occurrence of X on the others, see Table 1.1. Here, a learned irrelevance effect is shown when participants are slower to respond to presentations of X when it was cued by the preexposed letter than the novel letter.

Table 1.1

Experimental design: learned irrelevance with single cues (Schmidt-Hansen et al., 2009)

Preexposed Stage		Test Stage	
<i>Preexposed stimulus</i>		<i>Training</i>	
S → X (4)	S (16)	S → X (16)	
		H → X (16)	
<i>Filler trials</i>		<i>Filler trials</i>	
D → X (4)	D (16)	D → X (4)	D (50)
M → X (4)	M (16)	M → X (4)	M (50)
T → X (4)	T (16)	T → X (4)	T (50)
V → X (4)	V (16)	V → X (4)	V (50)

The second paradigm used to generate learned irrelevance arranges for cue(s) to always be followed by an outcome, but the predictive validity of these cues differs – thus one cue will reliably predict a specific outcome whilst another cue will not. A particularly clear demonstration of this learned irrelevance paradigm is illustrated in an experiment by Le Pelley and McLaren (2003) that used an allergist task (see Larkin, Aitken & Dickinson, 1998), in which participants are required to learn about the effects of different foods on ‘Mr X’. During stage 1, compound-cues (pictures of two different fruits) were followed by a given outcome - an allergic reaction experienced by the patient as a consequence of consuming these fruits. There were eight pairs of cues, and two possible outcomes (outcome 1 and 2). Table 1.2 shows that some food types (A-D) were established as being relevant predictors of an allergic reaction to the food (e.g. nausea): they consistently predicted an outcome on each trial. Whereas cues V-Y were irrelevant: being inconsistently followed by an outcome. In the second stage of training, new compounds of foods were created which each consisted of one previously relevant-cue and one previously irrelevant cue (i.e., AX, BY, DV, and DW), these were paired

with different allergic reactions to stage 1 (outcomes 3 and 4). Importantly, in this stage, the objective statistical relationship all the stimuli and the outcome were equal. In the absence of any learned bias, therefore, participants should learn as much about A, B, C and D as W, X, Y and Z. In a final test stage, participants had to rate the likelihood that new compounds (AC, BD, VX, and WY) would result in outcomes 3 and 4. Participants rated compounds AC and BD as significantly more predictive of outcomes 3 and 4 respectively, than compounds VX and WY. As the cues and compounds were all equally predictive of outcomes 3 and 4 during stage 2 the results at test are taken as evidence for the acquisition of differences in attention to these cues during the initial stage of training (see also: Le Pelley, Oakeshott, Wills & McLaren, 2005; Le Pelley, Turnbull, Reimers & Knipe, 2010b). Furthermore, stage 1 training cannot directly influence stage 2 learning, as the outcomes in stage 2 are (i) different and (ii) statistically independent as cues paired with outcome 1 during stage 1 were equally likely to be paired with outcome 3 or outcome 4 in stage 2. Thus, learning that a particular cue predicts outcome 1 during stage 1 does not inform the participant in any way about the effect of that cue in stage 2. That the objective contingency between previously relevant and previously irrelevant cues is identical during stage 2 makes it difficult to account for these findings in terms of a bias in learning favouring previously relevant over previously irrelevant cues. As such, compared to explanations of latent inhibition (cf, Garety et al., 1991; Sellen et al., 2005), this variant of learned irrelevance (compared to the variant which instead involves exposure to inconsistent/uncorrelated presentations of a cue and a target; see Schmidt-Hansen et al., 2009) is less amenable to non-attentional accounts of its occurrence as it cannot readily be explained by conditional probabilities or statistical inference.

Le Pelley and McLaren's (2003) finding suggests attention is determined by stimulus relevance and in turn supports the role of attention in learning. In further support of this

contention, eye-tracking studies have demonstrated that overt attention (attending to a stimulus or location by moving our eyes to look at it; Deubel & Schneider, 1996) is influenced by learning about stimulus relevance. Using the compound cue learned irrelevance procedure described above, Beesley, Le Pelley & Griffiths (2011) revealed that healthy adults reduced overt attention, measured using eye-tracking, to the previously non-predictive cues during stage 2 of the procedure (see also; Beesley & Le Pelley, 2011; Kruschke, Kappenman, & Hetrick, 2005; Wills, Lavric, Croft, & Hodgson, 2007). Therefore, studies of learned irrelevance provide support for an attentional bias toward predictive cues and away from irrelevant cues in healthy adults, which is consistent with theories of learned attention (Kruschke, 2001; Le Pelley, 2004; Mackintosh, 1975). The following sections explore the relationship between learned irrelevance task performance in individuals with schizophrenia and high schizotypal individuals (section 1.5.2.1).

Table 1.2

Experimental design: learned irrelevance with compound cues (Le Pelly & McLaren, 2003)

Stage 1	Stage 2	Stage 3
AV – 1	AX – 3	AC 3? 4?
AW – 1	BY – 4	BD 3? 4?
BV – 2	CV – 3	VX 3? 4?
BW – 2	DW – 4	WY 3? 4?
CX – 2		
CY – 2		
DX – 1		
DY – 1		

1.5.2.1 Learned irrelevance, schizophrenia & schizotypy

1.5.2.1.1 Attenuated learned irrelevance in schizophrenia and schizotypy

Similar to *some* of the existing schizophrenia and schizotypy literature that proposes a reduction in latent inhibition is associated with positive symptomatology; variations of the single-cue learned irrelevance task (see Table 1.1) have been reported to show an attenuation of learned irrelevance in participants with acute schizophrenia (see Gal et al., 2005; Young et al., 2005). However, in contrast to the latent inhibition literature that states latent inhibition attenuation is *predominantly* associated with the acute stages of schizophrenia, the studies carried out by Gal et al and Young et al also demonstrate some degree of learned irrelevance impairment in chronic schizophrenia patients. This impairment was however, ascribed to an effect of a more general deficit in associative learning as opposed to a specific failure to ignore the pre-exposed irrelevant cue. However, the experimental and control conditions in those studies differed in level of preexposure to the to-be-conditioned cue, making it possible that the effects observed, relative to acute schizophrenia individuals, reflect latent inhibition rather than learned irrelevance. Interpretation of these effects is made more complicated by the fact that the stimuli used to represent the preexposed and non-preexposed cues were not counterbalanced. Similar experimental limitations can be found in the schizotypy-learned irrelevance literature (e.g., Schmidt-Hansen et al., 2009)

Using the single-cue learned irrelevance task described in Table 1.1, Schmidt-Hansen et al. (2009) reported reduced ‘learned irrelevance’ in individuals scoring highly on the unusual experiences dimension of the O-LIFE (Mason et al., 1995). However, similar to the single-cue learned irrelevance paradigms utilised by see Gal et al. (2005) and Young et al. (2005), the learned irrelevance task described by Schmidt-Hansen et al. also presents the preexposed cue an unequal number of times with the target. Thus there were more presentations of the

preexposed cue without consequence (not followed by the target), than there were pairings of the preexposed cue followed by the target during the preexposure stage, resulting in the paradigm being potentially confounded by latent inhibition and/or conditioned inhibition.

The compound-cue learned irrelevance task described by Le Pelley and McLaren (2003); see Table 1.2 however equates latent inhibition by presenting all cues an equal number of times. Using a variant of Le Pelley and McLaren's learned irrelevance task; Morris, Griffiths, Le Pelley & Weickert (2012) assessed whether an inability to discriminate between relevant and irrelevant cues, as measured by the amount of learning in a novel test of attention, is related to the positive symptoms of schizophrenia. Across two experiments, results were consistent with models of attention which suggest that cues predictive of an outcome attract more attention than cues non-predictive of an outcome in healthy individuals (Kruschke, 2001; Le Pelley, 2004; Mackintosh, 1975). However, in individuals with schizophrenia, this normal attentional bias was impaired as patients were unable to distinguish between previously relevant and irrelevant cues and there was a positive correlation between learning about the previously irrelevant cue and high-positive symptom severity, measured using the Positive and Negative Syndrome Scale (PANSS) for schizophrenia (Kay, Fiszbein & Opler, 1987). These results provide evidence consistent with a failure of selective attention in schizophrenia and that this deficit may be critical in the formation and experience of psychotic symptoms (Corlett, Honey & Fletcher, 2007; Corlett, Murray & Honey, 2007). In an extension of these findings Le Pelley et al (2010a) assessed whether an observed attentional bias towards previously established relevant cues is reduced in high schizotypy individuals, again using a variant of the compound-cue learned irrelevance task described by Le Pelley and McLaren (2003; see section 1.5.2).

Le Pelley et al. (2010a) demonstrated an effect of learned irrelevance when participants were taken as a whole; participants learnt faster in stage 2 about previously relevant cues, relative to previously irrelevant cues. Importantly, however, individuals scoring highly on the unusual experiences dimension of schizotypy measured using the O-LIFE questionnaire (Mason et al., 1995) showed no effect of learned irrelevance: high schizotypal individuals showed no significant difference in learning about previously relevant or irrelevant cues in stage 2, relative to low schizotypal individuals who demonstrated increase learning towards previously relevant cues. This finding supports the suggestion that schizotypy is associated with a deficit in the appropriate allocation of attention to stimuli based on their previously experienced relevance; with a specific inability to reduce attention to irrelevant information (see Lubow & Weiner, 2010; Haselgrove et al., 2015). This finding is consistent with attentional interpretations of latent inhibition, consistent with some of the existing schizotypy and schizophrenia literature (see Lubow & Weiner, 2010) that proposes a reduction in learned variations in attention is associated with positive symptomatology. This finding does however encourage the parsimonious suggestion that masked latent inhibition tasks (which generate a procedure that align themselves with learned irrelevance, rather than latent inhibition, see section 1.5.1.2.2) show sensitivity to schizotypy because it is actually generated by learned irrelevance. This casts doubt on the assumption that masked latent inhibition in humans is comparable to simple latent inhibition in animals, which could undermine the use of animal latent inhibition preparations as models of schizophrenia; and other pathologies that are associated with reduced masked latent inhibition (see section 1.6.1 for a discussion with anxiety). These arguments are further explored in Chapter 3.

An additional line of research that might explain some of the controversies in the latent inhibition literature (i.e., whether latent inhibition is attenuated or enhanced in individuals with

schizophrenia/high in schizotypality) is that proposed by Braunstein-Bercovitz (2000). Suggesting, selective attention dysfunction may not be specific to schizophrenia and may instead be related to the anxiety components of schizotypality and its related pathologies. The most commonly reported attentional biases observed in individuals experiencing anxiety, are briefly reviewed next; before moving on to discuss the research (albeit limited) with latent inhibition and anxiety, and crucially, with latent inhibition and the anxiety components of schizotypy. To date, there are no studies that have directly investigated the relationship between learned irrelevance and anxiety (see section 1.6.2).

1.6 Attention Dysfunction in Anxiety

Anxiety disorders constitute a major worldwide health burden with sizeable psychological, social and economic costs (Beddington et al., 2008). The impact of anxiety on cognitive function is a major contributing factor to these costs; anxiety disorders can augment focus upon negative life events and make concentration difficult, leading to problems in both social and work environments. In such situations the state of anxiety can be seen as *maladaptive*. Anxiety can, however, also improve the ability to detect and avoid danger, which under the right circumstances- such as walking home alone in the dark- can be adaptive. The precise impact of anxiety on cognition is, however, unclear (Robinson et al., 2013).

Recent psychological models suggest that core deficits in attention control are involved in the etiology and maintenance of mood and anxiety disorders (e.g. de Raedt & Koster, 2010; Sylvester et al., 2012). According to cognitive theories (e.g. Williams, Watts, MacLeod & Mathews, 1988; Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg & Van, 2007) anxiety is associated with biased allocation of attention towards threat-related stimuli because one function of anxiety is the detection of threat, enabling the individual to react quickly.

To understand cognitive biases of attention, psychological theories and clinical research have increasingly turned to information-processing paradigms derived from experimental cognitive psychology. A modified version of the Stroop (1935) colour-naming task is one of the most frequently adapted paradigms to show attentional biases in high anxiety individuals. In this task, participants are asked to name the ink colour of words, whilst ignoring their semantic content. Consistent with the hypothesis that people with heightened vulnerability to anxiety are less able to ignore negative information, the general finding is that, anxious individuals display disproportionately longer colour-naming latencies with threatening words such as ‘tragedy’ compared to neutral words such as ‘corner.’ This effect has been reported in individuals clinically diagnosed with having a generalised anxiety disorder (e.g., Eysenck et al., 1987; Mathews & MacLeod, 1985; Mogg et al., 1989, 1995), post-traumatic stress disorder (Cassiday et al., 1992; Thrasher & Yule, 1994) and also non-clinical, healthy individuals scoring highly on self-report measures of anxiety (e.g., Dalgleish, 1995; Fox, 1993, 1994; MacLeod & Hagan, 1992; Van-Den-Hout et al., 1995; Edwards, Burt & Lipp, 2006).

More direct measures of selective attention have served to confirm that individuals with high levels of anxiety-vulnerability do indeed orient attention towards negatively-valenced stimuli. For example, the ‘dot probe’ procedure described by MacLeod, Mathews, and Tata (1986) assessed attentional responses to emotional information. In this task, participants were presented, briefly, with two words simultaneously, one negative threat-related word and one neutral word. Following the termination of this display, a small dot probe appears in the prior location of one of these two words and participants were required to press a response button, corresponding to target identity, as quickly as possible whenever the probe is detected. Consistent with existing attentional bias related research, generalised anxiety disorder patients were quicker to detect probes that appeared in the spatial vicinity of the more negative words.

Non-anxious controls tended to detect probes more slowly when they appeared in the vicinity of the negative words as opposed to the more neutral words, suggesting that low levels of anxiety vulnerability may be associated with a disposition to selectively orient attention away from negative information. This pattern of findings with the dot probe task has been replicated in patients with generalised anxiety disorder (e.g. Mogg, Mathews & Eysenck, 1992) and also non-clinical, healthy individuals scoring highly on self-report measures of anxiety (Broadbent & Broadbent, 1988; MacLeod & Mathews, 1988; See also: MacLeod et al., 2007; Koster et al., 2006; for a review see Cisler & Koster, 2010).

In addition to an attentional bias towards threat-related stimuli, data also point to a *general* attentional bias toward irrelevant stimuli, in the absence of threat. For example, in a modified version of the Stroop task, participants were required to name the colour of a centrally located colour-patch, which was flanked top and bottom by either a neutral-, colour- or threat-related distractor word. As we might expect, high anxious individuals produced slower colour-patch naming times when the patch was flanked by threat-related distractor words, relative to neutral distractor words. However, in addition to this finding, high anxious individuals also show distraction by the colour-related distractor words (when the colour word was separate from the colour patch) relative to the neutral-related distractor words). By contrast, low anxious individuals did not show any Stroop interference, when the colour words were conflicting with the colour-patch (Fox et al., 1993). In general, high anxious individuals produced slower colour-patch naming latencies than the low anxious individuals regardless of whether the distracting words were conflicting colour words, neutral or threat-related words.

These findings have been taken as evidence for a general inability to maintain attentional focus in high anxious individuals, rather than an automatic attentional bias that is

specific towards threat-related information. In further support of this contention, Derryberry and Reed (2002) have previously reported a high negative correlation between individual's trait anxiety scores and self-report of attentional control (see also; Enright and Beech, 1993; Fox, 1993, 1994; Mathews et al., 1990; Poy et al., 2004; Bishop, 2009; Pacheo-Unguetti, Acosta, Callejas & Lupiáñez, 2010).

To date, many existing selective attention paradigms have been influential for determining attentional biases in anxious individuals: indicating a bias in attentional processing for irrelevant information (either in the presence or in the absence of threat; for a review see: Eysenck et al., 2007). At this juncture, the selective attention tasks used in existing research (highlighted above) are able to advocate a well-established difference in attentional capture for individuals high and low in anxiety. What is less clear is *how* this difference in attention to relevant/irrelevant stimuli affects how well these stimuli are attended to, and learnt about in subsequent, novel situations. Based on associative theories of learning for example, the prior predictive history of a stimulus will affect how well that stimulus is attended to, and thus learnt about in the future (e.g., Mackintosh, 1975; Pearce & Hall, 1980). Similar to the schizophrenia literature, one prominent example of a learned attention task that has been used to investigate impaired attentional processes in anxiety is the latent inhibition paradigm (Lubow, 1989).

1.6.1 Latent inhibition and anxiety

1.6.1.1 Attenuated latent inhibition and anxiety

As previously stated, the latent inhibition procedure (Lubow, 1989) has been used to investigate attentional biases, for both schizophrenia and schizotypy (for a review see: Braunstein-Bercovitz, Dimentman-Ashkenazi & Lubow, 2001, and section 1.5.1). Latent inhibition has typically been used for this task because it has been proposed to provide an index

of the degree of distraction by irrelevant stimuli (for a review see: Braunstein-Bercovitz et al., 2002), and it has a well-established pharmacological basis (Moser, Hitchcock, Lister & Moran, 2000). Indeed, a variety of animal and human studies support a disruption of selective attention with increased anxiety and stress levels, as reflected in studies of latent inhibition (see Weiner, 1990; Weiner & Feldon, 1997; Braunstein-Bercovitz, 2000, 2002). More specifically, Braunstein-Bercovitz (2002) report that anxiety modulates latent inhibition, as individuals high in trait anxiety (Braunstein-Bercovitz, 2000) and state anxiety (Braunstein-Bercovitz, 2001) show an attenuation of latent inhibition. These data have been taken as further evidence for an attentional bias in anxious individuals. Furthermore, this relationship between anxiety and latent inhibition has been proposed to effectively account for the attenuation of latent inhibition in high-schizotypal individuals and schizophrenia patients that is often reported in *some* of the existing literature (for a review see Braunstein-Bercovitz, 2002). Evidence for this suggestion is discussed in the following section.

1.6.1.2 Latent inhibition: The Anxiety components of schizotypy

Similar to schizophrenia, and as noted earlier, several lines of existing research suggest anxiety is associated with a reduced ability to ignore irrelevant stimuli/information, reflecting a general inability to maintain attentional focus (Eysenck et al., 1987; Mathews & MacLeod, 1985; Mogg et al., 1989). As such, the disruption of latent inhibition reported in schizophrenia, high-schizotypals (for a review see Lubow & Weiner, 2010) and anxious individuals (for a review see Braunstein-Bercovitz, 2002) is most commonly attributed to the relatively high distractibility in these groups. Few studies, however, have attempted to bridge the gap between schizotypy and anxiety in relation to learned attentional functioning to assess whether the anxiety that characterises schizophrenia and schizotypy accounts for the difficulties individuals with schizophrenia and schizotypal individuals have in ignoring irrelevant information. This is

surprising given the high co-morbidity rate between schizophrenia and anxiety (Buckley et al., 2009; see section 1.1.4) and the overlap between psychometrically identified schizotypy and anxiety symptoms (Braunstein-Bercovitz, 2000). Both at clinical and sub-clinical levels, the SPQ and State Trait Anxiety Inventory are highly correlated (Braunstein-Bercovitz, 2000) and several studies report a positive correlation between symptom type in patients with schizophrenia and level of anxiety (Huppert et al., 2001; Lyons et al., 2001; Norman & Malla, 1993a, b).

In addition, as previously highlighted (see section 1.5.1.1.1), latent inhibition is mediated by dopaminergic activity (for reviews see: Gray, 1998; Moser et al., 2000; Weiner & Feldon, 1997), and both schizotypy (Caplan & Guthrie, 1994; Silver, 1994, 1995) and anxiety (McIvor et al., 1996; Nutt et al., 1998; Peroutka et al., 1998) are also characterized by increased dopaminergic activity. The high correlations of schizotypal scale scores with anxiety scale scores suggest that schizotypal scales may contain an anxiety factor (or vice versa). This, together with data that anxious individuals are distracted by irrelevant stimuli as measured by latent inhibition (as well as other tasks which show slower learning/distraction towards previously non-reinforced irrelevant stimuli, such as negative priming; Fox, 1993, 1994; and Stroop tasks; Mathews et al., 1990), reinforces the possibility that an anxiety component of the disorder may account for selective attention deficits in high schizotypals and individuals with schizophrenia. Furthermore, that disrupted latent inhibition in high schizotypals may be a result of the high levels of anxiety which accompanies this state.

One attempt to cross the boundary between schizotypy and anxiety, and investigate cognitive performance was in a study conducted by Braunstein-Bercovitz (2000). This study carried out a factor analysis to assess whether schizotypy is accompanied by sub-clinical levels

of anxiety. This analysis produced two factors; one factor that was correlated with trait-anxiety scores, and labeled ‘anxiety- loaded;’ the second factor represented thought and perception disorders, and was labeled ‘perceptual-disorganisation.’ Consistent with *some* of the existing research, disrupted latent inhibition was observed in high as compared to low schizotypy individuals. However, latent inhibition was also disrupted in patients with high trait anxiety scores and on the anxiety-loaded factor. Latent inhibition deficits, then, appear not to represent a specific marker for schizotypy, nor, by extension, for schizophrenia. Instead, such latent inhibition deficits may be a contribution of the heightened anxieties that accompany many different types of pathology.

1.6.2 Learned irrelevance and anxiety

Whilst there are studies that have looked at latent inhibition with anxiety, there are no studies that have *directly* investigated the relationship between anxiety and learned irrelevance. It is important to bear in mind however that, as previously highlighted, existing latent inhibition preparations including a masking task, generate a procedure that align themselves with learned irrelevance, rather than latent inhibition (see section 1.5.1.2.2). Therefore, the conclusions of these findings reported in the preceding sections, relating to disrupted latent inhibition with schizophrenia schizotypy and anxiety remain open to debate.

C. Learning Theory Background

1.9 Associative Learning Theory

Abnormalities of association formation have been considered to have a role in the pathogenesis of schizophrenia since Bleuler described ‘loosening of associations’ as ‘contradictory, competing, and more or less irrelevant responses [that] can no longer be excluded’ to epitomise the core deficits observed in schizophrenia (Bleuler, *Dementia Praecox*,

or the Group of Schizophrenias, p. 511). As discussed previously, considerable evidence of impairments in associative learning has accumulated; leading to the development of the idea that a disruption in learning might be of relevance to understanding the fragmented thinking and delusions that characterise schizophrenia. As such, associative learning theory provides a framework that can aid understanding of the disrupted psychological processes that give rise to impaired behaviour observed in neuropsychiatric disorders, which in turn, may help to clarify the nature of these deficits. Considered here, are some fundamental features of attention in associative learning that are of relevance to the attentional view of schizophrenia and anxiety, focusing on the Mackintosh (1975) and Pearce and Hall (1980) theories, in particular.

1.9.1 Attention in associative learning

Decades of research have been spent discovering how animals, including humans, are able to learn relationships between cues and events in the environment surrounding them. For it is the ability to learn about and use these cues to predict events of motivational significance (reinforcers) that enables organisms to adapt and survive in a changing environment. Exactly how both animals and humans come to attend to the appropriate cues has been of long standing debate amongst learning theorists (see Le Pelley, 2004, for a review). Some theories postulate that *attention* is a crucial mediating variable allowing the use of prior experience to determine which cues are, and which cues are not, processed for learning. Other theories focus on the nature of the association that is formed (see: Le Pelley, 2004; Mitchell & Le Pelley, 2010).

One of the major goals of associative learning theory is to determine the factors that influence learning; why under some conditions we learn more about one stimulus than another. Research from animal conditioning studies suggests that one factor which determines learning about the consequences of stimuli is the prior predictive history of a stimulus. For example,

previous experience with a cue (e.g., a light) as being predictive or nonpredictive of reinforcement (e.g., food) will affect how well that stimulus is learnt about in subsequent conditioning (see Le Pelley, 2004; Le Pelley et al. 2016, for a review). Research with human learning also provides support for this suggestion (see Le Pelley & McLaren, 2003; Le Pelley, Schmidt-Hansen, Harris, Lunter & Morris, 2010a). The rate of learning about the cue is commonly referred to as the cue's *associability* (α) which is related to the amount of *attention paid to the cue* (Le Pelley, 2004)⁴.

However, exactly how the prior predictiveness of a cue determines α is inconsistent across the literature, with findings supporting opposing theories of associative learning. According to Mackintosh's (1975) theory cues that have reliably predicted an outcome in the past, acquire attention (α) whilst poorer predictors lose attention and thus come to be ignored – facilitating or attenuating subsequent learning, respectively. In contrast, Pearce and Hall (1980) posit that attention should decrease to cues that reliably predict the outcome with which they are paired. Instead, the Pearce-Hall model assumes attention is allocated to cues that are inaccurate or uncertain predictors of reinforcement, so as to facilitate learning about the exact significance of those cues. In accordance with these theories, there are certain studies which are in line with the Mackintosh model; suggesting that stimuli previously established as reliable predictors of reinforcement, attain a higher α and are subsequently learnt about faster, than stimuli established as non-predictive (see Le Pelley, 2004). In opposition, other studies demonstrate faster learning about stimuli previously established as being uncertain/unreliable predictors of reinforcement, compared to those experienced as being continuously predictive (see Haselgrove, Esber, Pearce & Jones, 2010); thus fitting well with the Pearce-Hall model.

⁴ Associability and attention are often used (perhaps incorrectly) interchangeably to describe alpha (α).

The following sections provide a brief history and overview of these theories and their ability to explain latent inhibition and learned irrelevance, in particular.

1.9.1.1 Mackintosh (1975): The predictiveness principle

According to the Mackintosh model, attention to a stimulus is increased when it is the best predictor of an outcome, and decreases otherwise. The change in associative strength between the stimulus (CS A) and the outcome (US B) is formalised by Equation 1.

$$\Delta V_A = \alpha \cdot \Theta \cdot (\lambda - V_A) \quad (1)$$

In this equation, the error term $(\lambda - V_A)$ is the discrepancy between the magnitude of the US (λ) and the associative strength of the CS A (V_A). Θ is determined by the properties of the US and is a learning rate parameter. The most crucial aspect of this equation is that α is not a fixed parameter of CS-processing (c.f. Rescorla & Wagner, 1972), but a variable parameter that changes as a result of experience with the CS; it increases when the CS is a good predictor of the US (participants attend to relevant stimuli that predict trial outcomes) and decreases when it is a poor predictor of the US (participants ignore irrelevant stimuli that do not predict trial outcomes). The rules for determining these increases and decreases in α are formalised in Equation 2a and 2b.

$$\Delta \alpha_A > 0 \text{ if } |\lambda - V_A| < |\lambda - V_x| \quad (2a)$$

$$\Delta \alpha_A < 0 \text{ if } |\lambda - V_A| \geq |\lambda - V_x| \quad (2b)$$

Here, V_x is the summed associative strength of all CS's, besides V_A , present on that trial. If $(\lambda - V_A)$ is smaller than $(\lambda - V_x)$, then CS A is a better predictor of the outcome on that trial than any other available stimuli; if it is bigger, then CS is a poorer predictor.

Much research from animal studies provides evidence for a mechanism operating on this predictiveness principle offered by the Mackintosh model, which provides an explanation for many standard conditioning effects including the intra- and extradimensional-shift effect, blocking and overshadowing, overtraining-reversal effects, learned irrelevance and latent inhibition (for reviews, see Le Pelley, 2004; Pearce, 2008; Pearce & Mackintosh, 2010; Le Pelley et al., 2016). These conditioning effects are also well documented in human associative learning, commonly being observed in serial-reaction-time tasks (Beesley & Le Pelley, 2010) and eye-gaze fixations (Beesley & Le Pelley, 2011; Le Pelley, Beesley & Griffiths, 2011). The results of these studies support the suggestion that attention to a stimulus is governed by learning about its predictive-validity i.e., its ability to predict the occurrence of significant outcomes. A particularly clear demonstration of the importance of learned predictiveness /irrelevance is illustrated in the experiment reported by Le Pelley and McLaren (2003); this experiment was discussed at length in section 1.5.2, see also Table 1.2.

According to the Mackintosh (1975) model, attention to a stimulus is increased when it is the best predictor of an outcome, and decreases otherwise. In this way, Mackintosh describes learned irrelevance as a decrease in attention (more specifically ‘decreased associability’) to the previously uncertain/inconsistent cues, because the participant learns these cues are irrelevant (i.e., as it is an uncertain predictor of a given outcome), in contrast to the previously predictive cues. By the same token, Mackintosh describes latent inhibition as a decrease in attention/associability to the preexposed cue, as both the pre-exposed cue and the context are established as (at best) equally good predictors of non-reinforcement. Equation 2b will therefore ensure that the associability of the preexposed cue will reduce during stage 1. Therefore, at the outset of conditioning, the associability of the pre-exposed cue will be lower than the associability of the novel (non-pre-exposed cue), hence reduced learning to the pre-

exposed familiar cue relative, to the novel cue. Therefore, learning that a cue is ‘irrelevant’ to the occurrence of an outcome will result in reduced learning about this cue when these events are eventually paired; a unitary mechanism underlying both latent inhibition and learned irrelevance.

1.9.1.2 The uncertainty principle (Pearce & Hall, 1980)

Despite the success of the Mackintosh model, Pearce and Hall (1980) argued that, rather than devoting attentional resources to stimuli that are accurate predictors of reinforcement, attention should be directed towards stimuli which are inaccurate predictors of their outcomes. According to the Pearce and Hall model, when a stimulus is initially presented for conditioning, the stimulus is a poor predictor of its consequence and thus attention to the stimulus should be increased to facilitate learning on subsequent trials. Throughout conditioning, attention to the stimulus may then decrease as it becomes a better predictor of its outcome, and ultimately cease once the outcome is fully predicted by the stimulus. This change in associative strength between the stimulus (CS A) and the outcome (US) is formalised by Equation 3.

$$\Delta V_A = S \cdot \alpha_A \cdot \lambda \quad (3)$$

In this equation S is determined by the intensity of the CS and is a fixed learning-rate parameter and λ represents the asymptote of conditioning, determined by the intensity of the US. The parameter α again represents the associability of the CS (assumed to be high for a novel CS) and is modified by experience according to Equation 4.

$$\alpha^{n+1} = |\lambda - \Sigma V^n| \quad (4)$$

Where ΣV represents the sum of the associative strengths of all stimuli present on trial n ; the value of α on trial n is determined by the absolute discrepancy between the asymptote of conditioning and the summed associative strength experienced on the preceding trial n . In simple conditioning, Equation 4 predicts that a CS which is reliably paired with a US will lose

associability and approach zero as asymptote is reached. Studies that are consistent with these predictions are, for example the Hall and Pearce (1979) negative-transfer effect, in which acquisition of conditioning between a CS and a strong US is attenuated as a consequence of previous continuous reinforcement with the same CS and a weaker US. Another implication of Equation 4 refers to the effect of a partial reinforcement schedule and how this determines the degree of attention paid to a stimulus. By intermittently presenting a US after a CS, the parameter $|\lambda - \Sigma V|$ will always be positive no matter how many trials are given. Therefore, where associability (and thus attention) to a continuously reinforced CS will ultimately reach zero, the associability of a partially reinforced CS will remain at a relatively high level.

Direct support has since been provided for this prediction by using the associability of a stimulus as a measure of degree of attention paid to it. For example, Haselgrove et al., (2010) conducted an appetitive conditioning experiment using rats and four auditory stimuli, A, B, X and Y. The training stage was designed to modify attention to stimuli in accordance with the central tenets of the Pearce-Hall model; with A and B consistently paired with a food reward and X and Y intermittently paired with food. From this treatment it was expected, on the basis of the Pearce-Hall model that the associability of A and B would be lower than that of X and Y. In a subsequent test discrimination stage, rats were presented with an AY+, AX-, BY- discrimination. The results support that more attention was paid to X and Y during test, as the discrimination between the compounds that differed in terms of partially reinforced CSs (AY and AX) was acquired more readily than the discrimination between the compounds that differed in terms of the continuously reinforced CSs (AY and BY). Thus, suggesting that attention in rats is modulated in the way the Pearce-Hall model anticipates. Other studies (see Kaye & Pearce, 1984) have used the orienting response that the stimulus elicits to provide an index of attention paid to the stimulus; when a cue for the occurrence of food was only partially

reinforced, orientation towards the predictor was maintained relative to a continuously reinforced cue (see also: Wilson, Boumphrey, & Pearce, 1992).

There is only limited direct support for the Pearce-Hall model in studies of human learning; Hogarth, Dickinson, Austin, Brown and Duka (2008) used an eye-gaze measure as an index of attention to visual cues associated with an aversive noise outcome. The visual cue associated with an uncertain noise outcome, attracted a longer gaze-time, than cues which consistently predicted either the outcome (A), or its omission (C). These findings however fail to explore whether or not learning is facilitated for these cues predictive of uncertain outcomes (although see Le Pelley et al., 2010b; discussed at length in Chapter 3). More recent work by Beesley et al. (2015) also supports an increase in overt attention (as measured by eye-gaze) to cues trained in uncertain compounds (compounds that were paired with outcomes in a probabilistic manner: i.e., Outcome o1 occurred on 70% of trials, and o2 occurred on the remaining 30%). However, in a subsequent test of learning involving new cue-outcome relationships, there was no evidence of a carryover effect of participants' previous experience of uncertainty on overt attention or learning about these uncertain cues.

Applied to latent inhibition, the Pearce-Hall model suggests that the associability of a stimulus declines during preexposure because it is consistently followed by no consequence, therefore its outcome, nothing, is well predicted. Therefore, the model anticipates nominal learning on the first conditioning trial when the preexposed stimulus is paired with the US. By a similar token, Pearce and Hall attempt to describe learned irrelevance as a decrease in associability to the preexposed cue due to the random presentations of the CS and US, resulting in the growth of a context-US association. Consequently, whenever the US is, by chance, paired with the CS, it will be accurately predicted by the contextual stimuli, and thus attention to the

CS will decline because it is followed by an accurately predicted event. However, as there are trials in which the CS is followed by no consequence, the US will always be surprising; presenting a problem for the Pearce-Hall model in being able to explain learned irrelevance as a decrease in associability to the preexposed cue. Nevertheless, the Pearce-Hall model suggests that learning a cue is 'irrelevant' to the occurrence of an outcome will result in reduced learning about this cue when these events are eventually paired; suggesting a unitary mechanism (in this case, attentional) underlying both latent inhibition and learned irrelevance.

1.9.2 Overview of applications to latent inhibition and learned irrelevance

Many researchers have adopted the view that latent inhibition and learned irrelevance are the result of reduced stimulus processing, and explain the effects in terms of mechanisms that deal with attention and/or association (Le Pelley, 2004; Lubow, Weiner & Schnur, 1981; Mackintosh, 1975; McLaren & Mackintosh, 2000; Pearce & Hall, 1980; Wagner, 1978, 1981). These models assume that latent inhibition is generated by an attention-like mechanism, resulting from a reduction in the processing of the stimulus during non-reinforced preexposure. And, learned irrelevance is viewed as reflecting a reduction in the processing (in terms of a change in attention or associability) as a result of unpaired correlations between a stimulus and target during irrelevance pre-training. Theories which adopt this approach are referred to as 'attentional models' as they can explain latent inhibition and learned irrelevance as the result of a failure to encode the relationship between the preexposed stimulus and the US (Le Pelley, 2004; Lubow et al., 1981; Mackintosh, 1975; McLaren & Mackintosh, 2000; Pearce & Hall, 1980; Wagner, 1978, 1981). Therefore, despite the very different principles on which their theories are based, both Mackintosh (1975) and Pearce and Hall (1980) suggest the mechanism (in this case, attentional) underlying an effect of latent inhibition is the same mechanism underlying an effect of learned irrelevance. Whilst attentional accounts of latent inhibition and

learned irrelevance remain dominant, non-attentional accounts do exist (e.g. Hall, 1991; Bouton, 1993; 1997; Miller & Matzel, 1988; Oswald, 2001) and these are considered in the general discussion.

D. Aims of Thesis

The above sections have reviewed the symptomology of schizophrenia, schizotypy and anxiety (clinical and sub-clinical); with particular focus on the role attentional abnormalities may play in the causes of the disorders and by extension, their related personality sub-types in the normal population. Given the numerous factors likely to play a role in the manifestation of clinically diagnosed schizophrenia and anxiety, evidence has been reviewed that supports the study of attentional dysfunction as a possible cognitive endophenotype. An endophenotype is a ‘halfway point’ between the genetic/biological abnormalities and the signs and symptoms that characterise the disorder and may further our understanding of schizophrenia and anxiety. Braff (2008) proposed for an endophenotype to be viable, it must have a genetic basis, confirming it is trait not state and therefore precedes disorder onset. One means of doing this is by testing for the hypothesised endophenotype in healthy individuals using scales to measure schizotypy and anxiety.

Latent inhibition has already been identified as a potential cognitive endophenotype and there are plausible theories (Howes & Kapur, 2009; Kapur, 2003; Kapur et al., 2005) that link empirical findings to the clinical picture of schizophrenia. There is however, significant co-morbidity between schizophrenia and anxiety. As anxiety also shows abnormalities in dopaminergic functioning it maybe that latent inhibition dysfunction relates to symptom level. The similar relationship reported between both schizotypy and anxiety with latent inhibition (see Braunstein-Bercovitz, 2002) suggests that latent inhibition disruption is possibly

associated with general psychiatric illness or the anxiety components of schizotypy and by extension schizophrenia, rather than being a specific endophenotype for schizophrenia. However, there are number of limitations encompassed within existing research, specifically regarding the nature of latent inhibition paradigms, and whether they instead reflect the operation of learned irrelevance (see: Le Pelley et al., 2010a). This questions the current status of latent inhibition as a viable endophenotype for both schizophrenia and anxiety disorders by constraining the comparison between human studies and animal models that instead produce latent inhibition using only simple preexposure (thus latent inhibition not confounded by alternative learning phenomena). Further studies are required to ascertain whether this is the case. The possibility that the learned irrelevance paradigm might be more reliable, considering it is less ambiguous in terms of attention, is also worth exploring as a potential endophenotype for schizophrenia and anxiety. Existing research findings which indicate an attenuation of learned irrelevance in high schizotypy individuals provides support for this exploration (see Le Pelley et al., 2010a, section 1.5.2.1). Whether the distinction between latent inhibition and learned irrelevance is an important one, is a focus of the current work.

The general aim of this thesis is to address, or begin to address, some of the key questions and limitations with existing research that evaluate latent inhibition and learned irrelevance as potentially useful cognitive endophenotypes for schizophrenia and anxiety disorders.

(a) Experiments 1-4

The purpose is twofold: first, to address the limitations of existing latent inhibition tasks by designing a paradigm that examines a purer effect of latent inhibition, by minimising the contribution of learned irrelevance, and assessing how this latent inhibition task co-varies with

schizotypy and anxiety (Chapter 2: Experiments 1 and 2). Secondly, latent inhibition has been argued, an equivocal measure of attentional processing (Weiner, 1990; Hall, 1991; Bouton, 1993; Gray & Snowden, 2005) which renders it difficult to draw inferences that attenuations of latent inhibition infer a disruption of attention processes implicated in schizophrenia and anxiety. Thus, whilst an effect of latent inhibition has been viewed as a consequence of *attention* that influences learning; as already highlighted- alternative, and less equivocal, attentional paradigms exist. The learned irrelevance paradigm has been proposed a less ambiguous measure of the impact of attention on associative learning, in contrast to latent inhibition (as previously discussed; see also Le Pelley, 2010a,b). Therefore, the second aim was to design a learned irrelevance paradigm, and assess the relationship between this task and measures of schizotypy and anxiety (Chapter 3: Experiments 3 and 4).

Examining the comparison between a true latent inhibition paradigm and a learned irrelevance paradigm, will allow an assessment of their *independent effects* on schizotypy and anxiety. By teasing apart the effects of latent inhibition and learned irrelevance we are attempting to disentangle, and constrain our understanding of attentional abnormalities observed in these sub-clinical traits and by extension, their related pathologies. We assess whether the learned irrelevance paradigm has the potential to produce converging and complimentary evidence to that of the latent inhibition work.

Based on the assumption then, that latent inhibition and learned irrelevance share similar psychological underpinnings (in this case, attentional), we should expect the effect of schizotypy and anxiety to be comparable in the two types of attention tasks here. This proposition is supported by attentional theories of associative learning, such as Mackintosh (1975) which suggests the mechanism underlying an effect of latent inhibition is the same mechanism underlying an effect of learned irrelevance. Consequently, if we see an effect of

schizotypy and anxiety with latent inhibition, then we would expect to see the same with learned irrelevance. If this does not turn out to be the case, a revision of existing attentional-associative models will be suggested.

(b) Experiments 5 & 6

To anticipate, the results from Experiments 3 and 4 demonstrated a reduced effect of learned irrelevance which was specific to individuals high in state anxiety. However, from these results it remains unclear whether high anxiety causes an inability to direct attention, or alternatively whether the inability to distinguish previously relevant from irrelevant cues induces a state of anxiousness. Therefore, the aim of chapter 4 (Experiments 5 and 6) was to explore the direction of causality between anxiety and learned irrelevance, using a mood manipulation procedure in which participants either received a negative mood inducing task (a speech stressor task) to elevate state-anxiety levels; a positive mood inducing task (relaxed breathing/meditation exercises) to reduce state-anxiety levels; or a neutral mood inducing task (passage from the National Geographic) to act as a control group. Experiment 5 sought to explore the effectiveness of these mood induction tasks in modulating state anxiety before assessing their ability to influence learned variations in attention using an established learned irrelevance procedure (Experiment 6).

Chapter 2:

Latent inhibition: The relationship with schizotypy and anxiety

2.1 Introduction

2.1.1 Latent inhibition: Recapitulation

Theoretical analyses of latent inhibition have focused upon an attentional explanation - proposing that during preexposure, attention diminishes to the preexposed stimulus so that, subsequently, participants take longer to learn the association between this stimulus and the outcome (Lubow & Gerwitz, 1995; Mackintosh, 1975; Pearce & Hall, 1980) than the non-preexposed cue. Despite over 50 years of research, there is still no generally accepted theory of latent inhibition (Wagner, 1978, 1981; Bouton, 1993; Weiner, 2003), but the absence of a theoretical consensus has not impeded the use of latent inhibition paradigms for practical applications (e.g., screening potentially therapeutic drugs for schizophrenia; see Lubow & Weiner, 2010). As such, the concept of latent inhibition and the notion that it might be reduced in patients with schizophrenia has been a powerful heuristic tool for cross-species studies (for a review see Swerdlow & Williams, 2010). However, what is less clear is the evidence that latent inhibition actually *is* reduced, as many latent inhibition tasks have failed to provide replicable modulation of latent inhibition in patients with schizophrenia (for a review see Swerdlow, 2010) and in high schizotypy individuals (for a review Lubow & Weiner, 2010). Crucially, what is even less clear is whether existing latent inhibition paradigms instead reflect alternative learning phenomena. Detailed description of these findings, as well as a discussion of possible conceptual and methodological ambiguities surrounding some of the existing latent inhibition procedures, are discussed in the following introductory sections; 2.1.2 to 2.1.5.

2.1.2 Latent inhibition and schizophrenia

Baruch et al (1988a) were the first to report an anomaly in latent inhibition in patients with schizophrenia. This task was based on a ‘masked’ procedure devised by Ginton, Urca & Lubow (1975) in which participants had to listen to a recording of nonsense syllables and count the frequency of one of them. For the preexposure group only, short bursts of white noise were provided as a background to the masking task. The subsequent task during the test phase consisted of both preexposed and non-preexposed groups learning that a burst of white noise (the CS) signalled the increment of a counter on a scoreboard (the US). The learning of the noise-increment association was slowed for control participants and patients with chronic schizophrenia who were preexposed to presentations of the white noise, whilst those with acute schizophrenia showed an *absence* of slower learning to the preexposure stimulus. Some studies have replicated this experiment reporting acute, rather than chronic patients with schizophrenia exhibit attenuated latent inhibition (Baruch et al; Gray, Hemsley & Gray, 1992; Rascle et al., 2001; Gray et al., 2002, Vaitl et al., 2002). This relationship has been suggested to account for the presence of spurious associations being formed between stimuli in the environment from which unusual thought patterns and positive symptoms may emerge (i.e., hallucinations and delusions; Kapur, 2005; Cassaday & Moran, 2010, Moran et al 2008).

However, a number of studies demonstrate controversy about the status of latent inhibition in schizophrenia. For example, there are some studies that suggest no disruption of latent inhibition in patients with schizophrenia (Lubow, Weiner, Schlossberg & Baruch, 1987; Swerdlow et al., 1996; Williams et al., 1998; Lubow, Kaplan, Abramovich et al., 2000; Serra, Jones, Toone & Gray, 2001), whilst others report an increased (or enhanced) effect of latent inhibition (Rascle et al., 2001; Cohen et al., 2004; Gal et al., 2009). Normal latent inhibition has even been reported in acute medicated patients with schizophrenia (Swerdlow et al., 1996;

but see Williams et al., 1996) which used the same auditory latent inhibition paradigm as discussed above (see Ginton et al., 1975). Authors using a slight variation of this task however reported an attenuation of latent inhibition but only in one or another subclinical subgroup or sex (Lubow et al., 1987; Lubow et al., 2000). Others have alternatively suggested that attenuated latent inhibition simply reflects generalised learning deficits observed in the non-preexposed group (Serra et al., 2001). Disagreement also appears when the effects of disease chronicity are taken into account. Some have suggested latent inhibition deficits reflect the acute stage of schizophrenia rather than the positive symptoms per se (Gray et al., 1992), whilst others have suggested latent inhibition is attenuated in acute negatively symptomatic patients (Rasclé et al., 2001) or levels of latent inhibition are normal in acute positively symptomatic patients (Cohen et al., 2004). Each of these studies that show discrepant results not only challenge the proposed relationship between attenuated latent inhibition and positive symptomology in schizophrenia (Kapur, 2005) but also highlight the number of reports that fail to detect attenuated latent inhibition. One possible explanation for the inconsistencies in the literature may be because the effect has an additional pole of expression – an enhanced, or abnormally persistent latent inhibition effect, with the chronic stage of schizophrenia (Weiner, 2003). For the first time, Rasclé et al. (2001) reported an enhanced latent inhibition effect with patients in a chronic stage of their illness, one that was positively correlated with the negative symptoms of schizophrenia using the between-participant latent inhibition task described by Ginton et al. (1975).

However, the between-participant paradigms that have typically been used to measure latent inhibition in patients with schizophrenia have several limitations. Primarily, the preexposed and non-preexposed groups are composed of *different* participants, making it difficult to match patients with identical states across groups. To avoid these problems, more

recent studies have tended to employ a within-participant procedure for detecting latent inhibition in which learning about a novel and familiar stimulus is measured in the same participant. In a task reported by Cohen et al. (2004), participants were presented with displays on a computer monitor that comprised 20 shapes. One of the shapes (X) was different from the remaining nineteen (Y), and it was the participants' task to respond, on a keyboard, whether the odd shape was on the left, or the right hand side of the screen. Following 96 trials in which the odd item, and the distracters, were presented to participants, participants received four types of test trials in which: (1) the stimulus that had previously served as a distracter, Y, now served as the odd-item target stimulus amongst an array of nineteen Xs - *the preexposed condition*; (2) trials in which a novel cue, Z, served as the target stimulus amongst an array of nineteen Xs - *the non-preexposed condition*; (3) filler trials identical to pre-exposure; and (4) trials in which the target and the distracts were novel. The results of Cohen et al's experiment demonstrated that reaction times during the preexposed condition were slower than during the non-preexposed condition. Furthermore, similar to Rascle et al. (2001) their results show that patients in a chronic stage of their illness, displaying high negative and low positive symptoms, show an enhanced latent inhibition effect. Gal et al. (2009) have also replicated this finding using a variation of this within-participant visual recognition latent inhibition procedure. Although Gal et al suggest enhanced latent inhibition is more specific to illness chronicity, rather than negative symptoms per se. To the best of current knowledge, reports by Rascle et al. (2001), Cohen et al. (2004) and Gal et al. (2009), are the first three studies to have shown that latent inhibition is abnormally persistent in chronic patients. On the basis of the studies reviewed thus far, it seems accurate to suggest that schizophrenia is associated with an abnormal expression of latent inhibition. Whether an attenuation or enhancement of the effect is observed, depends on the stage of the illness.

2.1.3 Latent inhibition and schizotypy

Comparable to the schizophrenia literature (e.g., Baruch et al., 1988a; Gray et al., 1992; Rascle et al., 2001), previous studies that have investigated the relationship between schizotypy and latent inhibition have revealed mixed results. Baruch et al (1988b) were the first to report a relationship between latent inhibition and schizotypy in the normal population using the masked between-participant procedure to measure latent inhibition described by Ginton et al. (1975). They report reduced latent inhibition in participants who scored high, but not low (as determined by a median split) on the Psychoticism dimension of the Eysenck psychoticism questionnaire (EPQ; Eysenck & Eysenck, 1975). Although there was no relationship between latent inhibition and the Launay and Slade (1981) hallucination scale and only a trend for a reduced latent inhibition effect in participants scoring high (again as determined by median split) on the STA; suggesting an apparent discrepancy in findings when alternative psychometric measurements are used. In addition, Lubow, Ingberg-Sachs, Zalstein-Orda and Gewirtz (1992) also found reduced latent inhibition in participants scoring high on the STA but this effect was driven by a difference in learning in the non-preexposed group, as opposed to the theoretically more interesting, preexposed group. Using Brauch et al's procedure (originally described by Ginton et al.), Allan, Williams, Wellman et al. (1995) were able to demonstrate reduced latent inhibition in participants who scored high (as compared to low) on the STA questionnaire, and critically, with a difference in learning only observed in the preexposed group. Varying modulation of latent inhibition in schizotypy individuals is thus widely reported across the literature.

Whilst the majority of existing studies have employed a 'masked' procedure to demonstrate latent inhibition (i.e., Baruch et al., 1988b; Allan et al., 1995), some studies have instead employed a differential conditioning procedure, in a between-participant comparison

to assess the generality of existing findings. For example, Lipp and Vaitl (1992) used a differential conditioning procedure in which two visual stimuli were presented; one of which served as the to-be-conditioned stimulus (CS+) and the other was the not-to-be-conditioned stimulus (CS-). The US that followed the CS+ was a tone that participants were required to make a rapid button press response to as soon as they heard it. One group received different stimuli during preexposure and conditioning (Group Different), serving as a control for the latent inhibition effect, whereas a second group received the same CS+ throughout both stages of the experiment (Group Same); and it is expected that latent inhibition would occur in this latter group. The measure of conditioning was differential skin conductance during the CS+ and CS- presentations to assess whether schizotypy measures co-vary with latent inhibition indexed by autonomic responses. Unlike Baruch et al's findings, EPQ scores did not co-vary with latent inhibition but consistent with Baruch et al's findings, Launay & Slade's (1981) hallucination scale also did not co-vary with latent inhibition. Regarding STA (Claridge & Broks, 1984) scores; participants scoring high as compared to low on this questionnaire, determined by median split, did however show differences in the extent of latent inhibition displayed. Differential conditioning was significantly higher in Group Different than in Group Same only for participants who scored low on the STA. For participants who scored high, differential conditioning was equivalently high in Groups Same and Different. Using a slight variant of this procedure (an electric shock was instead used as the US); Lipp, Siddle & Arnold (1994) also show differences in the extent of latent inhibition displayed between groups who were divided by median split on the STA into low and high groups. However, it is unclear whether this experiment reveals an effect of schizotypy that is specific to stimulus preexposure as the high and low groups did not differ in the differential conditioning to the preexposed CS. Instead these groups only differed in relation to the non-preexposed CS. In contrast to an attenuation of latent inhibition however, other studies have shown that, given limited

preexposure, individuals high in schizotypy can in fact demonstrate a latent facilitation effect (Burch, Hemsley & Gray, 2004; but see De la Casa, Ruiz & Lubow, 1993), these findings are discussed next.

Burch, Hemsley and Joseph (2004) employed a variant of the auditory between-participant task previously employed by those such as Baruch et al. (1988b) and Allan et al. (1995) involving a visual version of the task in which participants were required to complete a masking task which involved counting the number of instances that a particular trigram of letters was presented on screen during the preexposure stage of the experiment. For the preexposure group only, these trigrams appeared on screen accompanied by irregularly-shaped polygons that subsequently served as the to-be-conditioned stimulus. The number of times that the preexposed stimulus accompanied the trigrams during preexposure was either 0 (for a non-preexposed group), 5, 10, 40 or 80 trials. The subsequent task during the test phase consisted of both preexposed and non-preexposed groups learning that the polygon (CS) signaled the increment of an on-screen counter (US). The learning of the polygon-increment association was increased for participants scoring high as compared to low (determined by median split) on the unusual experiences sub-dimension of the O-LIFE questionnaire (Mason et al., 1995) after only 5 preexposures to the polygon. For this group, learning was faster than for the non-preexposed group. However, after 80 preexposures, no latent inhibition was observed in participants scoring high on the unusual experiences sub-dimension. Learning of the polygon-increment association was only slowed for participants scoring low on this sub-dimension. These findings suggest that latent inhibition is a positive function of the amount of stimulus preexposure, and that with very low numbers of preexposure, latent facilitation will occur in high schizotypy individuals relative to the positive symptom dimension of schizophrenia.

What is clear from the above literature review is that where some authors report a reduction in latent inhibition with higher levels of schizotypy, others do not, and some suggest a reversal of latent inhibition with schizotypy (see also: Lubow & Weiner, 2010; Lubow, Kaplan & De la Casa, 2001; De la Casa & Lubow, 2002; Shira & Kaplan, 2009; Kaplan & Lubow, 2001; Lubow & Kaplan 1997). Adding further complexity to these discrepant results however is that the association between schizotypy and latent inhibition is typically reported with only small-to-moderate effect size (see Gray et al., 2003; Swerdlow et al., 2003). This may first limit the success in detecting effects of schizotypy upon latent inhibition, and second, it may indicate that schizotypy is perhaps not the only, or most, meaningful determinant of latent inhibition modulation in schizotypal individuals (and by extension schizophrenia). In support of this proposal, attenuated latent inhibition has been reported in both state and trait anxiety which has led to the conclusion that high schizotypal's reduced ability to suppress attention to irrelevant stimuli is related to both high levels of anxiety and schizophrenia-like symptoms (Braunstein-Bercovitz, 2000, 2001, 2002). Curiously however, there are no data examining whether anxiety or stress levels play a role in the modulation of latent inhibition observed in patients with schizophrenia. The attempts to cross this boundary in sub-clinical populations are explored in the following section.

2.1.4 Latent inhibition, schizotypy and anxiety

Schizotypy is a personality characteristic that is co-morbid with a number of other traits (see section 1.6.1.2). It is therefore possible that some of the variations in latent inhibition with schizotypy are in fact a consequence of the influence of other, correlated personality traits. This issue was addressed by Braunstein-Bercovitz (2000) and in the first instance 219 participants completed the SPQ and the trait subscale of the STAI (Spielberger et al., 1970). A factor analysis of the items of the SPQ revealed two factors; the first that was correlated with trait

anxiety scores (labelled ‘anxiety- loaded’) and included interpersonal deficits and disorganization factors such as social anxiety, no close friends, constricted affect and suspiciousness. The second factor did not correlate with trait anxiety (labelled ‘perceptual-disorganisation’) and included factors such as odd beliefs or magical thinking, unusual perceptual experiences, odd or eccentric behavior, and odd speech. Participants were then required to complete a latent inhibition task, similar to the masked between-participants task used by Baruch et al (1988a, b) and Allan et al. (1995). In this task participants were required to complete a masking task by indicating whether a pair of letters, presented on screen, were the same or different. For the pre-exposed group only, these letters were accompanied by irregular polygons. For the non-preexposed group, only the letter pairs were presented. The subsequent task during the test phase consisted on both preexposed and non-preexposed groups learning that the polygons signaled the increment of an on-screen counter. Participants were required to make a response when they thought the counter would increment.

Using a median split of scores, participants were separated into high and low groups on either factor 1 (anxiety loaded) or factor 2 (not anxiety loaded) of the SPQ. Latent inhibition was attenuated only as a function of the anxiety loaded factor (factor 1), and not as a function of the perceptual disorganization factor (factor 2). Thus when participants were separated into high and low schizotypy groups on the basis of factor 1, latent inhibition was only evident in the low group. For the high group, learning was as rapid in the preexposed, as in the non-preexposed groups. Whereas, on the basis of factor 2; a reliable latent inhibition effect was detected in participants who were both high and low in schizotypy. Since the ‘interpersonal deficits’ component of factor 1 (anxiety loaded) is associated with the negative symptoms of schizophrenia and schizotypy (see Raine, 1992), it appears that the negative and not positive symptoms of schizophrenia are characterized by elevated levels of anxiety. However, both

schizotypy and anxiety modulated latent inhibition independently, suggesting high schizotypals' (and by extension, individuals with schizophrenia) reduced ability to suppress attention to irrelevant stimuli, is related to both high levels of anxiety and schizophrenia-like symptoms (Braunstein-Bercovitz, 2000). Further support for this finding stems from a subsequent study (see Braunstein-Bercovitz, 2001) in which participant's level of state anxiety was manipulated using an acute stress induction procedure (see also Chapter 4). Participants in the high, but not low, stress condition exhibited attenuated latent inhibition. However, the limitations associated with existing latent inhibition paradigms question the validity of these findings (both in relation to anxiety and schizotypy); these limitations are highlighted in the following section.

2.1.5 Experimental paradigms of latent inhibition: conceptual and methodological limitations.

The latent inhibition procedures described thus far have modified its basic procedure in order to ensure that participants engage within the experiment during preexposure. First, the outcome from the second stage of the experiment might also be included in the first stage of the experiment – unpaired with the cue (e.g. Swerdlow et al., 1996; Cohen et al., 2004; Gal et al., 2009; Lubow & Kaplan, 1997; De la Casa & Lubow, 2001; Lubow & De la Casa, 2002). Second, a masking task may be presented that accompanies the presentation of the stimulus during the preexposure stage (e.g. Baruch et al., 1988a,b; Gray, Hemsley & Gray, 1992). The explicit use of a masking task has been employed to divert participant's attention from the preexposed cue. It has been suggested that a masking task is a necessary condition for the production of the latent inhibition effect in human participants (see Lubow & Gerwurz, 1995). Given that animal latent-inhibition studies do not require the use of either of these modifications to observe latent inhibition, the suggestion that human and animal latent

inhibition are not mediated by the same underlying attentional processes undermines the use of latent inhibition as an animal model of schizophrenia (for a review see: Le Pelley & Schmidt-Hansen, 2010; Lubow & Weiner, 2010). More importantly, however, these modifications also align themselves with alternative learning phenomena, rather than latent inhibition. For example, by exposing the target outcome during the preexposure stage of the experiment in an uncorrelated (or unpaired) fashion with the preexposed cue may result in the establishment of learned irrelevance or conditioned inhibition to the preexposed cue; both of these effects are known to retard the acquisition of later learning (e.g.: Baker & Mackintosh, 1997; Rescorla, 1969) and are known to co-vary with schizotypy (Schmidt-Hansen et al., 2009; Le Pelley et al., 2010a; Migo et al., 2006). It could be argued, therefore, that all the studies that employed these modifications to the latent inhibition procedure (see Allan et al., 1995; Baruch et al., 1988b; Braunstein-Bercovitz & Lubow, 1998; Della Casa et al., 1999; Gray et al., 2002; Lubow et al., 1992) may instead demonstrate alternative learning phenomena, other than latent inhibition.

Evans et al. (2007) have described a within-participant latent-inhibition procedure that, they suggest, circumvents the inclusion of a masking-task during preexposure. In this task participants were presented with a series of letters, presented one after the other in the centre of the screen and instructed to press the spacebar as quickly as possible when the letter X was presented. The letter X was either preceded on some trials by a letter (e.g., H) that had been preexposed amidst the filler letters earlier in the experiment or by a letter (e.g., S) that had not been preexposed. This task showed a latent inhibition effect - participants were slower to respond to presentations of X when it was cued by the preexposed letter than the non-preexposed letter, and a trend for a reduction in latent inhibition with the positive symptom dimension of schizotypy was observed. As this procedure did not include a concurrent masking

task during the preexposure stage of the experiment, it is difficult to explain this result in terms of learned irrelevance. Furthermore, at first blush, it seems difficult to explain this result in terms of conditioned inhibition, as the target outcome was not presented to participants during the preexposure phase either. However, as Evans et al note, an expectation of the target-stimulus was established prior to the preexposure phase through instruction. Thus, conditioned inhibition might be generated because the target outcome was expected to appear (but did not) at a time when the preexposed stimulus was presented. This negative prediction error will lead standard associative models of learning (e.g. Rescorla & Wagner, 1972) to predict the formation of an inhibitory association between the preexposed stimulus and the target X, slowing later learning for reasons other than latent inhibition. Such limitations can be applied then, to other studies that have utilised a similar within participant paradigm and also report a deficit in latent inhibition related to the positive dimension of the O-LIFE questionnaire (Schmidt-Hansen et al., 2009; Granger et al., 2012). The problem of such confounds has not been addressed in the development of more recent paradigms. Overcoming interpretational problems in respect of latent inhibition dysfunction could enhance the development of cognitive explanations about psychotic phenomena.

2.1.6 Aims and research questions

Here we introduce a procedure that examines variations in latent inhibition with schizotypy under conditions where the contribution of conditioned inhibition and learned irrelevance are minimised in order to provide a less ambiguous measure of the impact of learned variations in attention. However, removing the masking task altogether would result in an experimental paradigm that participants have no requirement to engage in. An alternative strategy then is to keep the masking task in place during preexposure but in such a way as to establish it as task-relevant. The two experiments reported here explored this possibility.

Additionally, it is important to include a measure of anxiety based on existing propositions that a) attentional dysfunction in high anxiety individuals has also been indicated in latent inhibition studies (Braunstein-Bercovitz, 2000, 2002). And b) measures of anxiety have been shown to co-vary with schizotypal traits that appear to modulate latent inhibition performance (Braunstein-Bercovitz). Additional analyses are conducted to assess how the relationship between schizotypy and anxiety co-varies with latent inhibition (see section 2.3.2.3).

2.2 Experiment 1

The first aim of Experiment 1 was to create a within-participant latent-inhibition task that minimises the possibility of observing conditioned inhibition and learned irrelevance. The second aim was to examine how this task co-varies with schizotypy and anxiety. Presented here are two variations of a task by Evans et al. (2007; itself modified from that designed by Young et al., 2005, see section 2.1.5). The first version constituted a replication of the task described by Evans et al, to demonstrate latent inhibition, predominantly as a *positive control*. The second version constituted a modification of this task where no expectation of the target was established during the preexposure stage either through instruction or explicit exposure to the target outcome – thus removing the contribution of conditioned inhibition (where a reduction in learning of the cue-target association during the test stage would occur due to the cue predicting the absence of the target during preexposure). Instead, as suggested by Evans et al, during the preexposure stage participants were simply asked to count the number of instances of one of the filler letters (M). This manipulation also establishes all of the stimuli in stage 1 as task relevant as participants must process each letter in order to determine whether it is a letter M or not. Consequently, this task is also less amenable to an explanation in terms of learned irrelevance. In the subsequent test stage of both versions of the task, participants continued to be presented with a series of letters, one after the other in the centre of the screen,

but were now instructed to make a response as quickly as possible when the letter X appeared. On some occasions the letter X was preceded by a non-preexposed cue, whereas on other trials it was preceded by a cue that had been rendered familiar by being presented during the preexposure stage. Based on the results of Evans et al. it was expected that response-times would be shorter to X when it had been preceded by the non-preexposed, rather than the preexposed cue. We are interested in assessing whether the same effect was evident in the modified version of the task, as this would suggest the effect of a mechanism on stimulus preexposure that is not sensitive to alternative effects of learning, and whether this is modulated by schizotypy and/or anxiety.

2.2.1 Method

2.2.1.1 Participants

Sixty healthy Nottingham University participants and members of the general public (35 males and 25 females) took part, in exchange for course credit or a £4 inconvenience allowance. The age range was 18-54. Thirty participants completed the replicated version of the Evans et al. (2007) latent inhibition task ('replicated-task condition'), and thirty completed a modified version of this task ('modified-task condition'). Due to missing questionnaire data, three participants were excluded from the analysis leaving $n = 28$ in the replicated-task condition and $n = 29$ in the modified-task condition. A sample size of 60 was chosen based on an effect size (0.66) and a power of 0.95 for a linear regression with 3-4 predictors (see section 2.2.2.2 but also section 2.3.2.3 which uses a pooled sample size $n = 117$). Previous studies using a similar task design in a similar cohort of participants have used a comparable sample size to the current study (see Schmidt-Hansen et al., 2009).

2.2.1.2 Apparatus & Stimuli

All experimental stimuli appeared on a standard desktop computer running Windows XP, and were programmed using Psychopy (Peirce, 2007; www.psychopy.org). Stimuli were white capital-letters in Arial-font (7mm(H) x 5mm(W)) presented for 1 second each on a computer-screen (28cm(H) x 35cm(W)) with a grey background. The stimulus-letters were S and H, one of the letters served as the preexposed stimulus and the other was the non-preexposed stimulus, counterbalanced across participants. The target was the letter X, with filler-letters D, M, T and V; see Figure 2.1.

2.2.1.3 Procedure

2.2.1.3.1 Replicated-task Condition

The task had two stages: preexposure and test. After reading an information sheet and signing a consent-form, the following instructions were presented to participants on the computer monitor:

“In this task I want you to watch the sequence of letters appearing on the screen. Your task is to try and predict when a letter 'X' is going to appear. If you think you know when the 'X' will appear then you can press the space bar early in the sequence, that is before the 'X' appears on screen. Alternatively, if you are unable to do this please press the spacebar as quickly as possible when you see the letter 'X.' There may be more than one rule that predicts the 'X.' Please try to be as accurate as you can, but do not worry about making the occasional error. If you understand your task and are ready to start press the spacebar to begin.”

During the preexposure stage the preexposed stimulus was presented 20 times, intermixed in a random order with presentations of filler letters each of which was presented 15 times; each stimulus was presented for 1000ms separated by a 50ms inter-stimulus interval. The non-preexposed stimulus and target letter X were not presented during the preexposure stage. The test stage followed, without interruption, the preexposure stage, during which the preexposed stimulus and the non-preexposed stimulus were each presented 20 times followed by a 1000ms presentation of the target stimulus X. There were also 20 non-cued presentations of X during which the target was preceded by one of the 4 filler letters, each of which preceding the target 5 times. In total there were 64 presentations of the filler letters throughout the test phase. The whole task lasted 7 minutes. Participants were required to press the space-bar, either when X appeared on screen, or if they could predict when the X would appear as the next letter in the sequence.

2.2.1.3.2 Modified -task Condition

The procedure for the modified version of the task was as described for the replicated version of the Evans et al. (2007) latent inhibition task (section 2.2.1.3.1), with the exception that participants received two sets of instructions, one set appeared on screen prior to the preexposure stage, instructing the following:

“In this task I want you to watch the sequence of letters appearing on the screen. Your task is to count how many times the letter 'M' appears. This task will last about 3mins. When this task ends, you will be given a new set of instructions. Press any key when you are ready to start the experiment.”

Thus for the modified-task condition participants were not aware that the target stimulus would appear until after the preexposure phase. A second-set of instructions (identical to those administered at the outset of the replicated-task condition) were then presented prior to the test stage. Otherwise, all procedural details of the preexposure and test stages were identical to the replicated-task condition.

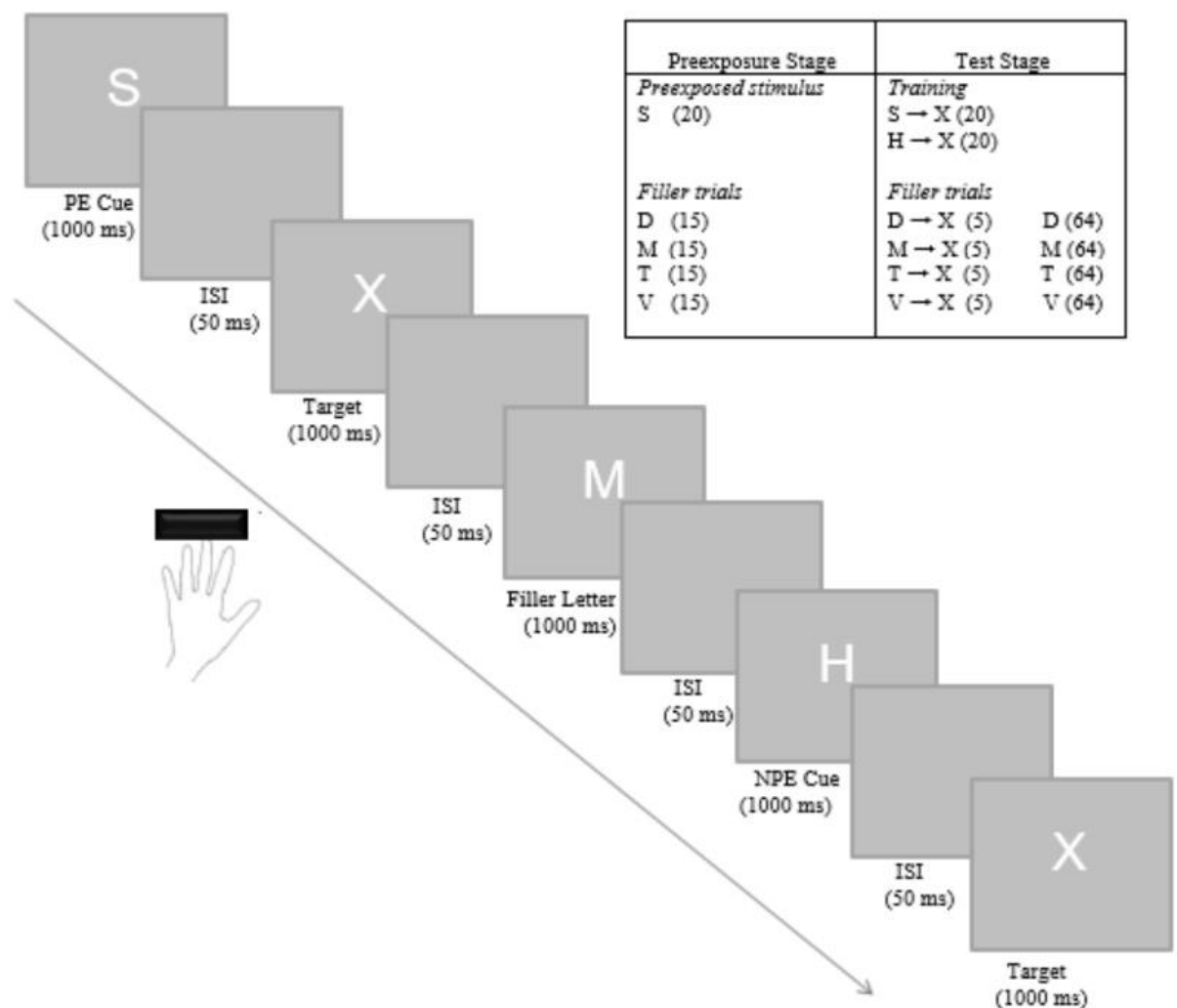


Figure 2.1. Experimental design and example stimuli for the test stage of the latent-inhibition task. Each trial comprised a 1000ms presentation of a stimulus separated by an inter-stimulus interval (ISI) of 50ms. Participants were required to press the spacebar either when the target stimulus ‘X’ appeared on screen, or before it appeared if they could predict it as the next letter in the sequence. The preexposed (PE) and non-preexposed (NPE) stimuli were counterbalanced across participants. Numbers in parentheses in the insert refer to trial frequencies.

A computer-based version of the O-LIFE (Mason et al., 1995) was administered to assess individual schizotypy, see Appendix 3. This questionnaire assesses four dimensions of schizotypy. The Unusual Experiences (UnEx) subscale measures auditory hallucinations, magical thinking and perceptual aberrations reflecting positive symptoms of schizophrenia (e.g., “Have you ever felt you have special, almost magical powers?”). The Introverted Anhedonia (IntAn) subscale reflects anhedonia (inability to experience pleasure); analogous to the negative symptoms of schizophrenia (e.g., “Do you feel lonely most of the time, even when you’re with people”). The Cognitive Disorganisation (CogDis) subscale assesses disruptions in attention/concentration; consistent with the disorganised symptoms of schizophrenia (e.g., “Do you ever feel that your speech is difficult to understand because the words are all mixed up and don’t make sense?”). Lastly, Impulsive Nonconformity (ImpNon) measures recklessness, impulsivity and antisocial behaviour (e.g., “Do you often have an urge to hit someone?”); similar to the Psychoticism scale of the Eysenck Personality Questionnaire (Eysenck & Eysenck, 1975). The O-LIFE questionnaire has good validity as it maps on to the same multi-dimensional structure as schizophrenia; assessing positive, negative and disorganised symptoms (Mason et al.).

A paper-version of the STICSA (Ree et al., 2008) was administered to assess individual anxiety-levels, see Appendix 4. This questionnaire assesses somatic symptoms of anxiety (e.g., increased heart rate, sweating) and cognitive symptoms of anxiety (e.g., difficulty concentrating, confusion), both in general; how often the statements are true of the participant (trait-anxiety) and their current symptoms of anxiety; right now, at this very moment (state-anxiety). Each scale (state and trait) encompasses 21 self-reported items, rated on a 4-point Likert-type scale (1 = *not at all* to 4 = *very much so*). The questionnaires were presented in a counterbalanced order across participants.

2.2.1.4 Scoring

Reaction times (RT's) in stage 2 were recorded from the onset of the preexposed and non-preexposed stimulus that preceded the target (X) for each participant. As each stimulus was presented for 1000ms separated by a 50ms inter-stimulus interval, participants' RT could range from 0-2050ms. If participants' RT was less than 1050ms they predicted the X; whereas if their RT was between 1050 and 2050ms, they responded to the X. Median RTs for responses to the preexposed stimulus and non-preexposed stimulus were calculated for each participant as it is less biased by extreme values compared to the mean. The scores derived for the four-schizotypy subtypes (complete for Experiment 1 and the subsequent Experiment 2) are presented in Table 2.2.

2.2.2 Results and Discussion

2.2.2.1 Latent inhibition

Figure 2.2 shows the mean of individual median reaction times to X across the 20 test trials⁵ with the preexposed and non-preexposed stimuli. Both the replicated-task and the modified-task groups showed faster RTs to the non-preexposed stimulus than the preexposed stimulus – latent inhibition. A 2 (condition: replicated-task, modified-task) x 2 (stimulus: preexposed, non-preexposed) mixed analysis of variance (ANOVA) of individual median reaction times revealed a significant main effect of stimulus $F(1,55) = 16.626, p < .001$, partial $\eta^2 = .23$, but no main effect of condition or interaction ($F_s < 1$), suggesting reaction times were similar for participants in both the replicated-task and the modified-task irrespective of target expectation during preexposure. Although not strictly warranted from the main effect of

⁵ Due to a program limitation, trial order could not be specified; hence the data were collapsed across the trials of the test stage. An updated version of the program was used for all subsequent experiments which circumvented this issue.

stimulus, and the absence of an interaction, it is instructive to examine whether the latent inhibition effect is present in both conditions. When median RT is employed as the measure of central tendency, repeated measures t tests revealed an effect of preexposure for the replicated task condition ($t(27) = 3.87, p=.001$) and an effect of preexposure for the modified task condition that just missed statistical significance ($t(28) = 2.02, p=.053$). When mean RT is employed as the measure of central tendency instead, both comparisons reach statistical significance (smallest $t(28) = 2.57, p=.016$). Thus, to increase statistical power for the subsequent analyses, the data were combined from the two test conditions for subsequent analyses.

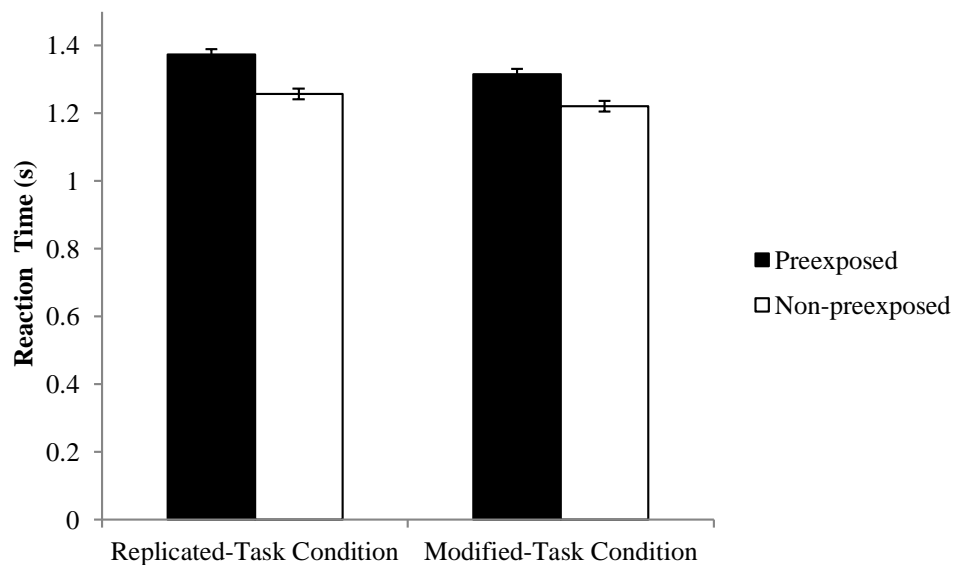


Figure 2.2 The mean of individual median reaction times to the target cued by preexposed stimuli and non-preexposed stimuli for participants in the replicated-task condition and the modified-task conditions in stage 2 of experiment 1. Error bars are ± 1 within-subject standard error of the mean (see: Cousineau, 2005).

2.2.2.2 Latent inhibition and schizotypy

A multiple regression analysis was carried out using the four schizotypy subscales taken from the O-LIFE: UnEx, IntAn, ImpNon and CogDis as the predictor variables, and median reaction time to the preexposed and non-preexposed stimuli as the dependent variables. If any of the predictor variables are associated with latent inhibition it would be expected that a

relationship would be found with the preexposed stimulus, but not with the control non-preexposed stimulus. When reaction time to the preexposed stimulus was entered as the dependent variable, UnEx was a significant predictor of RTs ($\beta = .362, p = .021$), reflecting *slower learning* to the preexposed stimulus with individuals *high* in UnEx, i.e. enhanced latent inhibition. ImpNon was also a significant predictor of reaction time to the preexposed stimulus ($\beta = -.360, p = .014$), reflecting *faster learning* to the preexposed stimulus for individuals *high* in ImpNon, i.e. an attenuation of latent inhibition. Neither of the remaining schizotypy subscales (CogDis and IntAn) were significant predictors of reaction time to the preexposed stimulus ($ps > .05$). When median reaction time to the non-preexposed stimulus was entered as the dependent variable, the only significant predictor of reaction time was ImpNon, which again was negatively correlated with RT ($\beta = -.318, p = .035$). None of the remaining schizotypy dimensions were significant predictors of reaction to the non-preexposed stimulus ($ps > .05$). All standardised regression coefficients and R^2 values can be seen in Table 2.1.

Table 2.1

Beta-coefficients from the multiple regression analyses of schizotypy subscales (predictor variables), with reaction times to preexposed and non-preexposed stimuli as dependent variables. Summary information includes all participants from the replicated-task and modified-task conditions of Experiment 1.

	Beta-coefficient	
	Preexposed	Non-preexposed
Unusual Experiences	.362*	.188
Cognitive Disorganisation	-.179	-.054
Introvertive Anhedonia	.032	.026
Impulsive Non-conformity	-.360*	-.318*
R^2	.164	.092

Note: * $p < .05$; Significant results are in bold.

The results indicate that individuals high in UnEx are slower to learn the association between the preexposed stimulus and the target than individuals low in UnEx. This, in conjunction with the finding that UnEx was not a significant predictor of reaction time to the non-preexposed stimulus, indicates that individuals high in this subtype are exhibiting an enhancement of latent inhibition. A relationship between ImpNon and RTs to both the preexposed and non-preexposed stimuli was also found, this suggests that ImpNon is associated with responding irrespective of whether the stimulus is familiar or novel, as opposed to being related to latent inhibition per se. Additional analyses which assess how the relationship between schizotypy and anxiety co-varies with latent inhibition are reported in section 2.3.2.3.

The enhancement of latent inhibition with high UnEx, does not agree with a number of schizotypy studies that have used a similar experimental procedure (Evans et al., 2007; Schmidt-Hansen et al., 2009; Granger et al., 2012). However, the attenuated latent inhibition effect with unusual experiences reported by Evans et al and Schmidt-Hansen et al did not reach the conventional cut-off point for statistical significance. A significant reduction in latent inhibition was attained by Granger et al, but this was a result of an association between the *difference* between the preexposed and non-preexposed stimuli and unusual experiences. Furthermore, it cannot be ruled out that the latent inhibition task employed in each of these studies could be showing alternative learning phenomena instead of latent inhibition, due to the limitations previously described. However, before we can draw any further conclusions, it is important to acknowledge the possibility that we still might be observing a co-variation of schizotypy with learned irrelevance in the current study, as opposed to latent inhibition. Whilst the modified-task condition successfully minimised the contribution of conditioned inhibition, it still included a masking task (count the letter M). Although this procedure – which requires continuous monitoring of the experimental stimuli - establishes a situation in which all of the

experimental stimuli are task relevant, it is conceivable that it still establishes learned irrelevance. In this task, participants are required to respond (albeit covertly) to the letter M, rather than any other stimulus. In this sense, then, the preexposed stimulus is irrelevant to the task in hand, thus learned irrelevance may still be the cause of the slower learning to the preexposed stimulus, rather than latent inhibition. As previously discussed, learned irrelevance is an effect which has been shown to influence human learning (Le Pelley & McLaren, 2003) and also co-vary with schizotypy (Schmidt-Hansen et al; Le Pelley et al., 2010a). However, as previously outlined, it would be problematic to remove the masking task altogether as participants would have no requirement to engage in the task during the preexposure stage. Therefore, the aim of Experiment 2 was to design a procedure that examined latent inhibition under conditions where the contribution of *both* learned irrelevance and conditioned inhibition were minimised, but keep the masking task in place during preexposure but in such a way as to establish it as *directly* relevant (as opposed to irrelevant) to the preexposed stimulus. If latent inhibition is still observed under these circumstances, it would permit an evaluation of the effect in terms of models of attention that do not emphasise the importance of learned irrelevance (e.g. Pearce & Hall, 1980; Esber & Haselgrove, 2011).

2.3 Experiment 2

To minimise the contribution of learned irrelevance (as well as conditioned inhibition), the purpose of Experiment 2 was to adjust the parameters of the modified-task condition from Experiment 1. In the preexposure stage, participants were now asked to say out loud each of the letters that appeared on the screen. This manipulation directly establishes all of the stimuli in stage 1 as task relevant as participants must process each letter by reading each of them aloud. Consequently, this version of the task rules out an explanation of any subsequent attenuation of learning to the preexposed stimulus with an appeal to learned irrelevance.

Furthermore, as no expectation of the target stimulus (X) is established prior to, or during, preexposure the task is also not amenable to an explanation in terms of conditioned inhibition. The test stage of the task remained the same as the modified-task condition from Experiment 1: participants were required to make a response as quickly as possible when the letter X appeared on screen. We are first interested in assessing whether an effect of stimulus preexposure is still observed under these different circumstances and second, to assess whether the task co-varies with schizotypy and anxiety. This being the case would suggest a relationship between these personality characteristics and stimulus preexposure that goes beyond learned irrelevance.

2.3.1 Method

2.3.1.1 Participants

In keeping with Experiment 1, sixty healthy Nottingham University participants and members of the general public (10 males and 50 females) took part, in exchange for course credit or a £4 inconvenience allowance. The age range was 18-33 years.

2.3.1.2 Apparatus

The apparatus were the same as described in Experiment 1.

2.3.1.3 Procedure

The procedure for Experiment 2 was as described in the modified-task condition in Experiment 1 with the exception that the instructions received prior to the preexposure stage asked participants to say aloud *each letter* that appeared on the screen. A second-set of instructions (identical to those administered at the outset of the test stage of the modified-task condition from Experiment 1) were presented prior to the test-phase. As per the previous

experiments, participants completed the O-LIFE (Mason et al., 1995) and the STICSA (Ree et al., 2008) questionnaires. All scoring was performed in the same manner as described in Experiment 1.

2.3.2 Results and Discussion

The scores derived for the four schizotypy subtypes (complete for Experiments 1 and 2) are shown in Table 2.2. Unpaired *t* test analyses were carried out to assess if the reported schizotypy means differ from the population norms for each subscale. While the means for CogDis and IntAn do not differ significantly from the normative values, the means for UnEx and ImpNon are both significantly lower than the normative values for the modified-task version of Experiment 1, and for Experiment 2. Significant differences are highlighted in bold in Table 2.2. Previous studies have also obtained mean schizotypy scores that are below Mason et al.'s (1995) normative values, and similar to those reported here (e.g. Evans et al., 2007; Granger et al., 2012; Sellen et al., 2005).

Table 2.2

Summary information for O-LIFE scores for the participants in the replicated-task and modified-task conditions of Experiment 1, and all participants from Experiment 2. All values are mean (SD). Population-norms taken from Mason et al., (1995), are also shown (mean (SD)).

	O-LIFE dimension			Mean (SD)
	UnEx	CogDis	IntAn	ImpNon
Experiment 1				
Replicated Task	10.1 (6.7)	11.4 (6.3)	6.7 (4.3)	8.2 (3.6)
Modified Task	6.9 (6.3)*	11.2 (6.3)	6.0 (5.1)	7.8 (3.3)*
Experiment 2	6.7 (5.4)*	12.3 (6.6)	5.0 (4.1)	7.1 (3.6)*
Population Norm	9.7 (6.7)	11.6 (5.8)	6.1 (4.6)	9.7 (4.3)

Note: * $p < .05$; Significant results that differ from the population norm for these subscales are in bold.

2.3.2.1 Latent inhibition

Figure 2.3 shows the median reaction times to X across the test trials of Experiment 2 (shown in two-trial blocks) with the preexposed and non-preexposed stimuli. It can be seen that reaction times became faster following the non-preexposed than the preexposed stimulus as this stage progressed. This impression was confirmed with a 2 (stimulus: non-preexposed, non-preexposed) x 10 (trial block 1-10) ANOVA of individual reaction times, which revealed a significant main effect of stimulus, $F(1,59) = 25.691$, $p < .001$, partial $\eta^2 = .303$ and a significant main effect of trial number, $F(9,51) = 7.949$, $p < .001$, partial $\eta^2 = .584$, but no significant interaction between these variables, $F < 1$.

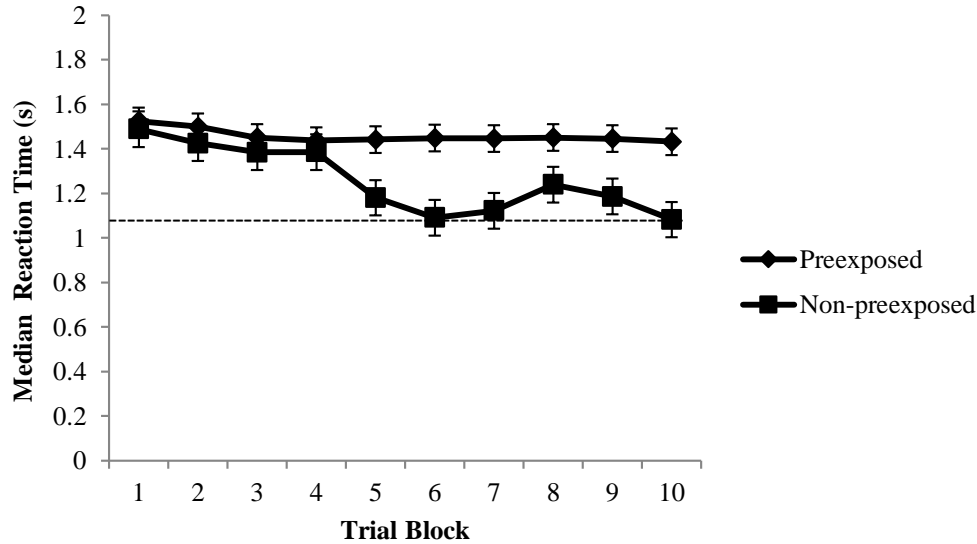


Figure 2.3. The median reaction times (sec) to the preexposed and non-preexposed stimuli over the 10 two-trial blocks of stage 2 of Experiment 2. Dotted line indicates the slowest reaction time at which participants can be regarded as anticipating the target (< 1005ms). Error bars represent 1+/- within-subject standard error (see: Cousineau, 2005).

In line with both conditions from Experiment 1; Experiment 2 successfully generated an effect of preexposure on reaction times during subsequent learning- latent inhibition. The task presented in Experiment 2 however, produced latent inhibition when the target was not expected during preexposure, and importantly, when using a masking-task that was not irrelevant to stimulus preexposure. These results encourage the suggestion that that an effect of exposure on learning is being observed here – that is to say latent inhibition rather than conditioned inhibition or learned irrelevance.

2.3.2.2 Latent inhibition and schizotypy

In keeping with Experiment 1, a multiple regression was carried out using the four schizotypy subscales from the O-LIFE (UnEx, IntAn, ImpNon and CogDis) as the predictor variables, and reaction time to the preexposed and non-preexposed stimuli as the dependent variables. Again, when reaction time to the preexposed stimulus was entered as the dependent variable, UnEx was a significant predictor of reaction times to the preexposed stimulus (β

=.402, $p = .021$), reflecting *slower learning* to the preexposed stimulus with individuals *high* in UnEx – replicating the enhanced latent inhibition effect observed in Experiment 1. Unlike Experiment 1, however, ImpNon was not a significant predictor of reaction time to the preexposed stimulus, nor were the remaining schizotypy subtypes. When median reaction time to the non-preexposed stimulus was entered as the dependent variable, none of the schizotypy subtypes were significant predictors of reaction time to the non-preexposed stimulus ($ps > .05$). Standardised regression coefficients and R^2 values can be seen in Table 2.3.

Table 2.3

Beta-coefficients from the multiple regression analyses of schizotypy subtypes (predictor variables), with reaction times to preexposed and non-preexposed stimuli as dependent variables.

	Beta-coefficient	
	Preexposed	Non-preexposed
Unusual Experiences	.402*	.238
Cognitive Disorganisation	-.249	.012
Introverted Anhedonia	.015	-.019
Impulsive Non-conformity	-.160	-.215
R^2	.111	.054

Note: * $p < .05$; Significant results are in bold.

In keeping with Experiment 1, the results of Experiment 2 show that individuals high in UnEx are slower to learn the association between the preexposed stimulus and the target than individuals low in UnEx. In both Experiments 1 and 2, we observed facilitation in RTs in individuals high in UnEx that was specific to the preexposed stimulus. These results encourage the suggestion that we are observing an enhancement of latent inhibition, rather than a more general effect of schizotypy on learning to both stimuli. Whilst the findings from both experiments presented here are comparable, the task employed in Experiment 2 is particularly

notable as it comprises a relatively ‘pure’ demonstration of latent inhibition, as it minimises the contribution of both conditioned inhibition and learned irrelevance to stimulus preexposure.

2.3.2.3 Latent inhibition, schizotypy and anxiety

The purpose of the subsequent analyses was to address the question posed by Braunstein-Bercovitz (2000); whether the attentional dysfunction in schizotypy is related to anxiety. The following analyses aimed to investigate the relationship between latent inhibition, schizotypy and anxiety. The scores for both anxiety-subtypes, for Experiment 1 (pooled data from the replicated and modified task conditions) and Experiment 2, are shown in Table 2.4.

Table 2.4

Summary information for STICSA-scores; all values are mean(SD). Values in brackets represent the range of scores for both anxiety-subtypes.

	Anxiety-Subtype			Mean(SD)		
	State	State Somatic	State Cognitive	Trait	Trait Somatic	Trait Cognitive
Experiment 1	31.3(8.4)	15.6(4.9)	16.4(6.1)	33.1(10.7)	14.9(5.1)	18.8(6.4)
Experiment 2	31.7(9.9)	15.5(4.7)	16.2(6.1)	33.6(9.5)	14.7(4.1)	18.6(6.0)
Population Norm	30.9(9.3)	13.6(4.0)	17.21(5.4)	32.4(8.1)	13.5(3.3)	18.8(4.8)

As a preliminary measure, Pearson product-moment correlation coefficients were run to assess whether the schizotypy dimensions were correlated with anxiety sub-types; given the exploratory nature of this analysis, no adjustments for multiple comparisons were made. There were significant correlations within each schizotypy dimension and each anxiety subtype (see Table 2.5); all p -values $<.01$, excluding IntrovAn in Experiment 1; $p >.05$. These significant relationships suggest an anxiety component in the schizotypy scale; on this basis subsequent analyses were continued to examine the effect of schizotypy on latent inhibition once anxiety had been controlled for. Two hierarchical multiple regressions were conducted with reaction time to the (1) preexposed stimulus and (2) non-preexposed stimulus as the

dependent variables. State and trait anxiety scores were entered into the model in step 1 to assess the main effect of anxiety on latent inhibition and to control for the effect of anxiety on the subsequent relationships between UnEx, CogDis, IntAn and ImpNon, and latent inhibition in step 2. These analyses were completed separately using the data from Experiments 1 and 2, as described below.

Table 2.5

Pearson product-moment correlation coefficients for anxiety and schizotypy variables: Experiments 1 (pooled data from the replicated and modified task conditions) and 2

	Trait	Unex	CogDis	IntrovAn	ImpNon
<i><u>Experiment 1</u></i>					
State	.375**	.513**	.527**	.080	.393**
Trait		.461**	.576**	.153	.290*
Unex			.484**	.088	.415**
CogDis				.248	.330*
IntrovAn					.039
<i><u>Experiment 2</u></i>					
State	.734**	.266*	.444**	.322*	.340*
Trait		.296*	.428**	.515**	.354**
Unex			.532**	.120	.498**
CogDis				.453**	.350**
IntrovAn					.253

Note. Values shown are Pearson's product-moment correlation coefficients.

** Correlation is significant at the 0.01 level.

* Correlation is significant at the 0.05 level.

Significant results are bolded.

2.3.2.3.1 Experiment 1

Hierarchical multiple regression analyses were carried out using the state and trait anxiety subtypes taken from the STICSA (step 1) and the four schizotypy subtypes taken from O-LIFE; UnEx, IntAn, ImpNon and CogDis (step 2), as the predictor variables. Md reaction time to the preexposed and non-preexposed cues were entered as the dependent variables.

When Md reaction time to preexposed trials was entered as the dependent variable, the effect of the predictor variables in step 1 was not significant $R^2 = .027$; $F < 1$. Neither State nor trait anxiety were significant predictors of reaction time to the preexposed cue ($p > .05$). When the schizotypy subtypes were entered into the regression in step 2, the change in the variance accounted for (ΔR^2) was significant; $\Delta R^2 = .209$, $p = .032$, whilst the overall model was close to significance; $F(6,56) = 2.206$, $p = .058$. The only significant predictor of reaction-time to the preexposed cue was ImpNon ($\beta = -.375$, $p = .011$). This finding reflects faster learning to the preexposed stimulus for individuals high in ImpNon and shows a comparable finding to that observed in the main analyses for Experiment 1. Also similar to the main analyses for Experiments 1 and 2, there was a trend for a relationship between UnEx and reaction time to the preexposed cue ($\beta = .299$, $p = .070$).

When Md reaction time to non-preexposed trials was entered as the dependent variable, the effect of the predictor variables in step 1 was significant $R^2 = .155$; $F(2,56) = 4.951$, $p = .011$. Both state and trait anxiety were significant predictors of reaction time to the non-preexposed cue (state anxiety; $\beta = -.354$, $p = .011$; trait anxiety; $\beta = .350$, $p = .012$); reflecting, faster learning to the non-preexposed cue for individuals high in state anxiety, and slower learning to the preexposed cue for individuals high in trait anxiety. There was no significant change in R^2 in step 2, but the effect of the predictor variables on learning to the non-preexposed were significant $R^2 = .239$; $F(6,56) = 2.619$, $p = .028$. Trait anxiety remained a significant

predictor ($\beta = .404, p = .013$), with state anxiety showing a trend for an association with the non-preexposed cue ($\beta = -.277, p = .085$). The only significant schizotypy predictor of reaction time to the non-preexposed cue was impNon ($\beta = -.293, p = .041$). Standardised regression coefficients and R^2 values can be seen in Table 2.6.

The results indicate a dissociation between state and trait anxiety for reaction time to the non-preexposed cue. Individuals high in state anxiety show faster learning to the non-preexposed cue, whereas individuals high in trait anxiety show slower learning to the non-preexposed cue. This could simply reflect a difference in the observed means between state and trait anxiety; as the mean (and range of scores) for trait anxiety is larger than those observed for state anxiety. Thus trait anxious individuals may be displaying slower learning compared to state anxious individuals (refer to Table 2.4) because their mean level of anxiety is higher. However, there was no relationship between state or trait anxiety and reaction time to the preexposed cue, suggesting anxiety influences basic associative learning, as opposed to latent inhibition more specifically. This finding is in opposition to the results reported by Braunstein-Bercovitz (2000) who found an abnormality in learning that was specific to the preexposed stimuli in high anxious individuals. Once the schizotypy sub-dimensions were added to the regression model in step 2, there was no increase in the predictive validity using reaction time to either the preexposed cue or the non-preexposed as the dependent variable. The key finding of interest here is that our earlier observation indicating enhanced latent inhibition with high UnEx (see Experiments 1 and 2; sections 2.2.2.2 and 2.3.2.2, respectively) approached significance ($p = .070$). Considering, this relationship is no longer significant though, suggests anxiety-subtypes *might* mediate the relationship between unusual experiences and latent inhibition. Once anxiety is controlled for, our previously observed effect is reduced below the significance threshold. This would lend support towards findings which suggest latent inhibition might not be a specific marker for schizophrenia/schizotypy, but a non-specific effect

associated with anxiety (Braunstein-Bercovitz, 2000). In line with Experiment 1 though, we observe a relationship between ImpNon and both the preexposed and non-preexposed cues, suggesting that ImpNon influences learning irrespective of whether the cue is familiar or novel—an effect, which appears to be, independent of anxiety. This finding adds to the heterogeneity in the literature regarding the relationship between latent inhibition and ImpNon; with some authors reporting a *trend* for enhanced latent inhibition (Evans et al., 2007) and others reporting reduced latent inhibition due to the high degree of correlation between ImpNon and UnEx (Gray et al., 2002).

2.3.2.3.2 Experiment 2

As in Experiment 1, hierarchical multiple regression analyses were carried out using the state and trait anxiety subtypes taken from the STICSA (step 1) and the four schizotypy subtypes taken from O-LIFE; UnEx, IntAn, ImpNon and CogDis (step 2), as the predictor variables. Md reaction time to the preexposed and non-preexposed cues were entered as the dependent variables.

When Md reaction time to preexposed trials was entered as the dependent variable, the effect of the predictor variables in step 1 was not significant $R^2 = .018$; $F < 1$. Neither state nor trait anxiety were significant predictors of reaction time to the preexposed cue ($p > .05$). When the schizotypy subtypes were entered into the regression, the change in R^2 was not significant; $\Delta R^2 = .168$, $p > .05$, similar to our main analysis for Experiment 2 (see section 2.3.2.2), unusual experiences was a significant predictor of reaction time to the preexposed cue ($\beta = .433$, $p = .017$), indicating an enhanced latent inhibition effect with high UnEx scores. In addition, we observe a novel relationship here as CogDis was also a significant predictor; ($\beta = -.404$, $p = .031$), indicating an attenuated latent inhibition effect with high CogDis scores.

When Md reaction time to non-preexposed trials was entered as the dependent variable, the effect of the predictor variables in step 1 was not significant $R^2 = .023$; $F < 1$. Neither state nor trait anxiety were significant predictors of reaction-time to the non-preexposed cue ($p > .05$). There was no significant change in R^2 in step 2, and the effect of the predictor variables on non-preexposed were not significant $R^2 = .073$; $F < 1$. None of the schizotypy variables were significant predictors of reaction time to the non-preexposed cue. Standardised regression coefficients and R^2 values can be seen in Table 2.6.

In contrast to the analyses of Experiment 1 (section 2.3.2.3.1), the results here indicate no relationship between state or trait anxiety and reaction time to the non-preexposed cue, which questions our previous observation indicating an influence of anxiety on basic associative learning. In addition, the pattern of results observed between state and trait anxiety and reaction time to the non-preexposed cue are in the opposite direction to those observed in Experiment 1; with high state anxious individuals now displaying slower learning towards the non-preexposed cue (albeit non-significantly) compared to high trait anxiety individuals. This discrepancy however, can possibly be explained by the difference in the observed range of scores between state and trait anxiety from Experiment 1 to Experiment 2, as the standard deviation of scores for trait anxiety is higher in Experiment 1 compared to Experiment 2 and the opposite is true for state anxiety (refer back to Table 2.4). Arguably of more importance though and comparable to Experiment 1, we observe no relationship between state or trait anxiety and reaction time to the preexposed cue. This encourages our previous suggestion that anxiety alone, does not appear to specifically influence latent inhibition. This contention is further supported from the results of Experiment 2, as both an enhanced effect of latent inhibition with high UnEx, and a reduced effect of latent inhibition with high CogDis, remain to be seen when anxiety is accounted for. Furthermore, the direction of results for each

schizotypy sub-domain relative to both the preexposed and non-preexposed cues are the same across both Experiments 1 and 2 thus indicating consistency in the observed findings (see Table 2.6).

These results from Experiment 2 suggest enhanced latent inhibition with UnEx and attenuated latent inhibition with CogDis are *specific* effects of schizotypy that are *not* related to anxiety. These findings appear to contrast with those observed by Braunstein-Bercovitz (2000), which suggest latent inhibition is attenuated in relation to the negative dimensions of schizotypy (including disorganisational factors) that are loaded with anxiety- a factor derived using factor analysis. Based on our preliminary correlations (see Table 2.5) we do also observe a relationship between CogDis and both trait and state anxiety, but this relationship does not account for the attenuated latent inhibition effect we observe. Here we observe an attenuation of latent inhibition that is specifically related to increased CogDis scores. We return to this issue in the general discussion (see section 2.4).

Table 2.6

Beta-coefficients from the hierarchical multiple regression analyses of schizotypy subtypes and anxiety subtypes (predictor variables), with reaction time to the preexposed and non-preexposed stimuli as dependent variables.

	Reaction-Time			
	PE	NPE	PE	NPE
	<i>Experiment 1</i>		<i>Experiment 2</i>	
Step 1				
State Anxiety	-.106	-.354*	.197	.045
Trait Anxiety	.172	.350*	-.125	-.183
R ²	.027	.155	.018	.023
Step 2				
State Anxiety	.008	-.277	.306	.077
Trait Anxiety	.270	.404*	-.099	-.272
Unusual Experiences	.299	.176	.433*	.266
Cognitive Disorganisation	-.303	-.138	-.404*	-.064
Introvertive Anhedonia	.027	.008	.031	.131
Impulsive Non-conformity	-.375*	-.293*	-.217	-.148
R ²	.209	.239	.168	.073

Note. * $p < .05$; Significant results are bolded.

2.3.2.3.3 *Summary of findings*

Consistent with some of the clinical literature (i.e., Rascle et al., 2001; Cohen et al., 2004; Gal et al., 2009), a positive association was found between the rate of learning to the familiar, but not the novel, stimulus and the UnEx dimension of schizotypy – implying abnormally persistent latent inhibition in these high schizotypy individuals. Once anxiety was controlled for, the previously observed positive association between UnEx and latent inhibition approached significance in Experiment 1 and was significant in Experiment 2. There was also a negative association between the rate of learning to the familiar, but not the novel, stimulus and the CogDis dimension of schizotypy – implying an attenuation of latent inhibition in these high schizotypy individuals. These findings lend support for an attentional difference in schizotypy (and by extension schizophrenia) that suggests attentional dysfunctions *are* specific effects of schizotypy, and *not* non-specific effects related to anxiety. This conclusion contradicts reports by Braunstein-Bercovitz (2000, 2001) - we return to a more detailed discussion of this, in the following section and in the overall general discussion (see Chapter 5).

2.4 General Discussion

Two experiments revealed slower learning of a stimulus-target association with a stimulus that had been rendered familiar through prior exposure than a stimulus that had not – latent inhibition. In both experiments learning about the preexposed, but not the non-preexposed stimulus was related to the UnEx dimension of the O-LIFE – revealing an enhancement of latent inhibition in individuals scoring higher on the positive dimension of schizotypy. Experiment 2, in particular, arranged preexposure in a manner that resulted in the subsequent retardation of learning to be explicable in terms of the effects of mere

exposure but not the confounding effects of conditioned inhibition or learned irrelevance. This is in contrast to other studies in the latent inhibition literature (e.g. Swerdlow et al., 1996; Braunstein-Bercovitz, 2000, 2001; De la Casa & Lubow, 2002; De la Casa & Lubow, 2001; Lubow & De la Casa, 2002; Evans et al., 2007; Schmidt-Hansen et al., 2009; Granger et al., 2012), which can be explained in terms of these alternative learning phenomena. Using the refined latent inhibition procedure described in Experiment 2, the previously observed enhanced latent inhibition effect in high schizotypal individuals remained significant once anxiety was controlled for. In addition, neither state nor trait anxiety were related to learning about the preexposed and non-preexposed cues, which also contrasts with previous research findings (see Braunstein-Bercovitz, 2000, 2001) that are confounded by alternative learning phenomena. The current findings suggest enhanced latent inhibition in individuals with high UnEx scores are specific effects of schizotypy that are *not* related to anxiety.

To the best of our knowledge, the current data constitute the first observation of enhanced latent inhibition in sub-clinical high schizotypy individuals. Three studies (Rasclé et al., 2001; Cohen et al., 2004; Gal et al., 2009) have reported enhanced latent inhibition in schizophrenia patients. The first study by Rasclé et al. used a between-participants design in which chronic schizophrenia patients in the preexposed group showed slower learning in comparison to controls, resulting in an enhancement of latent inhibition. The remaining studies, by Cohen et al. and Gal et al, like the current study, employed a within-subject manipulation of stimulus familiarity to demonstrate latent inhibition and were able to show an abnormality in learning that was specific to the preexposed stimuli. Both Cohen et al. and Gal et al. showed that latent inhibition enhancement was associated with the negative symptoms experienced by adolescents with schizophrenia. These results are what would be

predicted based on Weiner's (2003) model that suggests enhanced latent inhibition is associated with depleted levels of glutamate (see Javiit, 2007; Javiit, 2010), which may be related to the prevalence of negative symptoms. On the other side of the coin, is the reported relationship between the positive symptoms of schizophrenia and attenuated latent inhibition (e.g. Baruch et al., 1988a; Gray et al., 2002; Gray et al., 1992; Rascle et al.; Vaitl et al., 2002). This latter pattern of results is consistent with Gray et al.'s (1991) model for cognitive and neural associates of positive acute schizophrenia symptoms: that a loss of latent inhibition is due to over-activity in the mesolimbic dopaminergic system. At first glance, the results presented here, an enhancement of latent inhibition with the positive UnEx dimension of schizotypy, conflict with these analyses.

There has been considerable disagreement about the relationship between the attenuation of latent inhibition in schizophrenia and positive symptomatology: some authors have found a relationship between latent inhibition and positive symptoms (Baruch et al., 1988a; Gray et al., 2002; Gray et al., 1992; Vaitl et al., 2002), others have not (Rascle et al., 2001; Swerdlow et al., 1996; Williams et al., 1998; Cohen et al., 2004; Gal et al., 2009; for a review see: Schmidt-Hansen et al., 2012). In particular, Rascle et al. reported an attenuation of latent inhibition was associated with low levels of negative symptoms in patients with schizophrenia, rather than with levels of positive symptoms. Whereas Cohen et al. reported no difference in the magnitude of latent inhibition between high levels of positive symptoms in schizophrenia patients, and healthy controls. These findings, along with the current results, do not support the relationship between latent inhibition attenuation and positive symptomatology. On the other hand, the proposition by Weiner (2003) - that enhanced latent inhibition is related to negative symptoms, refers mainly to chronic patients. However, the findings reported by Cohen et al. and Gal et al. were able to show

an association between enhanced latent inhibition and clinical condition (chronic schizophrenia), but not with the level of negative symptoms per se. The discrepancy between these findings, and the results reported here are possibly due to the nature of the tasks employed by Cohen et al and Gal et al; as previously highlighted, these existing tasks confound learned irrelevance with latent inhibition itself. How the refined latent inhibition task reported here covaries with individuals with schizophrenia, is the focus of future research.

Only two other studies have attempted to bridge the gap between schizotypy and anxiety in relation to learned attentional functioning to assess whether the anxiety that characterises schizophrenia and schizotypy accounts for the difficulties individuals with schizophrenia and schizotypal individuals have in ignoring irrelevant information (see Braunstein-Bercovitz, 2000, 2001). In contrast to the results observed by Braunstein-Bercovitz, the current results suggest that neither component of anxiety, state nor trait, influence latent inhibition alone, or modulates the ability of schizotypy to modify learning about a preexposed stimulus. Although, as previously discussed, the limitations associated with existing latent inhibition paradigms question the validity of the findings reported by Braunstein-Bercovitz (2000, 2001). The latent inhibition task employed in their study included a secondary masking task (whether a pair of letters were the same or different) which accompanied the presentation of the preexposure stimulus (irregularly shaped polygons) during the preexposure phase of the experiment (see section 2.1.4). By presenting the preexposed cue in a manner that is irrelevant to the solution of the masking task raises the possibility of learned irrelevance being measured in this study instead of latent inhibition; an effect which has been shown to influence human learning (Le Pelley et al., 2010b). The current findings instead suggest that when a refined latent inhibition task is

used that removes the confound of such alternative learning effects, the variations observed in latent inhibition appear to be specific effects of schizotypy, as opposed to non-specific effects of anxiety. We return to a more detailed discussion of this finding in the general discussion (see Chapter 5).

One possible shortcoming of employing the multiple regression analysis that we have used in Experiments 1 and 2, see sections 2.2.2.2 and 2.3.2.2, respectively, is that the observed correlations between UnEx and RT to the non-preexposed stimulus could have been caused by any processes that impact upon the RTs to the preexposed stimulus, including those which also impact on RTs to the non-repexposed stimulus; that is to say, the common variance components affecting RTs to both preexposed and non-preexposed conditions. In order to evaluate this possibility, we pooled the data across Experiments 1 and 2 and conducted a hierarchical multiple regression in which RTs to the non-preexposed stimulus were added in the model in step 1 to act as a covariate, and examined the subsequent relationships between UnEx, CogDis, IntAn and ImpNon (as predictor variables), and RTs to the pre-exposed stimulus (as the dependent variable) in step 2. UnEx remained as a significant predictor of RT to the pre-exposed stimulus in step 2, $\beta = .230$, $t = 2.614$, $p = .010$, as did CogDis now, $\beta = -.175$, $t = 2.067$, $p = .041$. The remaining sub dimensions of the O-LIFE were not significant however, $\beta s < -.010$, $t s < 1.204$, $p s > .231$. It therefore appears that the relationship that we observed between schizotypy and RT in the current studies is specific to the pre-exposed stimulus. For the purposes of completeness, we also repeated the previous regression but this time with RTs to the pre-exposed stimulus entered as a covariate in step 1, and examined the subsequent relationships between UnEx, CogDis, IntAn and ImpNon (as predictor variables), and RTs to the non-preexposed

stimulus (as the dependent variable) in step 2. None of the beta coefficients were significant; $\beta s < .031$, $ts < 1.043$, $ps > .385$.

In order to ensure that participants were engaged with the task during the preexposure stage of Experiment 2, a secondary task was employed in which participants were required to repeat, out loud, each stimulus that was presented on the screen. We have argued that immersing preexposure within such a procedure precludes the current results from being explained in terms of learned irrelevance – as the preexposed stimulus was established as task relevant. This raises the question, then, of whether the current results are a demonstration of latent inhibition or, instead, a circumstance in which establishing a stimulus as task relevant in stage 1 might hinder learning in stage 2 when the same stimulus is established as an explicit cue for a target stimulus. On balance, this possibility seems unlikely, for a number of studies have established a stimulus as relevant to the solution of one task have then gone on to show that the same stimulus is subsequently better, not worse, at serving as a cue for a second stimulus in different task than a control stimulus (e.g. Le Pelley et al., 2010b; Bonardi, Graham, Hall & Mitchell, 2005), and performance in tasks of these sort has been shown to have a negative, not a positive, correlation with schizotypy (e.g Le Pelley et al., 2010a). To the best of our knowledge there is only one demonstration, in humans, of a stimulus being established as task relevant then going on to show a subsequent retardation in learning (Griffiths, Johnson & Mitchell, 2011). However, this negative transfer effect was demonstrated under circumstances in which the task type was the same between pre-exposure and learning (only the magnitude of the target outcome was changed). Furthermore, to date, there is no evidence of this effect having any relationship with schizotypy.

To summarise, the two experiments presented here show an effect of schizotypy (that is *not* underpinned by anxiety) on learning about a preexposed stimulus using a refined latent inhibition procedure. Both Experiments 1 and 2 show a comparable and novel effect of enhanced latent inhibition in individuals high in UnEx, that is not influenced by anxiety. We advocate the use of the task described in Experiment 2, as this task successfully minimised the contribution of both conditioned inhibition and learned irrelevance on the preexposure effect, and could be a useful tool for assessing attentional dysfunction in schizophrenia, as well as other clinical and sub-clinical populations. The aim of the following chapter is to explore the comparability of these findings using an alternative task that also measures an (arguably more direct) effect of attention on learning; learned irrelevance.

Chapter 3:

Learned irrelevance: The relationship with schizotypy and anxiety

3.1 Introduction

3.1.1 Latent inhibition: Overview & limitations

As discussed in the preceding chapters the association between latent inhibition, schizophrenia and schizotypy has a well-established framework that has been investigated both pharmacologically, neuropsychologically, and incorporated into a neuropsychological model for schizophrenia (see Gray et al., 1991; Gray, 1998; see Chapter 1 for a review). Latent inhibition has since become a prominent model of choice in studies investigating the attentional dysfunction view of schizophrenia; mostly because studies investigating latent inhibition have often assumed that latent inhibition provides a direct measure of attentional processing in human associative learning (Bender et al., 2001; Rascle et al., 2001). This approach explains latent inhibition as reflecting a reduction in attention to the stimulus during non-reinforced preexposure (Mackintosh, 1975; Pearce & Hall, 1980; Lubow, 1989; Kruschke, 2001).

However, the findings surrounding latent inhibition, schizophrenia and schizotypy have not been consistently demonstrated in the literature. Some authors suggest latent inhibition is either normal (Swerdlow et al., 1996; Williams et al., 1998; Rascle et al., 2001), or even enhanced (Rascle et al., 2001; Cohen et al., 2004; Gal et al., 2009, see also Chapter 2), with others suggesting that the anxiety components of schizophrenia are accountable for disruptions observed in latent inhibition (see Braunstein-Bercovitz, 2000). Adding further complexity to the interpretation of the latent inhibition-schizophrenia relationship however, is the fact that many existing latent inhibition paradigms either include an explicit masking

paradigm (e.g. Baruch et al., 1988a; Gray, Hemsley & Gray, 1992), or include the outcome from the second stage of the experiment in the first stage of the experiment – unpaired with the cue (e.g. Swerdlow et al., 1996; Cohen et al., 2004; Gal et al., 2009; Lubow & Kaplan, 1997; De la Casa & Lubow, 2001; Lubow & De la Casa, 2002). As a consequence, these paradigms encompass components of learned irrelevance, rather than true latent inhibition. Whether this is an important distinction; and whether learned irrelevance and latent inhibition are manifestations of similar cognitive processes, remains to be established and is a focus of the current chapter. The following sections provide a comparison of latent inhibition and learned irrelevance summarised from the existing literature, before moving on to explore the relationship between learned irrelevance, schizotypy and anxiety in more detail. How the results from Experiments 1 and 2, which observed an enhanced effect of latent inhibition in high schizotypy individuals using a refined latent inhibition task, corroborates with a learned irrelevance task that uses a similar task design is explored across Experiments 3 and 4.

3.1.2 Latent inhibition vs learned irrelevance

There are numerous accounts of latent inhibition that make no reference to attention (Weiner, 1990; Hall, 1991; Bouton, 1993; Gray & Snowden, 2005) which has raised concerns over the interpretation of attention dysfunction in schizophrenia and schizotypy (i.e., Le Pelley et al., 2010a). These accounts argue that attention is not reduced to the preexposed cue and instead regard latent inhibition as a deficit in the translation between learning and performance. For example, Bouton (1993; 1997) attributed latent inhibition to an effect of proactive interference in which memory for a cue-no target association is established during preexposure that subsequently interferes with memory for retrieval of the cue-target associations during conditioning. Bouton suggests that retrieval of these

opposing associations is determined by contextual stimuli, including time delay intervals between preexposure and conditioning (see McCloskey & Cohen, 1989). Miller and Matzel's (1988) comparator hypothesis instead argues that during preexposure an association is established between the cue and the context which subsequently strengthens an indirect activation of the target during conditioning (via cue-context and context-target links). This initial cue-context association reduces the strength of the direct target activation which thus hinders learning of the cue-target relationship. It has also been argued that latent inhibition can result from participants computing conditional probabilities, where the conditional probability of a particular outcome given the presence of a cue will be lower for a cue that has had extensive nonreinforced preexposure than for a cue that has not (see Le Pelley et al., 2010a,b; Lubow & Weiner, 2010).

Le Pelley et al (2010a) instead propose the use of the 'learned irrelevance' paradigm to investigate the attentional view of schizophrenia. The most commonly accepted view of learned irrelevance states that it reflects a reduction in learning rate to a cue as a result of prior experience of that cue's irrelevance with respect to an outcome. This retardation in learning is taken to reflect a decrease in attention to the cue (on the assumption that attention is determined by relevance; see Mackintosh, 1975; Kruschke, 2001) and there is experimental evidence (including eye-tracking data; Beesley et al., 2011) to support this view which was discussed in Chapter 1; for a review see Livesey, Harris & Harris (2009). In contrast to latent inhibition, learned irrelevance has been proposed a less ambiguous measure of the impact of attention on associative learning, as it is less amenable to non-attentional theories of its occurrence, such as rational inference (as discussed in the general introduction; see also Le Pelley et al., 2010a,b). Whether the true measure of latent inhibition used in Experiments 1 and 2 (Chapter 2) aligns itself with a comparable design

to measure learned irrelevance is explored in this chapter; this comparison will help to elucidate whether learned irrelevance and latent inhibition are manifestations of similar cognitive processes. A review of the experimental paradigms used to measure learned irrelevance are recapitulated in the following section (see also Chapter 1, section 1.5.2 for a review) before moving on to discuss existing research relative to patients with schizophrenia (Gal et al., 2005; Orosz et al., 2008; Young et al., 2005) and schizotypy individuals (Schmidt-Hansen et al., 2009; Le Pelley et al., 2010a).

3.1.3 Experimental paradigms of learned irrelevance

As described in Chapter 1, two different procedures have been employed to generate an effect of learned irrelevance. The first involves exposure to inconsistent/uncorrelated presentations of a cue and an outcome, or target (rather than the cue presented without a target in tasks of latent inhibition). Several authors have employed variations of the ‘letters sequence’ paradigm used in Experiments 1 and 2 to generate learned irrelevance in which participants are presented with a series of letters, presented one after the other in the centre of the screen and are instructed to press the spacebar as quickly as possible when a target letter, X, is presented. Amidst filler letters, the letter X is either preceded by either a novel letter (e.g., H) or by a letter that has been preexposed (e.g., S) in conjunction with uncorrelated presentations of X. Therefore, the preexposed letter (e.g., S) is presented without consequence on some trials, and precedes the occurrence of X on the others (e.g., Young et al., 2005; Gal et al., 2008; Orosz et al., 2009; Schmidt-Hansen et al., 2009; refer back to Table 1.1, Chapter 1). Here, a learned irrelevance effect is shown when participants are slower to respond to presentations of X when it was cued by the preexposed letter than the novel letter. However, the following section (3.1.4) discusses some limitations in the

task parameters chosen by these authors which questions whether learned irrelevance, or alternative learning phenomena are being measured.

The second paradigm used to generate learned irrelevance differs in that the cue(s) are always followed by a given outcome but the predictive validity of these cues (the degree to which they reliably predict an outcome) are established as either relevant cues (consistently predict an outcome) or irrelevant cues (inconsistently predict an outcome). A particularly clear demonstration of this learned irrelevance paradigm was described in detail in Chapter 1, section 1.5.2, but to reiterate, this task included eight compound cues (pictures of two different fruits) during stage 1, and two possible outcomes (i.e., nausea or diarrhoea; see Chapter 1, Table 1.2). One of the cues was established as being a relevant predictor of a reaction to the food, whereas the other cue in each compound was irrelevant, being followed by one outcome on 50% of the trials, and a second outcome on the remaining 50% of the trials. In the second stage of training, new compounds of foods are created which each consisted of one previously relevant cue and one previously irrelevant cue; these are paired with different reactions to stage 1, importantly, however, all cues were equally predictive of the novel outcomes in stage 2. In a final test stage participants rate the cues that were previously predictive of an outcome during stage 1 as significantly more predictive of an allergic reaction in stage 2, than compounds that were previously irrelevant as a predictor during stage 1. As the cues and compounds were all equally predictive of the outcomes during stage 2, the results at test are taken as evidence for the acquisition of differences in attention to these cues during the initial stage of training which biased subsequent learning in stage 2 (see: Le Pelley, Oakeshott, Wills & McLaren, 2005; Le Pelley et al., 2010b).

The following section provides an overview of existing studies which have utilised these two different learned irrelevance paradigms to examine their relationship with individuals with schizophrenia and high schizotypal individuals. The literature does not report on any studies that have examined the relationship between learned irrelevance and anxiety but the possible confound of learned irrelevance in some existing latent inhibition paradigms is discussed and it is parsimoniously suggested how these findings relate to anxiety (e.g., Braunstein-Bercovitz, 2000, 2001).

3.1.4 Learned irrelevance and schizophrenia

In comparison to the latent inhibition literature, there are only a limited number of studies that have explored the learned irrelevance effect as a way in which to study the cognitive disruptions observed in patients with schizophrenia (e.g., Young et al., 2005; Gal et al., 2005; Orosz et al., 2008; Morris et al., 2012). For example, using variations of the single-cue 'letter sequence' task to produce learned irrelevance, Young et al. (2005), Gal et al (2005) and Orosz et al. (2008) each showed attenuated learned irrelevance effect in patients with acute schizophrenia as acquisition of the cue-target associations for the preexposed irrelevant cue were just as fast as for the non-preexposed relevant cue, compared to healthy volunteer participants. Each of these studies also demonstrated some degree of learned irrelevance impairments with patients in a chronic phase of schizophrenia. Thus these findings are also in line with some of the latent inhibition-schizophrenia literature which has shown variations in latent inhibition with both acute and chronic schizophrenia patients (e.g., Baruch et al., 1988; Gray et al., 1992; Rascle et al., 2001; Gray et al., 2002; Vaitl et al., 2002). However, the task parameters utilised by Young et al. (2005), Gal et al (2005) and Orosz et al. (2008) to generate learned irrelevance can be criticised of being subject to measuring latent inhibition instead.

In the Young et al. (2005) study there were five 30 second presentation blocks which each used a different vowel as the preexposed irrelevant letter. Within each block one of the vowels and the target letter X were each presented 5 times in a random order, followed by a test phase in which the vowel was again presented 5 times but now consistently followed by the X- thus appearing to conform to a learned irrelevance procedure. However, the key issue here is that within each of the 5 blocks the stimuli were counterbalanced so that a vowel from the preceding block which would have previously presented without consequence (not followed by X), would then be used as the preexposed irrelevant letter (the to-be conditioned cue) in the next block. Thus this sequence reflects the influence of a preexposed cue that has in previous blocks been presented without consequence – thus conforming more to a latent inhibition rather than a learned irrelevance procedure. A similar limitation can be applied to the Gal et al and Orosz et al studies. In each of these studies, a single preexposure and test phase was included in which preexposure consisted of 5 cued presentations of the preexposed irrelevant cue followed by 5 presentations of the target, as well as 20 random presentations of the preexposed irrelevant cue. Therefore, there were more presentations of the preexposed irrelevant cue without consequence, than there were presentations of the preexposed irrelevant cue followed by the target. Thus, again presenting a paradigm that is potentially influenced by a preexposure effect akin to latent inhibition, rather than learned irrelevance. The confounding effect of latent inhibition in these paradigms thus permits interpretation of their effects in patients with schizophrenia to suffer from the same non-attentional accounts that *may* apply to the latent inhibition literature. The same limitation can be ascribed to the single cue learned irrelevance-schizotypy research, as Schmidt-Hansen et al. (2009) also presented the preexposed irrelevant cue without consequence on more occasions (16 presentations) than the preexposed irrelevant cue followed by the target (4 presentations), see section 1.5.2. Thus

their findings which suggest an attenuated effect of learned irrelevance in high schizotypy individuals is confounded by latent inhibition and possibly conditioned inhibition.

Instead, Morris et al. (2012) used a variant of the compound-cue learned irrelevance paradigm (described by Le Pelley and McLaren, 2003) to assess the co-variation of this task in patients with schizophrenia. This task instead equates latent inhibition by presenting all cues an equal number of times. The difference being, that the validity of these cues (the degree to which they reliably predict an outcome) is manipulated in order to establish them as either relevant cues (consistently predict an outcome on 100% of trials) or irrelevant cues (inconsistently predict an outcome – one cue followed by one outcome on 50% of trials, and a second outcome on the remaining 50% of the trials). Across two experiments, the results were consistent with models of attention which suggest that cues predictive of an outcome attract more attention than cues non-predictive of an outcome in healthy individuals (Kruschke, 2001; Le Pelley, 2004; Mackintosh, 1975). However, in individuals with schizophrenia, this normal attentional bias was impaired as patients were unable to distinguish between previously relevant and irrelevant cues and there was a positive correlation between learning about the previously irrelevant cue and high-positive symptom severity, measured using the PANSS assessment for schizophrenia (Kay, Fiszbein & Opler, 1987).

3.1.5. Learned irrelevance and schizotypy

Using a variant of the learned irrelevance compound-cue paradigm (Le Pelley & McLaren, 2003), Le Pelley et al (2010a) assessed whether an observed attentional bias towards previously established relevant cues is also reduced in high schizotypy individuals. Le Pelley et al. demonstrated an effect of learned irrelevance when participants were taken

as a whole; participants learnt more in stage 2 about previously relevant cues, relative to previously irrelevant cues. Importantly, however, individuals scoring highly on the unusual-experiences (UnEx) dimension of schizotypy showed an abolished effect of learned irrelevance, with high schizotypal individuals learning significantly more about the previously irrelevant cues, than previously relevant cues, compared to low schizotypal individuals. In an extension of these findings, Haselgrove et al. (2015) demonstrated that a schizotypy related difference in learning about previously relevant and irrelevant stimuli was accompanied by a corresponding difference in overt attention (measured using eye-tracking). These findings support the suggestion that schizotypy is associated with a deficit in the appropriate allocation of attention to stimuli based on their previously experienced relevance; with a specific inability to reduce attention to irrelevant information (see Lubow & Weiner, 2010). This finding is consistent with attentional interpretations of latent inhibition and consistent with *some* of the existing schizophrenia and schizotypy literature that proposes a reduction in latent inhibition is associated with positive symptomatology (e.g., Baruch et al., 1988a; Gray et al., 2002). It is important to bear in mind that these findings might be comparable because previous demonstrations of latent inhibition have been confounded by learned irrelevance.

3.1.6 Learned irrelevance and anxiety

Similar to schizophrenia, several lines of existing research suggest anxiety is associated with a reduced ability to ignore irrelevant stimuli/information, reflecting a general inability to maintain attentional focus (Eysenck et al., 1987; Mathews & MacLeod, 1985; Mogg et al., 1989). However, whilst there are studies that have looked at the relationship between ‘latent inhibition’ and anxiety, as discussed in preceding chapters (i.e., Braunstein-Bercovitz, 2000, 2001) there are no studies that have *directly* attempted to

investigate the relationship between anxiety and learned irrelevance. However, as discussed at length previously, the limitations encompassed within existing latent inhibition paradigms (i.e., the inclusion of an explicit masking task) makes it possible that these existing paradigms are actually generating an effect of learned irrelevance, instead of latent inhibition. In which case, these existing results might be interpreted as a reduction in learned irrelevance with high anxiety individuals. Therefore, how a task specifically designed to measure learned irrelevance, covaries with anxiety, as well as schizotypy, is explored in the following experiments.

3.1.7 Aims and research questions

Experiments 1 and 2 (Chapter 2) used a latent inhibition task which measured a pure effect of exposure. Thus, the finding that latent inhibition was enhanced in high schizotypy, but not high anxiety, individuals is difficult to explain in terms of an effect of learned irrelevance. Interestingly, the absence of a relationship between latent inhibition and anxiety seemingly contradicts previous research findings (i.e., Braunstein-Bercovitz, 2000, 2001) which claim that latent inhibition is reduced in high anxious individuals. However, as previously highlighted, the limitations encompassed within those existing latent inhibition designs makes it plausible that Braunstein-Bercovitz (2000, 2001) were actually observing an attenuation of learned irrelevance in individuals with high anxiety, and also high schizotypy. Thus, the first aim of Experiments 3 and 4 was to examine the relationship between learned irrelevance, anxiety and schizotypy. To ensure a direct measure of learned irrelevance, exposure to all cues were equated across these experiments; a description of these tasks are provided below.

The second aim of this chapter was to explore how the latent inhibition results from Experiments 1 and 2 corroborate with a learned irrelevance task that uses similar task parameters whilst removing the potential confound of latent inhibition. Thus allowing us to compare the effects of a pure effect of preexposure (latent inhibition; Experiments 1 and 2) with a direct measure of learned irrelevance (Experiments 3 and 4). If learned irrelevance is underpinned by the same unitary mechanism (i.e., attentional mechanism; e.g. Mackintosh, 1975) as latent inhibition, it would be expected that the effect of schizotypy, and anxiety, observed in the latent inhibition paradigm to be comparable in a learned irrelevance paradigm. Whether this assumption holds true, is assessed following the subsequent learned irrelevance experiments. Alternatively, if learned irrelevance and latent inhibition paradigms are not underpinned by the same psychological mechanism, then understanding this difference and exploring how it co-varies in the schizophrenia spectrum will allow further insights into the mechanisms of the disease.

One reason to question this prediction is based on the results provided by Le Pelley et al (2010a), which suggest that schizotypy individuals show a reduced (as opposed to the predicted enhanced) effect of learned irrelevance. Although, the learned irrelevance paradigm employed by Le Pelley et al (2010a) is a rather complex design that used compound cues, which is in contrast to the simple, single cue task that employed for the latent inhibition experiments in the preceding Chapter 2; making comparisons across these experiments difficult. What is desirable then is to generate a single-cue paradigm similar to that used for the latent inhibition design, to enable more direct comparisons, to examine the effects of latent inhibition and learned irrelevance on schizotypy and anxiety. To the best of current knowledge, an effect of learned irrelevance using single cue training has only been utilised in one other study (see Le Pelley et al., 2010b), which did not take measures

of schizotypy or anxiety into account; this omission is addressed in the following experiments.

3.2 Experiment 3

Experiment 3 presents a learned irrelevance task, the procedure of which is comparable to that employed in Experiments 1 and 2 to generate latent inhibition. In this learned irrelevance task, participants were presented with a series of letters, presented one after the other in the centre of the computer monitor, and required to make a response as quickly as possible when a target letter appeared. Immersed within this task was a relevant versus irrelevant target design employing four types of cues, U, O, C and D (see Table 3.1). During the training-stage, participants received trials in which two cues (U and O) were consistently followed by the same target (an X or a Y respectively), thus establishing U and O as task relevant cues. Two other cues (C and D) were each followed on half of the trials with one of the targets (X) and on the remaining trials with the other target (Y) thus establishing them as task irrelevant cues. In the second, test, stage all cues were established as reliable predictors of two novel targets (P and Q). If attention to U and O is greater than to C and D then learning about U and O, as measured by reaction times, should proceed more rapidly in stage 2. Table 3.1 provides a summary of the overall design of Experiment 3. Individual measures of schizotypy and anxiety were also taken to explore their relationship with learned irrelevance.

Table 3.1
Experimental Design of Experiment 3

Stage 1	Stage 2
U – X (10)	U – P (20)
O – Y (10)	O – Q (20)
C – X (5)	C – P (20)
C – Y (5)	D – Q (20)
D – X (5)	
D- Y (5)	
<i>Filler trials</i>	<i>Filler trials</i>
<i>J – (40)</i>	<i>J – (40)</i>
<i>T – (40)</i>	<i>T – (40)</i>
<i>L – (40)</i>	<i>L – (40)</i>

3.2.1 Method

3.2.1.1 Participants

Sixty-four healthy students from Nottingham University and members from the general public took part in exchange for course credit, or a £5 inconvenience allowance. There were 50 females and 14 males, age range 18-36. Given the comparable nature of the current procedure to Experiments 1 and 2, a comparable sample was also selected.

3.2.1.2 Apparatus

All experimental stimuli appeared on a standard desktop computer running Windows XP, and were programmed using Psychopy (Peirce, 2007; www.psychopy.org). Stimuli were white capital-letters in Arial-font (7mm(H) x 5mm(W)) presented for 1 second

each on a computer-screen (28cm(H) x 35cm(W)) with a grey background. All participants received acquisition training with four cues (D, U, O and C), two of which were consistently followed by an outcome (relevant-cues) and two of which were intermittently followed by an outcome (irrelevant-cues); counterbalanced across participants. During acquisition training, target letters were X and Y, the target letters during the test phase were changed to P and Q. Filler letters (L, T and J), were randomly interspersed throughout the acquisition and test phase. As in the previous experiments; a computerized version of the O-LIFE questionnaire (Mason et al., 1995) was administered to assess individual schizotypy levels, and a paper-version of the STICSA (Ree et al., 2008) was administered to assess individual anxiety levels.

3.2.1.3 Procedure

After reading an information sheet and signing a consent form, the following instructions were presented to participants on the computer monitor prior to commencement of the task:

“Thank you for participating in this experiment. In this experiment you will see individual letters appear in the centre of the screen. It is your job to press X when you see X appear and press Y when you see Y appear. At first you will only be able to respond to these letters when you see them, but as the experiment continues, you might be able to anticipate when they are going to be presented. If you think you know when either X or Y are going to appear, you can press them BEFORE they are presented. Please try to respond as quickly as you can when you think you know when X or Y are going to appear. If you have no questions, please have your fingers ready over the X and the Y, and then press the space bar to begin the experiment.”

During the acquisition stage, the relevant-cues and the irrelevant-cues (either U, O, C or D) were each presented 10 times in a random order, followed by a 1s presentation of the target-letters (either X or Y); the inter-stimulus interval was 1s. One relevant-cue was always followed by X (presented 10 times), and the other relevant-cue was always followed by Y (presented 10 times). Following each of the irrelevant-cues were 5 presentations each of X and Y. Filler letters were randomly interspersed within this sequence each presented a total of 40 times (but were not presented after U, O, C and D). Participants were required to press X when they saw the letter X on screen, and Y when they saw Y appear, or if they could predict when then these letters would appear as the next letter in the sequence. The test-phase followed on from acquisition, and prior to the test-phase participants were given a new set of instructions, stating the following:

“Now, we would like you to continue to watch a sequence of letters appearing on the screen. However, your task now is to press P when you see P appear and press Q when you see Q appear. Again, you will at first only be able to respond to these letters when you see them, but as the experiment continues, you might be able to anticipate when they are presented. If you think you know when either P or Q are going to appear, you can press them BEFORE they are presented. Please try to respond as quickly as you can when you think you know when P or Q are going to appear. Please have your fingers ready over the P and the Q, and then press the space bar to begin”.

During the test phase, the target letters were P and Q each presented 40 times and were consistently preceded by either the previously relevant or irrelevant cues. Thus during stage 2, the cues (D, U, O and C) were consistently predictive (100%) of the target (P or

Q). The previously relevant and irrelevant cues (D, U, O and C) were each presented 20 times. Each stimulus was presented for 1s separated by a 1s inter-stimulus interval. Filler letters were randomly interspersed within this sequence each presented a total of 40 times (but were not presented after U, O, C and D). Participants were required to press P when they saw the letter P on screen, and Q when they saw Q appear, or if they could predict when these letters would appear as the next letter in the sequence. The whole task lasted approximately 15 minutes. Following completion of the task, participants completed the O-LIFE (Mason et al., 1995) and the state and trait sub-scales of the STICSA (Ree et al., 2008) questionnaire.

3.2.1.4 Scoring

In keeping with Experiments 1 and 2, RT's were recorded for each participant. RT's could range from 0-3000ms, as the predictive and non-predictive letters were shown for 1000ms, followed by a 1000ms inter-stimulus interval, and the target-letter presented from 2000ms-3000ms. Therefore, if participants' RT was less than 2000ms they predicted the X or Y; whereas if their RT was between 2000 and 3000ms, they responded to the target. Mean RT for responses to the predictive and non-predictive cues were calculated for each participant.

3.2.2 Results and Discussion

The scores for each of the four schizotypy sub-dimensions and for both anxiety-subtypes are shown in Tables 3.2 and 3.3, respectively. Unpaired *t* test analyses were carried out to assess if the reported schizotypy and anxiety means differ from the population norms for each subscale. Comparable to Experiments 1 and 2 for schizotypy, the means for CogDis

and IntAn do not differ significantly from the normative values but the means for UnEx and ImpNon are both significantly lower than the normative values. As discussed in the preceding chapter, previous studies have also obtained mean schizotypy scores that are below Mason et al.'s (1995) normative values, and similar to those reported here (e.g. Evans et al., 2007; Granger et al., 2012; Sellen et al., 2005). Significant findings are highlighted in bold in Table 3.2. For the anxiety subtypes, means were not significantly different from the normative values.

Table 3.2

Summary information for O-LIFE scores; all values are mean(SD). Values in brackets represent the range of scores for each schizotypy-dimension. Population-norms taken from Mason et al., 1995, are also shown (mean (SD)).

	O-LIFE-dimension		Mean (SD)	
	UnEx	CogDis	IntAn	ImpNon
All Participants (N= 64)	7.6 (6.1)*	12.2 (6.1)	5.7 (4.0)	7.8 (3.4)*
Population Norm	9.7 (6.7)	11.6 (5.8)	6.1 (4.6)	9.7 (4.3)

Table 3.3

Summary information for STICSA-scores; all values are mean(SD). Values in brackets represent the range of scores for both anxiety-subtypes.

	Anxiety-Subtype			Mean(SD)		
	State	State Somatic	State Cognitive	Trait	Trait Somatic	Trait Cognitive
All Participant (N= 64)	33.5(9.2)	17.0(5.1)	16.3(5.8)	35.0(8.8)	16.0(4.2)	18.9(5.7)
Population Norm	30.9(9.3)	13.6(4.0)	17.21(5.4)	32.4(8.1)	13.5(3.3)	18.8(4.8)

3.2.2.1 Learned irrelevance

Figure 3.1 shows the mean reaction-times across 10 2-trial blocks of stage 1. There was a small trend for reaction-times to be faster to relevant-cues than irrelevant-cues. The relevant trials were compared with the irrelevant-trials using a 2 (cue: relevant-cue, irrelevant-cue) x 20 (trials 1-20) repeated measures ANOVA. For stage 1 this analysis revealed a significant main-effect of cue; $F(1,63) = 5.739$, $p = .020$, partial $\eta^2 = .083$, and a significant main-effect of trial number; $F(19,45) = 5.232$, $p < .001$, partial $\eta^2 = .688$, with no significant interaction; $F(< 1)$.

Figure 3.2 shows the mean reaction times across the 20 2-trial blocks of stage 2. Reaction times remained marginally faster to the cues that had previously been a consistent predictor of an outcome than those that had been an inconsistent/uncertain predictor. The relevant-trials were compared with the irrelevant-trials using a 2 (cue: relevant-cue, irrelevant-cue) x 20 (blocked trials 1-20) repeated measures ANOVA but this analysis revealed no significant main-effect of cue $F < 1$, a significant main-effect of trial number; $F(1, 19) = 10.827$, $p < .001$, partial $\eta^2 = .821$, with no significant interaction; $F < 1$.

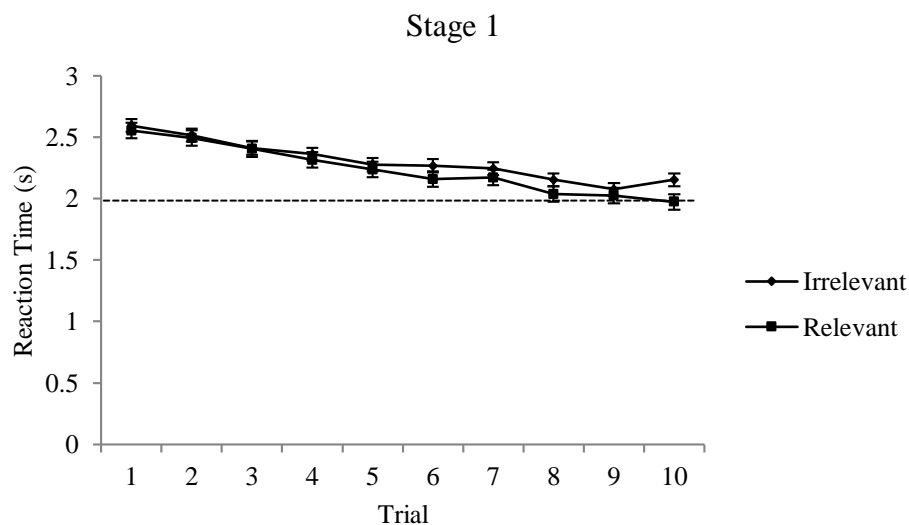


Figure 3.1. Reaction times to target cued by relevant and irrelevant cues for stage 1. Dotted line indicates the point of anticipation for predicting the target (< 2000ms). Error bars represent 1+/- within-subject standard error (see: Cousineau, 2005).

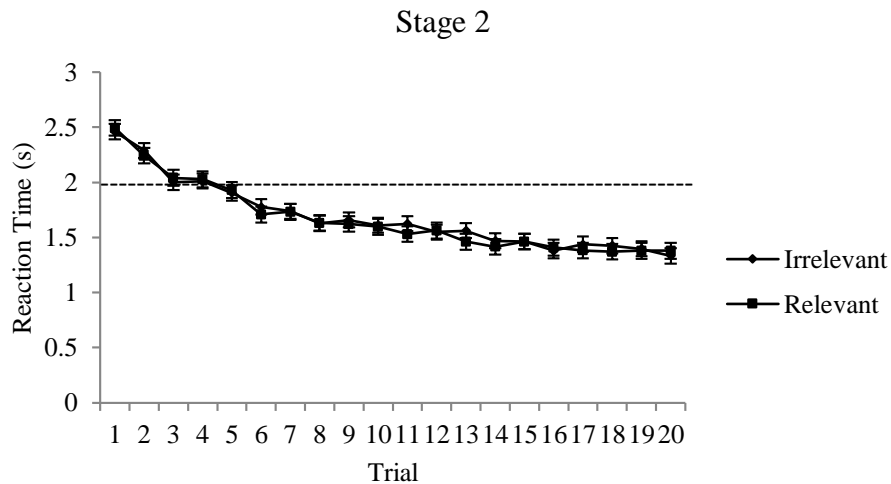


Figure 3.2. Reaction times to target cued by relevant and irrelevant cues for stage 2. Dotted line indicates the point of anticipation for predicting the target (< 2000ms). Error bars represent 1+/- within-subject standard error (see: Cousineau, 2005).

In contrast to the single-cue learned irrelevance task employed by Le Pelley et al (2010b), the current findings fail to observe a learned irrelevance effect. It is not entirely clear why the relevant and irrelevant cues were learnt about at comparable rates in stage two. Perhaps the amount of training in stage 1 was not sufficient to observe variations in stimulus attention which is supported by the fact that participants were not responding below <2000ms by the end of stage 1 and thus not predicting the occurrence of the target. Alternatively, it is possible that the data do contain an effect of relevance and irrelevance on cue associability, but this is being masked by a personality characteristic, which we go on to address next.

3.2.2.2 Learned irrelevance, Schizotypy and Anxiety

3.2.2.2.1 Preliminary analyses

Pearson product-moment correlation coefficients were computed between the learning scores (calculated for each participant by subtracting the difference in RT between relevant and irrelevant cues; higher learning scores indicate better learning about the predictive cues) for stage 1 and stage 2 data, and each of the four schizotypy dimensions and both state and trait anxiety subscales (Pearson's r , using all participants; see Table 3.4). Given the preliminary, exploratory nature of this analysis, no adjustments for multiple comparisons were made. For stage 1 learning score, correlations were significant for; CogDis; $r = -.269$, $p = .031$, ImpNon; $r = -.276$, $p = .027$ and stage 2 learning score; $r = .384$, $p = .002$. Stage 1 data thus provides evidence for a general deficit in learning the difference between relevant and irrelevant cues associated with high schizotypy (ImpNon and CogDis sub-dimensions), but not with state or trait anxiety. The significant correlation between stage 1 and stage 2 learning scores suggests a possible transfer of reaction time from stage 1 to stage 2; this possibility is further explored in the general discussion). During stage 2, the only correlation that was significant was that between the learning score and state anxiety; $r = -.313$, $p = .012$. The direction of this correlation indicates a reduced learned irrelevance effect in high state anxious individuals. Contrary to expectations, there were no correlations with schizotypy. The results of experiments 1 and 2, in direct contrast, showed an augmentation of a purported attentional effect (latent inhibition), in high schizotypy individuals. This omission also contrasts with existing research findings that support an attentional dysfunction in high schizotypy individuals (see Le Pelley et al., 2010a). We return to a more detailed discussion concerning this finding in the General Discussion (see section 3.4).

Table 3.4

Correlation matrices among study variables

	Stage 2						
	Learning Score	UnEx	CogDis	IntrovAn	ImpNon	State	Trait
Stage 1 Learning Score	.384**	-.160	-.269*	-.012	-.276*	-.203	-.157
Stage 2 Learning Score		-.113	-.074	.046	-.104	-.313*	-.147
UnEx			.515**	-.031	.194	.344**	.490**
CogDis				.135	.186	.359**	.622**
IntrovAn					-.219	.016	.155
ImpNon						.353**	.352**
State							.691**

Note. Values shown are Pearson's product-moment correlation coefficients.

** Correlation is significant at the 0.01 level.

* Correlation is significant at the 0.05 level.

Significant results are bolded.

3.2.2.3 *Learned irrelevance and Anxiety*

Based on the preliminary correlational analyses participants were assigned into a 'low' state anxiety group ($N = 31$) if their score lay on or below a mean state anxiety score of 31, and to a 'high' state anxiety group ($N = 33$) if their score lay above this mean. This split was determined by the population norm (mean = 30.9) reported for state anxiety in a healthy student population (see Ree et al., 2008), similar to the sample representative of the current studies. To investigate whether there was a significant effect of high or low state anxiety on attention to relevant and irrelevant cues, a 2 (state anxiety: high, low) \times 2 (cue: relevant-cue, irrelevant-cue) mixed ANOVA was carried out for stage 1 and stage 2.

Figure 3.3 shows the mean reaction-times to relevant and irrelevant-cues collapsed across all trials for the high and low anxiety groups in stage 1. It is evident from this figure that reaction-times were faster to the relevant-cues compared to the irrelevant-cues for all participants. This impression was confirmed for stage 1 as there was a significant main-effect of cue $F(1, 62) = 6.274, p = .015$, partial $\eta^2 = .092$, and no significant main-effect of state-anxiety ($F < 1$) and no significant stimulus \times state anxiety interaction $F(1, 62) = 3.678, p > .05$.

Figure 3.4 shows the mean-reaction times to the relevant and irrelevant-cues, for high and low anxiety groups in stage 2. Low-anxiety individuals showed faster reaction-times to cues that had previously been a consistent predictor of an outcome than those that had been an inconsistent/uncertain predictor. In contrast, high-anxiety individuals show, if anything, the reverse pattern of results. Analysis of stage 2 revealed no significant main-effect of cue ($F < 1$), and no significant main-effect of state-anxiety ($F < 1$) but a significant state-anxiety \times cue-interaction; $F(1, 62) = 5.644, p = .021$, partial $\eta^2 = .083$. Follow-up

simple effects analysis revealed a significant effect of cue for the low-anxiety group, $F(1, 62) = 5.057, p = .028$, partial $\eta^2 = .075$ but not for the high-anxiety group ($F < 1$), see Figure 3.4.

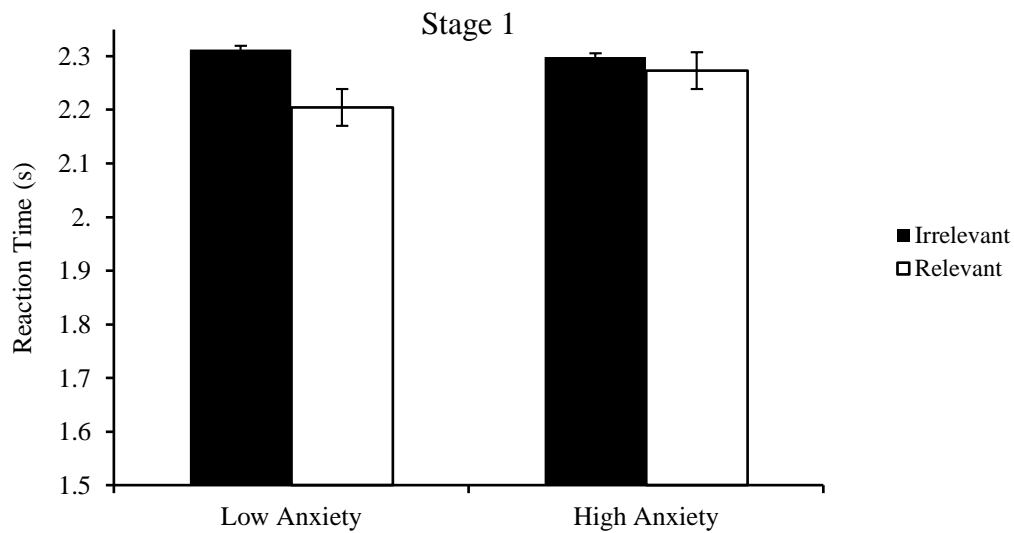


Figure 3.3. Reaction times to target cued by relevant and irrelevant cues for stage 1. Error bars represent 1+/- within-subject standard error (see: Cousineau, 2005).

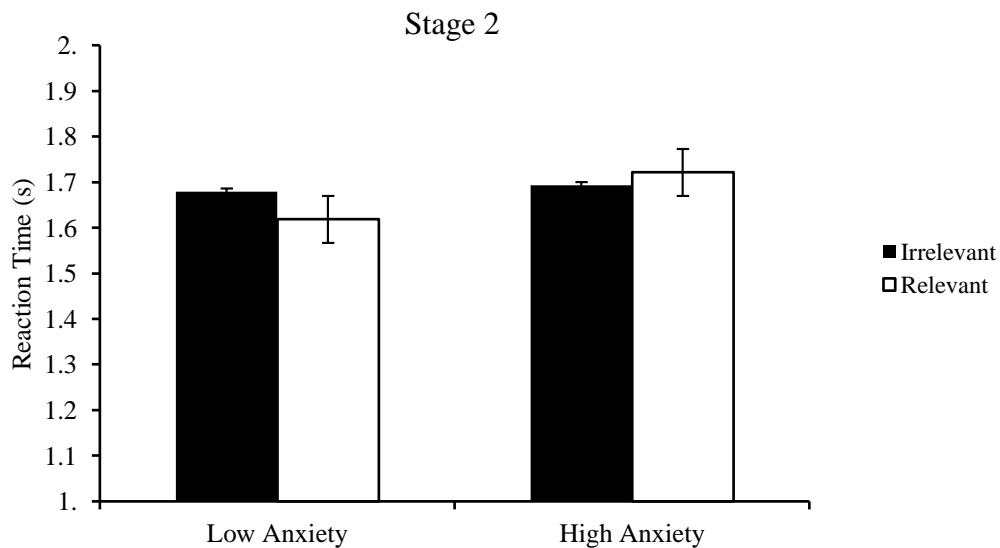


Figure 3.4. Reaction times to target cued by relevant and irrelevant-cues for stage 2. Error bars represent 1+/- within-subject standard error (see: Cousineau, 2005).

The results from the reaction-time data for stage 2 indicate that individuals low in state-anxiety are faster to learn the association between the relevant-cues and the target than between the irrelevant-cues and the target; suggesting that low state-anxiety individuals devote more attention to stimuli that are good predictors of subsequent events than to stimuli that are followed by irrelevant/uncertain events. In contrast, there appeared to be no influence of prior relevance on the cues on novel learning for individuals high in state-anxiety, as the learning rate between the relevant-cues and the irrelevant-cues with the target was not significant. Indicating that, high-anxious individuals show approximately equal learning about these cues in stage 2. However, Figure 3.4 illustrates, a reverse in the direction of results for high anxiety individuals (increased learning to irrelevant-cues), in comparison to low anxiety individuals. The significant state-anxiety x cue-interaction does not survive, however, if we include participants' schizotypy scores (for each subscale) and mean RT responses to the predictive and non-predictive cues during stage 1 (to control for any differences in learning rates between high and low state anxiety individuals) as covariates; $F(1, 55) = 2.133, p = .150$. This analysis suggests that the effect of anxiety on the current learned irrelevance task is influenced by both stage 1 learning and individuals schizotypy scores.

Based on our findings from Experiments 1 and 2 which indicated an enhanced effect of latent inhibition in high schizotypy individuals (but not in high anxiety individuals), we anticipated to find a comparable effect of schizotypy on learned irrelevance. More specifically we expected to observe a superior learned irrelevance effect with individuals high in unusual experiences, with no effect of anxiety on learned irrelevance. This follows from single-process models of learning and attention (e.g. Mackintosh, 1975) which employs the same (single) algorithm to vary attention to a cue- whether it be in a case of

simple pre-exposure (latent inhibition) or in a situation where the cue is more (or less) predictive of an outcome (learned irrelevance). That we can double-dissociate latent inhibition and learned irrelevance with schizotypy and anxiety suggests a single mechanism of attention is not sufficient (e.g., Le Pelley, 2004; Le Pelley, Haselgrove & Esber, 2012; Pearce & Mackintosh, 2010).

3.2.2.4 Summary of findings

The current findings fail to observe an overall effect of learned irrelevance when participants are taken as a whole. Additionally, and contrary to expectations, there was no effect of schizotypy on learned irrelevance but there was an effect of anxiety on learned irrelevance with high state anxiety individuals - who demonstrated insensitivity to the difference between relevant and irrelevant information, relative to low state anxiety individuals (who shown increased learning towards the previously predictive cue). This finding is consistent with the existing literature that high anxiety individuals are impaired in their ability to distribute attention appropriately between previously experienced relevant and irrelevant information; with an inappropriate allocation of attention to irrelevant stimuli. This finding has previously been indicated by existing studies of latent inhibition (Weiner, 1990; Weiner & Feldon, 1997; Braunstein-Bercovitz, 2000; 2001; 2002). However, before we attempt to draw any conclusions from the results obtained here, it is important to acknowledge the possibility that we might simply be observing a transfer of reaction time from stage 1 to stage 2; (i.e., low anxious individuals were learning faster about the predictive cues in stage 1, which might explain faster learning about these cues in stage 2 - based on the similarity between stage 1 and stage 2 tasks). This possibility is further supported by the fact that the cue x anxiety interaction did not remain significant once stage 1 learning was included as a covariate in the ANOVA model and based on the

significant correlation observed between stage 1 and stage 2 learning scores (see Table 3.4). The aim of Experiment 4 was to circumvent this problem by using an entirely different task and a different cover story between stage 1 and stage 2 of the task (see Le Pelley et al., 2010b). Using a novel task during stage 2 will ensure attention to all cues for novel outcomes, begin stage 2 at zero (no difference in the α of the cues); thus providing a paradigm that can assess a pure difference in associability. Therefore any subsequent difference in learning rate to these cues can be attributed to a difference in attention to cues previously experienced as being relevant or irrelevant. Using this task, the purpose of Experiment 4 was to assess the generality of Experiment 3.

3.3 Experiment 4

As per Experiment 3, this study used single-cue training design during stage 1 (Le Pelley et al., 2010b). Here, participants were asked to predict which of two background colours (pink or orange) a particular fictional company had used for their business cards. Letters A-Y in Table 3.5 represents different company names. Stage 1 comprised each of the 6 trial types shown in Table 3.5; each company appeared twice in each block. Throughout stage 1 companies A-D were consistently paired with the same colour; cues A and D were paired with pink and B and C with orange. Thus cues A-D are referred to as relevant cues. Whereas, companies X and Y were inconsistent predictors; in each block, each company was paired once with pink and once with orange. Thus cues X and Y are referred to as irrelevant cues. It is important to highlight that all cues were trained individually; on each trial, only one company name was presented. If participants thought the background colour for the business cards was 'orange' they had to press 'O' or if they thought the background colour was 'pink' they had to press 'P' on the computer keyboard.

During each stage 2 trial, participants were told that they had invested in a company and had to predict whether that company would make a profit or a loss. In Table 3.5, ‘A-profit’ for example, indicates that investment in a company would be profitable, whereas ‘B-loss’ indicates that investment would be loss-making. In stage 2 cues were either paired with all profits or all losses. The point of interest here is how quickly participants are able to learn about profitability during stage 2. The objective statistical relationship between the cues and profitability was identical for companies that had been predictive of business card colours during stage 1, and for those that had been non-predictive. Therefore, companies A and C (relevant-cues) were paired with the same amount of profitability as was company X (an irrelevant-cue), and companies’ B and D (relevant-cues) were paired with the same amount of losses as was company Y (an irrelevant-cue). Thus, any subsequent differences in learning rate about these cues can be attributed from differences in their learned relevance/irrelevance regarding stage 1 colours. On the basis of Le Pelley et al.’s (2010b) findings, more rapid learning is expected about relevant-cues, than irrelevant-cues. Learning was assessed using participant’s responses during stage 2 of the task, i.e., if the participant thought the company would make a loss they had to rate the company low on a 21-point scale, and if they thought the company would make a profit, they had to rate the company high on the 21-point scale. Here there is a change in the dependent variable from stage 1 (keyboard response to business card colour) to stage 2 (mouse click to rate the company profitability on the 21-point scale), so unlike Experiment 3 the results will be more difficult to interpret in terms of a straightforward transfer of responding.

Table 3.5
Experimental Design of Experiment 4

Stage 1	Stage 2
A – Pink (12)	A – Profit (10)
B – Orange (12)	B – Loss (10)
C – Orange (12)	C – Profit (10)
D – Pink (12)	D – Loss (10)
X – Pink/Orange (12)	X – Profit (10)
Y – Pink/Orange (12)	Y – Loss (10)

Note. The number in parentheses indicates the number of each repetition of each trial type.

3.3.1 Method

3.3.1.1 Participants

Eighty-eight healthy university of Nottingham students and members of the general public took part in exchange for course credit, or a £5 inconvenience allowance. There were 68 females and 20 males, age range 18-54. A sample size of 88 was based on previous studies using a similar learned irrelevance task in a similar population of participants (see Haselgrove et al., 2015).

3.3.1.2 Apparatus

All experimental stimuli appeared on a standard desktop computer running Windows XP, and were programmed using Psychopy (Peirce, 2007; www.psychopy.org). The six company names were Stonedge, Hedgend, Woodrow, Cornfield, Lakeside and Maylawn. These names were independently assigned to the letters A-Y in the experimental design, and fully counterbalanced, for each participant. As per previous experiments, the O-LIFE questionnaire (Mason et al., 1995) was administered to assess individual

schizotypy levels, and a paper-version of the STICSA (Ree et al., 2008) was administered to assess individual anxiety levels.

3.3.1.3 Procedure

After reading an information sheet and signing a consent form, the following instructions were presented to participants on the computer monitor prior to commencement of the task:

“Thank you for participating in this experiment. Six companies have purchased several batches of business cards. It is your task to decide which colour the company has used for the background of their cards. On each trial, two different coloured business cards (PINK and ORANGE) will appear on the screen, each bearing the company name. At first you will have to guess the colour, but after each trial you will be told which colour that company used for their business cards, and you can use this feedback to guide your subsequent decisions. If you think the background colour for that particular batch is ORANGE, press 'O' or if you think the background colour is PINK press 'P' on the computer keyboard. To continue press the 'SPACE' bar on your keyboard.”

The task was self-timed and on each trial, the message “which colour did [company name] use for this batch of business cards?” appeared above images of two cards, each stating the name of the company listed at the top of the screen and differing only in their background colour (one pink, the other orange), see Figure 3.5(a). The colour of the business cards and their position on the screen (presented on either the left or the right) was determined randomly for each participant, but remained consistent across stage 1.

Participants made their decision by pressing 'P' on the computer keyboard if they thought the background colour was 'Pink' and "O" if they thought the colour was 'Orange'. Stage 1 comprised 6 training blocks, with each of the 6 trial types shown in Table 3.5, occurring twice per block in a random order. Stage 2 followed on from stage 1, and prior to stage 2, participants were given a new set of instructions, stating the following:

"For the next part of the task you will be told that you have invested in a company and it is your task to predict whether that company will make a profit or a loss. If you think that the company will make a loss then rate that company low on the 21 point scale. If you think that company will make a profit then rate that company high on the scale. If you think that company is equally likely to make a profit or a loss then rate that company in the middle of the scale. Please try to be as accurate as you can with your ratings and use the feedback you get to guide your ratings. Please press the 'SPACE' bar to begin the next part of the task."

On each trial the message at the top of the screen read "You have invested in [company name]. What do you think will happen?" Below the message was a horizontal scale with 21 marked gradations. The low anchor point of the scale was labeled "Sure to make a loss" and the upper anchor point of the scale was labeled "Sure to make a profit", see Figure 3.6(a). After participants made their selection on the rating scale, and confirmed their choice by clicking the box containing the number underneath the rating scale, immediate feedback was provided. If the trial was a *profit* trial, the message "You made a profit" appeared in green; if it was a *loss* trial, the message "You made a loss" appeared in red, see Figure 3.6(b). During stage 2, each of the 6 trial types shown in Table 3.5, appeared once per block in a random order, with 10 blocks in total. Following completion of the task,

participants completed the O-LIFE (Mason et al., 1995) and the state and trait sub-scales of the STICSA (Ree et al., 2008) questionnaire.

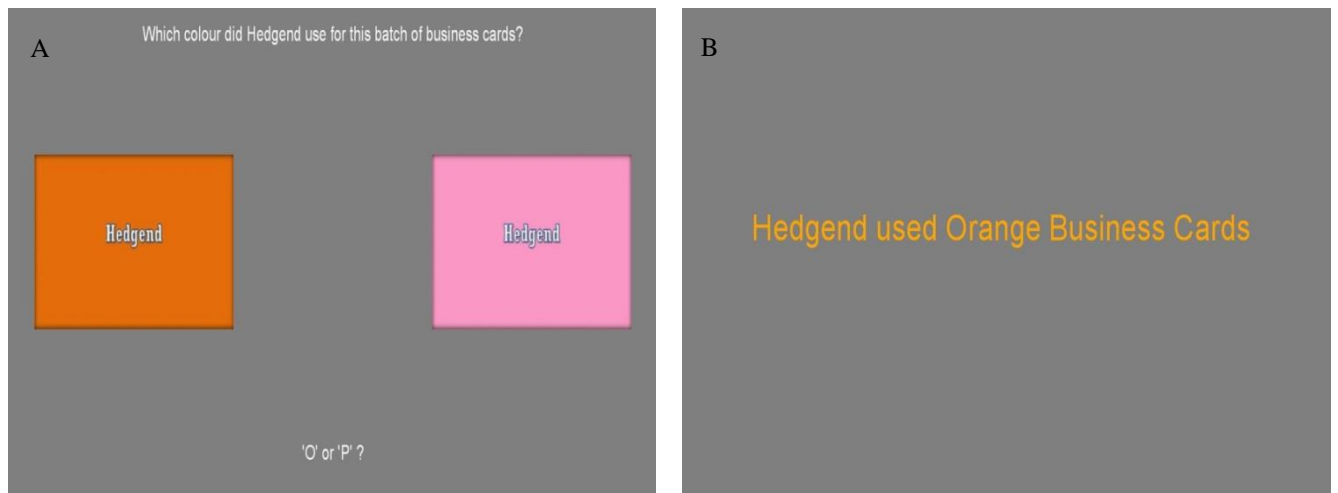


Figure 3.5(a) Screenshot example of a typical trial from stage 1; (b) Screenshot example of stage 1 trial feedback

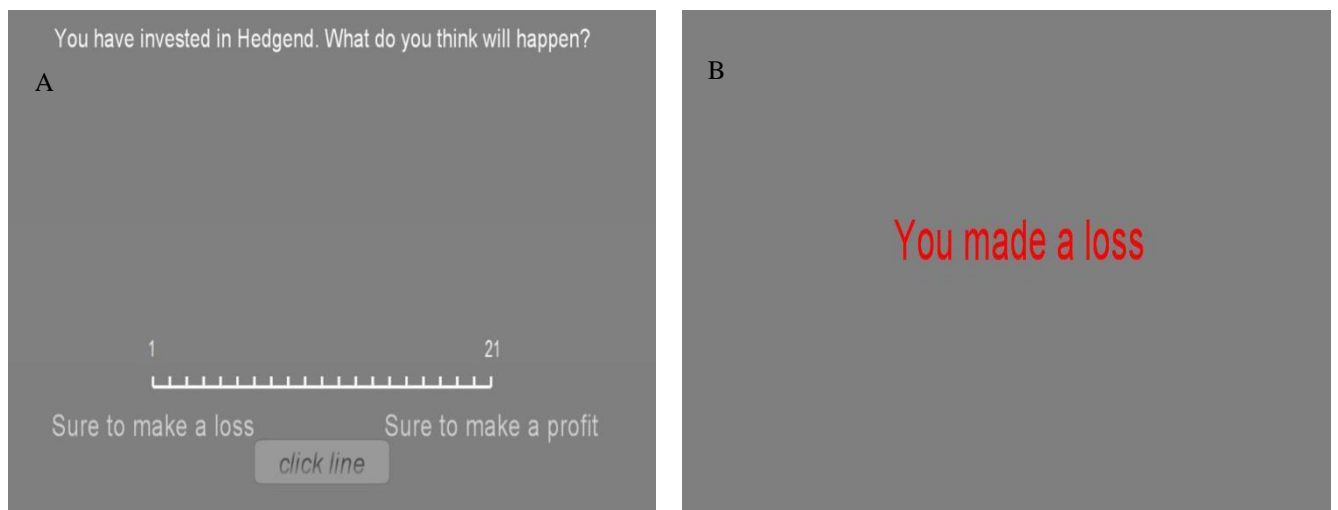


Figure 3.6(a) Screenshot example of a typical trial from stage 2; (b) Screenshot example of stage 2 trial feedback

3.3.1.4 Scoring

For stage 1 the mean percentages of correct responses were averaged separately for relevant and irrelevant cues. For stage 2, mean discrimination scores were calculated separately for relevant and irrelevant cues. These scores were calculated by subtracting the

mean rating for loss making companies from that received by profit making companies, to remove valence as a factor. An overall discrimination score was then calculated for each participant by subtracting relevant-cues from irrelevant-cues.

3.3.2 Results and Discussion

The scores derived for the four schizotypy subtypes and the two anxiety subtypes are shown in Tables 3.6 and 3.7, respectively. Unpaired *t* test analyses were carried out to assess if the reported schizotypy and anxiety means differ from the population norms for each subscale. Comparable to previous experiments for schizotypy (Experiments 1, 2 & 3), the means for CogDis and IntAn do not differ significantly from the normative values but the means for UnEx and ImpNon are both significantly lower than the normative values. As discussed previously, existing studies have also obtained mean schizotypy scores that are below Mason et al.'s (1995) normative values, and similar to those reported here (e.g. Evans et al., 2007; Granger et al., 2012; Sellen et al., 2005). Significant findings are highlighted in bold in Table 3.6. For the anxiety subtypes, means were not significantly different from the normative values.

Table 3.6

Summary information for O-LIFE scores; all values are mean(SD). Values in brackets represent the range of scores for each schizotypy-dimension. Population-norms taken from Mason et al., 1995, are also shown (mean (SD)).

	O-LIFE-dimension	Mean(SD)		[Range]
	UnEx	CogDis	IntAn	ImpNon
All Participants (N= 88)	6.5 (5.9)*	11.8 (6.1)	5.2 (4.3)	7.7 (3.8)*
Population-Norm	9.7 (6.7)	11.6 (5.8)	6.1 (4.6)	9.7 (4.3)

Table 3.7

Summary information for STICSA-scores; all values are mean(SD). Values in brackets represent the range of scores for both anxiety-subtypes.

	Anxiety-Subtype			Mean(SD)		
	State	State Somatic	State Cognitive	Trait	Trait Somatic	Trait Cognitive
All Participants (N= 88)	32.7(8.7)	15.5(3.8)	17.1(6.1)	35.6(9.1)	15.6(3.5)	20.1(6.4)
Population Norm	30.9(9.3)	13.6(4.0)	17.21(5.4)	32.4(8.1)	13.5(3.3)	18.8(4.8)

3.3.2.1 Learned irrelevance

Figure 3.7 shows the mean percentages of correct-responses per block across the 6 blocks of stage 1. As expected, accuracy increased rapidly for the relevant cues as the participants learnt the correct responses, in comparison to the irrelevant cues, which remained slightly below the chance level of 50% throughout stage 1 (as the irrelevant cues were only 50% predictive of an outcome). One-sample t tests using the mean percentages correct data for the irrelevant and cues collapsed across the 6 blocks of stage 1, revealed that participants did score significantly below chance (50%) for the irrelevant cues; $t(87) = -7.010$, $p < .001$, and significantly above chance for the relevant cues; $t(87) = 14.815$, $p < .001$. Subsequently, the relevant trials were compared with the irrelevant trials using a 2 (cue: relevant cue, irrelevant cue) x 6 (block 1-6) repeated measures ANOVA. For stage 1 this analysis revealed a significant main effect of cue; $F(1,87) = 299.265$, $p < .001$, partial $\eta^2 = .775$, a significant main effect of trial number; $F(5, 435) = 8.217$, $p < .001$, partial $\eta^2 = .086$, and a significant interaction; $F(5, 435) = 4.341$, $p < .01$, partial $\eta^2 = .048$. Follow-up simple effects analysis revealed a significant effect of cue across all 6 trial blocks- trial 1; Smallest $F(1, 87) = 21.529$, $p < .001$, partial $\eta^2 = .196$.

Figure 3.8 shows the mean discrimination scores across stage 2; the mean discrimination scores for previously relevant-cues appear higher than previously irrelevant-cues during the first few blocks, with equal discrimination scores by the end of stage 2. The relevant trials were compared with the irrelevant trials using a 2 (cue: relevant cue, irrelevant cue) x 10 (blocked trials 1-10) repeated measures ANOVA but this analysis revealed no significant main effect of cue; $F(1,87) = 2.034$, $p = .157$, a significant main-effect of trial number; $F(9,783) = 37.190$, $p < .001$, partial $\eta^2 = .299$, with a trend towards a significant interaction $F(9,783) = 1.698$, $p = .086$.

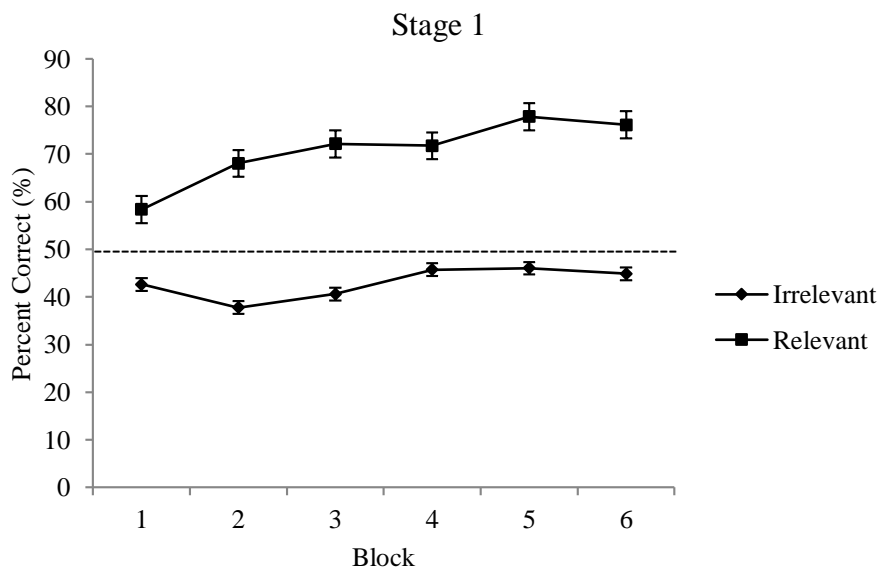


Figure 3.7. Mean percentages of correct responses across the six blocks of stage 1, averaged separately for relevant and irrelevant cues. Dotted line shows theoretical level of chance responding (50%). Error bars represent 1+/- within-subject standard error (see: Cousineau, 2005).

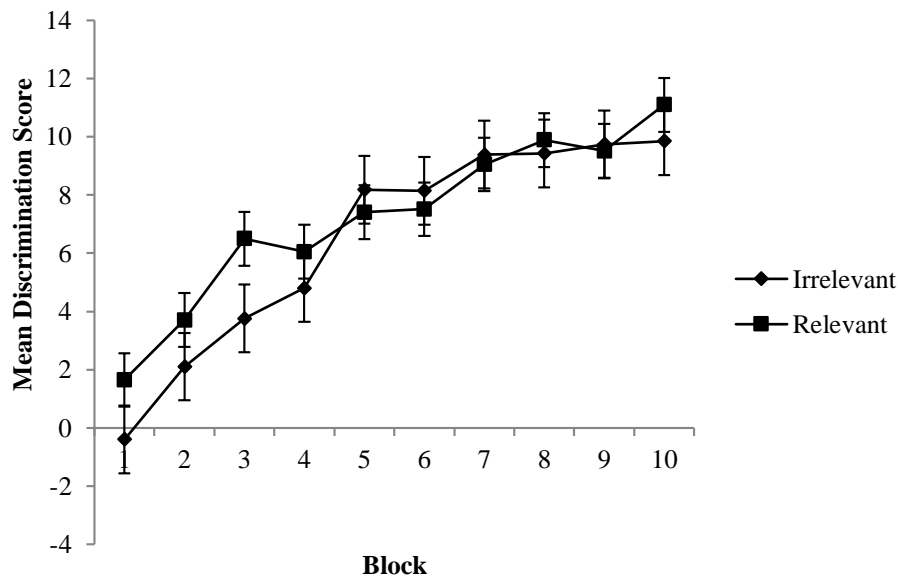


Figure 3.8. Mean discrimination scores for stage 2, averaged separately for relevant and irrelevant cues. Error bars represent 1+/- within-subject standard error (see: Cousineau, 2005).

Whilst the overall cue x trial interaction did not reach the conventional threshold for significance the current findings do show suggest an effect of learned irrelevance which is present early on in stage 2 (between blocks 1-5) with the mean discrimination score for previously relevant-cues appearing higher than previously irrelevant-cues. This impression was confirmed across the first five trials using a 2 (cue: relevant cue, irrelevant cue) x 5 (blocked trials 1-5) repeated measures ANOVA which revealed a significant main effect of cue; $F(1,87) = 4.837$, $p = .031$, partial $\eta^2 = .053$, a significant main effect of trial number; $F(4,348) = 26.321$, $p < .001$, partial $\eta^2 = .473$, with no significant interaction $F(4,348) = 2.036$, $p = .089$. This finding lends support to the study by Le Pelley et al (2010b). However, it is possible that the data across all 10 trials do contain an effect of predictiveness and uncertainty on cue associability, but this is being masked by a personality characteristic. It is arguable that participants in the study carried out by Le Pelley et al. were less varied in their personality traits, thus allowing an overall effect of learned irrelevance to be demonstrated.

3.3.2.2 Learned irrelevance, Schizotypy and Anxiety

3.3.2.2.1 Preliminary Analyses

Pearson product-moment correlation coefficients were computed between: the mean percentages of correct responses for relevant and irrelevant cues for stage 1; the mean discrimination scores for relevant and irrelevant cues for stage 2; the overall difference scores (relevant cues minus irrelevant cues) for both stage 1 and stage 2; and each of the four schizotypy dimensions and both state and trait anxiety subscales (Pearson's r , using all participants; see Tables 3.8 & 3.9). Given the preliminary, exploratory nature of this analysis, no adjustments for multiple comparisons were made. For stage 1, there were no significant correlations for any of the personality variables with either overall discrimination score, relevant or irrelevant cues. For stage 2, correlations were only significant for the relevant-cue and state anxiety; $r = -.229$, $p = .032$. In keeping with experiment 3, there were no correlations with schizotypy. We return to a more detailed discussion concerning this finding in the General Discussion (section 3.4).

Table 3.8

Correlation matrices among study variables for stage 1

	Stage 1 Relevant Cue	Stage 1 Irrelevant Cue	State	Trait	Unex	Cogdis	Introvan	Impnon
Discrimination Score	.784**	-.506**	-.065	-.111	-.090	.009	.110	-.074
Stage 1 Relevant cue		.139	-.094	-.099	-.071	-.038	.013	-.038
Stage 1 Irrelevant cue			-.027	.039	.046	-.067	-.157	.065
State				.757**	.524**	.672**	.280**	.301**
Trait					.584**	.811**	.395**	.273**
UnEx						.653**	.531**	.293**
CogDis							.540**	.304**
Introvan								.239*

Note. Values shown are Pearson's product-moment correlation coefficients.

** Correlation is significant at the 0.01 level.

* Correlation is significant at the 0.05 level.

Significant results are bolded.

Table 3.9

Correlation matrices among study variables for stage 2

	Stage 2 Relvant Cue	Stage 2 Irrelevant Cue	State	Trait	Unex	Cogdis	Introvan	Impnon
Discrimination Score	.380**	-.500**	-.048	-.065	.049	.000	-.050	.114
Stage 1 Relevant cue		.612**	-.229*	-.146	-.157	-.116	.002	.021
Stage 1 Irrelevant cue			-.173	-.081	-.189	-.109	.044	-.077
State				.757**	.524**	.672**	.280**	.301**
Trait					.584**	.811**	.395**	.273**
UnEx						.653**	.531**	.293**
CogDis							.540**	.304**
Introvan								.239*

Note. Values shown are Pearson's product-moment correlation coefficients.

** Correlation is significant at the 0.01 level.

* Correlation is significant at the 0.05 level.

Significant results are bolded.

3.3.2.3 *Learned irrelevance and Anxiety*

Based on the preliminary correlational analyses, participants were assigned into a ‘low’ state anxiety group ($N = 46$) if their score lay on or below a mean state anxiety score of 31, and to a ‘high’ state anxiety group ($N = 42$) if their score lay above this mean. This split was determined by the population norm (mean = 30.9) reported for state anxiety in a healthy student population (see Ree et al., 2008). To investigate whether there was a significant effect of high or low state anxiety on attention to relevant and irrelevant cues, a 2 (state anxiety: high, low) \times 2 (cue: relevant cue, irrelevant cue) mixed ANOVA was carried out for stages 1 and 2.

Figure 3.9 shows the mean percentages of correct responses to the relevant and irrelevant cues collapsed across the six blocks for high and low anxiety groups in stage 1. It is evident from this figure that the percentage of correct responses was higher to the relevant-cues compared to the irrelevant cues for all participants. This impression was confirmed for stage 1 as there was a significant main effect of Cue $F(1, 86) = 296.919, p < .001$, partial $\eta^2 = .775$, no significant main-effect of State anxiety ($F < 1$) and no significant Stimulus \times State anxiety interaction ($F < 1$).

Figure 3.10 shows the mean discrimination scores for the relevant and irrelevant-cues collapsed across all trials of stage 2, for the high and low anxiety groups. Low anxious individuals show increased learning to previously relevant-cues, than to previously irrelevant-cues. In contrast, high-anxious individuals show, if anything, the reverse pattern of results. Analysis of stage 2 revealed no significant main effect of Cue $F(1, 86) = 1.395, p = .241$, and no significant main effect of State anxiety $F(1, 86) = 2.787, p = .099$ but a significant State anxiety \times Cue interaction; $F(1, 86) = 4.183, p = .044$, partial $\eta^2 = .046$. Given the significant state-anxiety \times cue interaction, follow-up simple effects analysis revealed a significant effect

of cue for the low anxiety group, $F(1, 86) = 5.452$, $p = .022$, partial $\eta^2 = .060$, but not for the high anxiety group ($F < 1$), see Figure 3.10. Additionally, the significant state-anxiety x cue- interaction survives if we include participants schizotypy scores (for each subscale) and mean accuracy responses to the predictive and non-predictive cues during stage 1 (to control for any differences in learning rates between high and low state anxiety individuals) as covariates; $F(1, 79) = 7.052$, $p = .010$. This analysis suggests that the effect of anxiety on the current learned irrelevance task is not influenced by stage 1 learning and the effect is specific to the state anxiety subscale.

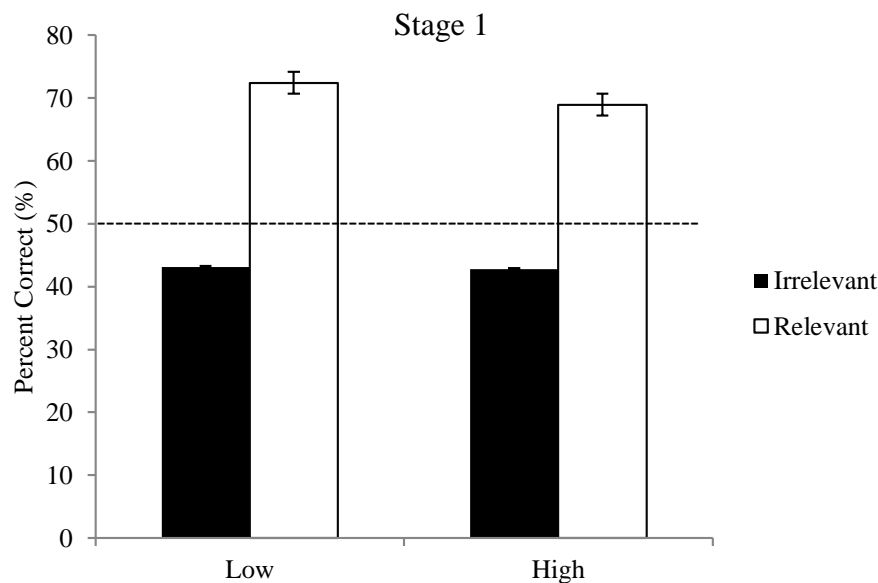


Figure 3.9. Percentage of correct responses to target cued by relevant and irrelevant cues for stage 1. Dotted line shows theoretical levels of chance responding (50%). Error bars represent 1 \pm within-subject standard error (see: Cousineau, 2005).

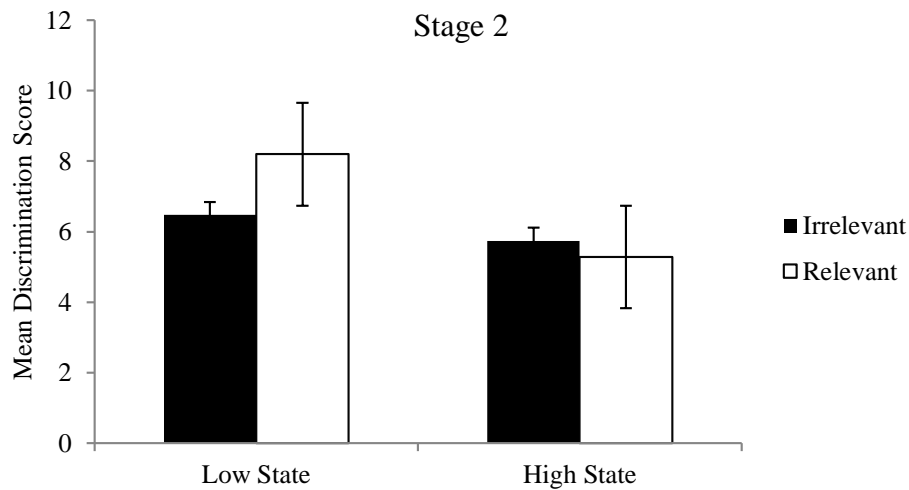


Figure3.10. Mean discrimination scores for stage 2, averaged separately for relevant and irrelevant cues for the low and high anxious groups. Error bars represent 1+/- within-subject standard error (see: Cousineau, 2005).

When participants are taken as a whole, the current results suggest a trend towards an effect of learned irrelevance early on in stage 2 (between trials 1-5). This finding is comparable to that observed by Le Pelley et al. (2010a) who also observed better discrimination for relevant cues than for irrelevant cues during trial blocks 1-5. Crucially, and in keeping with Experiment 3, the results from stage 2 indicate that individuals low in state anxiety are faster to learn the association between the previously relevant cues and the target than between the previously irrelevant cues and the target; suggesting that low state-anxiety individuals devote more attention to stimuli that are good predictors of subsequent events than to stimuli that are followed by uncertain events. In contrast, there appeared to be no influence of prior relevance of the cues on novel learning for individuals high in state-anxiety, as the learning rate between the relevant cues and the irrelevant cues with the target was not significant. Indicating that, high anxious individuals show approximately equal learning about these cues in stage 2. The results from Experiment 4 thus indicate a replication of the direction of results presented in Experiment 3, but extend their generality; as the current Experiment 4 employed a task design

that directly examined a difference in associability, and therefore the amount of attention paid to the predictive and uncertain cues.

3.3.2.4 Summary of findings

From these results it appears we are observing insensitivity to the difference between relevant and irrelevant information in high state anxiety individuals. This finding is however in contrast to our predictions; based on our findings from Experiments 1 and 2. Across all 4 experiments (presented in the current and preceding chapter) it appears that we are observing a double dissociation; an effect of schizotypy (but not anxiety) that co-varies with latent inhibition, and an effect of anxiety (but not schizotypy) that co-varies with learned irrelevance. This possibility is explored in more detail, in the general discussion.

3.4 General Discussion

Two experiments revealed that learning about a cue that was previously predictive of an outcome was higher than the cue that was previously irrelevant, but only in low state-anxious participants. Therefore, low anxious individuals, successfully demonstrated a significant learned irrelevance effect, whereas high anxious individuals showed a disruption of this effect. In contrast to predictions, there was no relationship between schizotypy and learned irrelevance; suggesting variations observed in learned irrelevance are specific to state anxiety. This suggestion is supported, particularly by the findings reported for Experiment 4, which show that when variations in the schizotypy subscales were statistically controlled for, the critical interaction between state anxiety x cue persisted.

Based on the results from Experiments 1 and 2, these findings contradict our predictions; we expected no effect of anxiety on learned irrelevance, as we saw no effect of

anxiety on latent inhibition. We did however expect to observe an enhanced effect of learned irrelevance in high schizotypy individuals, comparable to the enhanced effect of latent inhibition observed across Experiments 1 and 2. This prediction is based on the assumption of single-process models of attention and learning such as Mackintosh (1975) and Pearce and Hall (1980) which assume that the mechanism underlying an effect of latent inhibition (in this case, attentional) is the same mechanism underlying an effect of learned irrelevance.

These opposing findings suggest that learned irrelevance and latent inhibition may not underpinned by the same unitary, attentional mechanism as predicted by attentional theories of associative learning (i.e., Mackintosh, 1975). A more detailed discussion of this double dissociation is discussed in the overall General Discussion (see Chapter 5). Whilst the difference in learning rate between the previously relevant cues and irrelevant cues are not significant for high anxiety individuals, in either Experiment 3 or 4; Figures 3.4 and 3.10 illustrate a reverse in the direction of the results in comparison to low anxiety individuals. This tentative direction of results suggests that high-anxiety is associated with faster learning to previously irrelevant cues, and falls in line with the Pearce and Hall (1980) theory of attention on learning. Whereas the finding that low anxiety is associated with significantly faster learning to the previously relevant/predictive cues falls in line with the predictions of the Mackintosh (1975) model. These results may suggest a dual-process model of attention (e.g.: Le Pelley, 2004) on anxiety, in which the relative weightings of Pearce-Hall-like and Mackintosh-like effects are determined by state anxiety.

The results of Experiments 3 and 4 are however comparable, suggesting reduced learned irrelevance is related to high state (but not trait) anxiety scores – suggesting an impaired ability to distribute attention appropriately between cues on the basis of their previously

experienced relevance, is specific to state anxiety using single cue learned irrelevance paradigms. At first glance, this finding does appear consistent with the existing literature. For example, others have reported that high anxiety individuals are impaired in their ability to distribute attention appropriately between previously experienced relevant and irrelevant information; with an inappropriate allocation of attention to irrelevant stimuli. This finding has previously been indicated by existing studies of latent inhibition (Weiner, 1990; Weiner & Feldon, 1997; see Braunstein-Bercovitz, 2002). However, as previously discussed, the limitations encompassed within existing latent inhibition task designs, makes it possible that existing latent inhibition tasks are actually generating an effect of learned irrelevance. In light of this limitation, it is possible that previous observations of reduced latent inhibition with anxiety (i.e., Braunstein-Bercovitz, 2000, 2001), are actually generating reduced learned irrelevance, which would be consistent with the results we are observing here. If the effect of prior relevance of cues on subsequent learning depends on the ability to unequally distribute attention between relevant/irrelevant cues, then naturally we might anticipate that individuals with impaired ability to equally distribute attention will show a reduced effect of prior relevance of cues. Therefore, the reduced attentional bias towards previously relevant-cues in high anxious individuals may be taken as evidence of an attentional deficit- but, is an effect restricted to observations of learned irrelevance, not latent inhibition. This possibility could also lend support to the null finding observed with anxiety and latent inhibition, observed in the previous Experiments 1 and 2. The fact that schizotypy did not however have an effect on learned irrelevance contradicts existing research findings which report a reduced learned irrelevance effect in high positive schizotypy individuals using a compound cue learned irrelevance task (see Le Pelley et al., 2010a). This could however have something to do with the inherent differences between compound cue tasks (e.g., Le Pelley et al., 2010a) and single

cue tasks (used in the current experiments); this idea is explored further in the overall general discussion (see Chapter 5).

It is important to note this disrupted learned irrelevance effect was observed using only neutral (non-emotional/non-threat related) information (See also: Derryberry and Reed, 2002; Eysenck et al., 2007; Pacheco-Unguetti et al., 2010). Great difficulty to disengage attention from threat related information in anxious participants has been shown in different studies (for a review see: Pergamin-Hight et al., 2014). These studies have typically used compound cues as it has previously been claimed that no associations have been found in tasks where one emotional or neutral stimulus is presented as a single cue (e.g. Mathews & Milroy, 1994). Therefore, an important contribution of the current findings is that we observed the effects typically expected for anxious individuals dealing with threatening stimuli, in spite of using stimuli presented as single cues with no affective value. Furthermore, the current results corroborate this and extend it to circumstances in which attentional biases are acquired *during learning*. Here, people with high levels of state anxiety failed to show the normal attentional bias towards information that was relevant to the solution of a learning task. This suggests that everyday anxiety disrupts people's appropriate allocation of attention to stimuli based on their previous experiences. This discovery is important because the natural variation in attention that stems from people's interaction with the environment permits them to tune out irrelevance. If this is disrupted, then the repercussions are substantial, as a diminished ability to tune out irrelevance may slow the solution of complex tasks and perpetuate a focus on unimportant information (see Hullinger, Kruschke & Todd, 2014). To the best of current knowledge, this result constitutes the first observation of disrupted learned irrelevance in high state anxious individuals.

Pacheo-Unguetti et al. (2010) demonstrate that state and trait anxiety influence attentional processes differently and suggest the effects of state and trait anxiety on attentional bias can be dissociated. More specifically, they report high state anxiety involves a vigilant state associated with assessing cue relevance and the detection of infrequent stimuli. Whereas high trait anxiety is linked to attentional processes underpinned by the executive control network, involving conflict resolution between two stimuli presented in compound. On this basis then, it is not surprising that we only observe a disruption in high state anxious individuals using the single cue learned irrelevance tasks employed here. As the relevant and irrelevant cues are presented singularly, rather than in compound, there is no need for the activation of a mechanism where conflict resolution (i.e., between two stimuli) is required. The cues are trained to be either predictive (100%) or irrelevant (50%) to the occurrence of the outcome, and thus providing an apt situation for the effects of state anxiety to be detected. Thus, it would be of interest for future research to assess whether a comparable compound cue learned irrelevance task would elicit a disruption with high trait anxiety individuals. This remains for future research to determine.

The current findings propose a more ambitious framework to explain the attentional functioning of anxious individuals. Currently, the hypervigilance theory (Eysenck, 1992), suggests that anxious individuals, as compared with non-anxious individuals, have a greater tendency to scan the environment regardless of the presence of threat or aversive stimuli (see also: Mathews, May, Mogg, & Eysenck, 1990). Our results suggest this framework does not only operate when multiple neutral cues are competing for attention, but when single, neutral cues are presented. Therefore the learned irrelevance paradigm could be a useful tool to investigate the attentional view of anxiety; more specifically, for how individuals in a transient state of anxiety learn and shift their attention to everyday cues.

At this juncture however, the causal status of the relationship between disrupted *learned attention* and anxiety is unclear. It is unclear whether high anxiety causes an inability to direct attention, or alternatively whether the inability to distinguish previously relevant from irrelevant cues induces a state of anxiousness. Existing research has served to establish the causal nature of the relationship between anxiety and an attentional bias for *threat related* information (see Mathews & MacLeod, 2002). Such research has focused on the hypothesis that induced processing biases can cause anxiety, while leaving open the possibility that causal effects could also operate in the reverse direction, providing a feedback loop (see also Chapter 4). Findings that implicate a threat-related attention bias in anxiety (i.e., Mathews & MacLeod, 2002) have generated interest in a novel ‘Attention Bias Modification Treatment’ (ABMT). ABMT arises from the notion that cognitive biases result in pathological anxiety. This idea also underlies Cognitive Behavioural Therapy (CBT) which targets a range of biases, for example; exposure to feared situations in order to learn that feared situations/objects are safe. However, in contrast to CBT, ABMT currently has a direct target of therapeutic action that focuses on a specific bias in threat-related attention (For reviews see: Bar-Haim et al., 2007; Hakamata et al., 2010). Whilst previous research findings are promising in showing support for ABMT as a novel treatment for anxiety, the findings from the current study and those of others (e.g. Pacheco-Unguetti et al., 2010) also using neutral information in the absence of affective stimuli, urges the continued development of these cognitive-training programmes. In relation to learned attention tasks, for example; there are important ramifications for this type research on learning and shifting attention to everyday cues for individuals experiencing stressful situations that might elevate current levels of anxiety. Part of therapy could not only include retraining of attention but also retraining, more generally, what the cues are associated with.

In conclusion, the findings of the present chapter contribute to existing knowledge highlighting the disrupted attentional mechanisms that are involved in individuals experiencing anxiety and how they could be related to the day-to-day difficulties associated with clinical anxiety. It is important to highlight that we have identified an effect of state anxiety on these disorders by using neutral, single cue, information. The current findings allow a greater opportunity to generalise existing knowledge; with insights that have potential implications for the treatment of anxiety problems in general and attentional control strategies in particular. The causal direction of the relationship between anxiety and learned attention to cues with a history or relevance or irrelevance, is the focus of the following chapter before more specific conclusions can be drawn regarding the future development of cognitive-training programmes, such as ABMT.

Chapter 4:

Learned irrelevance: The relationship with induced anxiety and schizotypy

4.1 Introduction

Chapter 3 investigated the relationship between anxiety, and learning about stimuli that have a history of learned-predictiveness or irrelevance. Across two experiments, learning about the cue that was previously predictive (100%) was higher than the cue that was previously irrelevant (50%), but only in low state-anxious individuals. High state-anxious individuals demonstrated a reduced attentional bias towards previously established predictive cues, suggesting an impaired ability of high anxiety individuals to distribute attention appropriately between cues based on their previously experienced relevance (e.g., Braunstein-Bercovitz, 2001; Eysenck et al, 2007). At this juncture however, the causal status of the relationship between disrupted *learned attention* and anxiety is ambiguous. It is unclear whether high anxiety causes an inability to direct attention appropriately, or alternatively whether the inability to distinguish previously relevant from irrelevant cues induces a state of anxiousness. The experiments reported in this chapter aim to address this question. The following sections discuss the literature which has previously endeavoured to establish the causal status of the relationship between attentional biases and anxiety, before moving on to discuss, in more detail, how the current experiments provide advancement in this literature.

4.1.1 Attentional bias and vulnerability to anxiety

Existing research has served to establish the causal nature of the relationship between anxiety and an attentional bias for *threat related* information (see Mathews & MacLeod, 2002; MacLeod, Rutherford, Campbell, Ebsworthy & Holker, 2002). Such research has focused on the hypothesis that induced processing biases (i.e., experimentally biasing participants'

responses towards processing negative/threat information) can cause anxiety, while leaving open the possibility that causal effects could also operate in the reverse direction (i.e., anxiety causing a bias towards processing negative/threat information), providing a feedback loop. For example, MacLeod et al. employed a dot probe task designed to induce a temporary attentional bias either towards or away from threat-related information, followed by exposure to a mildly stressful task to assess the effects of an induced attentional bias (i.e., toward negative information) on emotional vulnerability to subsequent stress. During this dot probe task, participants were presented, briefly, with two words simultaneously, one negative threat-related word and one neutral word. Following the termination of this display, a small dot probe was presented in the prior location of one of these two words and participants were required to press a response button, corresponding to target identity, as quickly as possible, whenever the probes were detected. The discrimination latencies relative to the probes occurring in either location provided a measure of individual's attentional response to emotional/threat-related stimuli. During the training trials, the probes always appeared in the vicinity of threat-related word for half of the participants, to induce an attentional bias towards negative stimuli. For the other half of participants, the probes always appeared in the vicinity of the neutral word to induce an attentional bias away from negative stimuli and toward neutral stimuli. During the test trials the probes were presented in the vicinity of either the neutral or the threat-related word, with equal frequency and the discrimination latencies to detect the probes in each location served to indicate the attentional impact of the training manipulation. At the end of this task, all participants were exposed to a stressor task involving the attempt to complete 30 difficult or insoluble anagrams under timed conditions whilst being videotaped and anxiety levels measured pre- and post-test (MacLeod et al).

For participants exposed to the training procedure designed to induce an attentional bias towards the threat-related words, reaction times were faster to the probes in the vicinity of these words relative to the neutral words, thus resulting in an attentional vigilance to this information. Whereas those individuals exposed to the training procedure designed to induce an attentional avoidance away from threat-related words, reaction times were faster to the probes in the vicinity of the neutral words relative to the neutral words. Thus the dot probe training procedure effectively manipulated participant's attentional responses. Furthermore, the induction of a differential attentional bias served to modify individual's reactions to the subsequent stressor task. Participants trained to exhibit an attentional bias towards threat-related stimuli, demonstrated increased elevations of anxiety in response to the anagram stress task relative to those participants trained to orient attention away from emotionally negative information. These findings therefore provide support for the hypothesis that attentional biases towards threat-related information can exert a causal influence on increased emotional vulnerability.

On the basis of the above results it appears that induced biases can affect vulnerability to anxiety through their influence on how stimuli are processed or interpreted. However, whilst findings using tasks such as the dot probe (Mathews & MacLeod, 2002) can tell us how *forced* selective attention, either towards or away from threat related stimuli, (by experimentally inducing a processing bias) can serve to establish individuals vulnerability to a situational level of anxiety, it cannot tell us how *learned* selective attention (i.e., attention that is governed by whether a stimulus reliably predicts an outcome or not) towards or away from cues correlates with individuals level of situational anxiety or what the causal direction of this relationship might be. To date there are only two experiments that have looked at the causal relationship between anxiety and learned variations in attention (see Braunstein-Bercovitz, 2001), and these are discussed in the following section.

4.1.2 Experimentally induced anxiety and latent inhibition

As discussed in the preceding chapters (see Chapter 1, section 1.6), there is empirical evidence that shows a general attentional bias towards irrelevant stimuli, in the absence of threat, in individuals who are characterised by high levels of anxiety (e.g. Derryberry & Reed, 2002; Poy et al., 2004; Bishop, 2009; Pacheco-Unguetti, Acosta, Callejas & Lupiáñez, 2010). As with latent inhibition, for example, high trait anxious individuals show an inability to gate out irrelevant information resulting in high distractibility and difficulty in focusing attention on information that is task relevant; the consequence of which is attenuated latent inhibition (Braunstein-Bercovitz, 2000). In an extension of these findings, Braunstein-Bercovitz et al. (2001) suggested that situational stress should also disrupt latent inhibition because it is known to elicit anxiety (e.g., Houston, 1987) and to increase scores on the state anxiety scale of the STAI (Spielberger et al., 1970), which is correlated with trait anxiety. Thus on the basis that state and trait anxiety are related then task-induced stress should attenuate latent inhibition, comparable to trait anxiety.

To test this prediction Braunstein-Bercovitz (2001) conducted two experiments using two separate stress manipulation procedures and an established latent inhibition procedure (Braunstein-Bercovitz & Lubow, 1998a, 1988b). In this latent inhibition task, participants were either preexposed, or not preexposed to an irrelevant shape (preexposed stimulus), whilst they completed a masking task in which they had to indicate whether a pair of letters, presented on screen, were the same or different. In the subsequent test stage of the experiment participants had to make a response when they thought an on-screen counter would increment. The increment in the counter was preceded by presentation of the polygon (see Chapter 2, section 2.1.4 for the full procedure). In experiment 1, stress was induced by threats to self-esteem in a difficult number-series completion task said to be related to intelligence (high stress group).

For the low stress group, the number task was easy and not related to intelligence (Keinan, Friedland, Kahneman & Roth, 1999). In experiment 2, the participants were job seekers and the latent inhibition task was described as part of the interview selection process (high stress group) or not (low stress group). Across both experiments latent inhibition was attenuated in high as compared to low stress induced individuals; suggesting induced stress/anxiety impairs selective attention caused by disrupted attentional inhibition. This finding adds to the generality of previous findings and suggests that the attentional processes governing latent inhibition (if we accept the attentional view of latent inhibition; i.e., Mackintosh, 1975; Pearce & Hall, 1980) are impaired by trait anxiety, as well as by situations such as induced-stress which elevate levels of state anxiety. As previously discussed, Braunstein-Bercovitz (2000) also report attenuated latent inhibition is the result of high levels of anxiety experienced in high schizotypal individuals (see Chapter 2, section 2.1.4). However, one reason to question these findings is based on the inherent limitations encompassed with latent inhibition designs. For example, the latent inhibition procedure described by Braunstein-Bercovitz (2000, 2001) includes an explicit masking task, consequently encompassing components of learned irrelevance within the paradigm. Thus the conclusion of the findings reported by Braunstein-Bercovitz (2000, 2001) remains open to debate. Whether there is, however, an important distinction between latent inhibition and learned irrelevance; and whether they are manifestations of similar cognitive processes, is an on-going question that this thesis aims to answer. As discussed in the preceding chapters, the learned irrelevance paradigm is a less ambiguous measure of the impact of attention on associative learning. Therefore, the current experiments make use of the learned irrelevance paradigm employed in Chapter 3, Experiment 4 (see section 4.1.3 for a rationale) to establish the causal status of the relationship between anxiety and disrupted *learned attention*. Therefore, the focus of the following experiments is to establish the relationship between induced state anxiety and its effect on learned attention,

in a similar way to that of previous studies (i.e., Braunstein-Bercovitz, 2001). In a further extension of this literature, we also include a relaxation task (low anxiety) and a neutral task (control condition) to compare with a group of individuals induced with a state of anxiety, using a stressor task. Failure to find evidence of the existence of a relationship between induced state anxiety and disrupted learned attention may suggest that the causal effect operates in the reverse direction.

4.1.3 Aims and research questions

Here, we introduce a mood induction procedure to examine the relative influence of state anxiety on *learned attention*, using the learned irrelevance task previously employed in Chapter 3, Experiment 4. This learned irrelevance task was used over that employed for Experiment 3 because it has the sensitivity to examine a pure difference in associability using a different cover story between stages 1 and 2 of the task. For the mood induction procedure, participants either received a negative mood inducing task (a speech stressor task) to elevate state-anxiety levels; a positive mood inducing task (relaxed breathing/meditation exercises) to reduce state-anxiety levels; or a neutral mood inducing task (passage from the National Geographic) to act as a control group. The first part of this chapter explores the effectiveness of these mood induction tasks in modulating state anxiety (Experiment 5) before assessing their ability to influence learned variations in attention using an established learned irrelevance procedure (Experiment 6). In a second part to this chapter, mediation analyses are run to explore whether there is a direct causal relationship between state anxiety and learned irrelevance or whether schizotypy is a mediator of this relationship.

Part 1: Mood Manipulation

4.2 Experiment 5

The aim of Experiment 5 was to investigate the effectiveness of the mood induction procedures; here we assess the ability of a negative and positive mood induction procedure to induce a state of anxiety different from baseline mood state scores, and the ability of a neutral mood induction procedure to maintain state anxiety levels relative to baseline. Participants were either exposed to: a speech stressor task (see Sayette, Martin, Perrott, Wertz, and Hufford's, 2001)⁶ designed to elicit a transient anxious state; a relaxation response task (NHS Choices, 2015) to induce a calming state by reducing state anxiety (or at least not increase their level of state anxiety if it is already of a low level at baseline); or a neutral reading task (see Dyson & Haselgrove, 2000) designed to neither increase or decrease state anxiety levels.

4.2.1 Method

4.2.1.1 Participants

Eighteen healthy Nottingham University participants (3 males and 15 females) took part, in exchange for course credit. The age range was 18-27. The participants were randomly allocated to one of three conditions, with 6 participants in each. One group of participants was designated the 'speech stressor condition,' and given a task designed to induce a transient state of anxiousness. The second group were designated the 'relaxation response condition' and were given a task to induce a state of relaxation. The third group made up the control group and designated the 'neutral reading condition' designed to maintain participants state anxiety score comparative to their baseline measure. The sample size was kept deliberately low prior to

⁶ These task instructions have been chosen for the following study due to the sensitivity and effectiveness of these tasks being established in an undergraduate population (see Phillips & Giancola, 2008).

Experiment 6 as the effectiveness of the mood induction conditions, in our lab, was unknown thus a small pilot study was necessary to explore the ability of the mood induction tasks to modulate levels of state anxiety. In addition, based on previous research findings (see Phillips & Giancola, 2008) it was anticipated that the stress induction would be effective and thus a large sample size would be redundant. An n of 18 also ensured equal counterbalancing across the 3 mood conditions.

4.2.1.2 Materials

4.2.1.2.1 Speech Stressor Task

A Canon DVD DC95 video camera and a full screen on-line stopwatch (<http://www.online-stopwatch.com/full-screen-stopwatch/>) presented on a standard desktop computer were used to enhance the subjective stressfulness of this procedure.

4.2.1.2.2 Relaxation Response Task

Relaxation meditation music (taken from:

<https://www.youtube.com/watch?v=n17BzBecv8w>) was played using Windows Media

Player through a standard desktop computer. Lightening in the laboratory was darkened and mood lights used to create ambient and relaxing lighting effects.

4.2.1.2.3 Mood Assessment Scale

To assess individual state anxiety levels, the state anxiety sub-scale of the STICSA questionnaire (Ree et al., 2008) was administered. The state anxiety sub-scale of this questionnaire assesses somatic and cognitive-symptoms of anxiety; right now, at this very moment. The scale encompasses 21 self-reported items, rated on a 4-point Likert-type scale (1 = *not at all* to 4 = *very much so*).

4.2.1.3 Procedure

After reading an information sheet and signing a consent form, participants completed the state anxiety subscale of the STICSA (Ree et al., 2008) questionnaire to measure each individual's baseline level of state-anxiety upon entering the study. One of the three task conditions ('speech stressor,' 'relaxation response' or 'neutral reading': see below) was then completed before the state anxiety subscale was administered for a second time. The comparison between the scores on this mood scale immediately before and immediately after the designated task enabled an examination of the degree to which the mood manipulation procedure served to elevate, reduce or maintain individual level of state-anxiety. This procedure lasted 25 minutes. At the end of the session participants were fully debriefed about the true purpose of the study and for participants in the stressor condition, the relaxation exercises, which formed the relaxation condition, was offered as a way to lower individual's level of state anxiety back to baseline before leaving the laboratory.

4.2.1.3.1 Speech Stressor Task

This task was an adaptation of the procedure introduced by Sayette, Martin, Perrott, Wertz, and Hufford's (2001), administered to elicit a transient state of anxiousness. In this task participants were informed that their 'thinking style' was being assessed by their ability to prepare and deliver a short speech in front of a video camera. Informed consent for the video recording was sought after participants were read aloud the following task instructions:

"This part of the study is to test your thinking style. We are interested in your ability to think quickly with limited time for preparation. Research has shown that these skills are related to cognitive ability. For this task you must quickly prepare and then deliver a short speech about what you like and dislike about your body while standing

directly in front of this video camera that will record your speech. You will have 5 minutes to prepare a 3-minute speech. Your speech will be delivered later in the study when prompted by the researcher. It is very important that you think about the speech you are about to give and how best to present this to the video camera. This stopwatch will now give you a 5-minute countdown. You will have this time to prepare your speech in your mind. When the 5 minutes are up, you will be given your next instructions”.

At the end of the session, participants were debriefed about the true purpose of the study, informed that they did not have to deliver a speech, and given the assurance that no video record of their performance had actually been taken.

4.2.1.3.2 Relaxation Response Task

A relaxation response task (recommended by NHS Choices as an effective relaxation procedure:

<http://www.nhs.uk/Conditions/stress-anxiety-depression/Pages/ways-relieve-stress.aspx>) was administered to reduce the level of state anxiety in each participant. In this task participants were informed that they would practice deep breathing exercises for 5 minutes whilst listening to relaxation meditation music (taken from:

<https://www.youtube.com/watch?v=n17BzBecv8w>). The following instructions were read aloud and presented visually to participants on the computer screen:

“For this part of the study you will be given 5 minutes to practice deep breathing exercises whilst listening to relaxation meditation music. Please sit comfortably in your chair, placing your arms on the chair arms with your palms up. Good relaxation always starts with focusing on your breathing, and the way to do this is to breathe in and out

slowly and in a regular rhythm as this will help to relax the body and induce a calming state. Please follow the step by step instructions in front of you, and repeat for 5 minutes. The researcher will inform you when the time is up.”

At this stage, the relaxation meditation music was started and the following step by step instructions were read aloud once to participants (and presented visually on the computer screen for the duration of the exercises) before being left to practice the exercises unaided:

- “1. Fill up the whole of your lungs with air, without forcing. Imagine you're filling up a bottle, so that your lungs fill from the bottom.*
- 2. Breathe in through your nose and out through your mouth.*
- 3. Breathe in slowly and regularly counting from one to five (don't worry if you can't reach five at first).*
- 4. Then let the breath escape slowly, counting from one to five.*
- 5. Keep doing this for approximately 3 minutes, or until you feel calm. Breathe without pausing or holding your breath.”*

Once the 5 minutes were up, the researcher turned off the meditation music, and in their own time participants were asked to let the researcher know when they felt ready to begin the next part of the experiment. At the end of the session, participants were debriefed about the true purpose of the study.

4.2.1.3.3 Neutral Reading Task

A neutral reading task (passage taken from the National Geographic) was administered to elicit/maintain a neutral mood state, providing a neutral control group. In this task

participants were simply asked to read a passage provided on paper in front of them for 5 minutes. At the end of the session, participants were fully debriefed about the true purpose of the study.

4.2.2 Results and Discussion

Figure 4.1 shows the mean, pre and post-test state anxiety scores for each mood induction condition. It is evident from this figure, that prior to any mood induction condition; mean state anxiety scores were similar across all participants. Whereas observation of state anxiety scores, post mood induction, show an increase in mean state anxiety scores for participants in the speech stressor condition; a decrease in mean state anxiety scores for the relaxation condition and little or no change in mean state anxiety scores for the neutral condition. This impression was confirmed using a 2 (state anxiety: pre, post) x 3 (mood condition: stress, relaxation and neutral) mixed ANOVA which revealed no significant main effect of pre and post state anxiety ($F < 1$), but a significant pre post state anxiety x mood condition interaction $F(2, 15) = 7.188, p = .006$, partial $\eta^2 = .489$. Follow up simple main effects analysis with applied Bonferroni adjustment⁷ revealed no significant effect of state anxiety between each of the mood conditions at pre-test ($F_s < 1$), whereas, there was a significant effect of state anxiety between each of the mood conditions at post-test $F(2, 15) = 4.853, p = .024$, partial $\eta^2 = .393$. At post-test, state anxiety scores were only significantly different between the speech condition ($M = 41.00, SD = 13.84$) and the relaxation condition ($M = 25.33, SD = 3.88$), $p = .028$.

⁷ Bonferroni adjustment was applied for the current analyses due to multiple comparisons made between the 3 mood conditions which is in contrast to Experiments 3 and 4 that only compared high versus low anxiety.

Simple main effects analysis also revealed state anxiety scores were: significantly higher posttest than pretest in the speech stressor condition $F(1, 15) = 6.902, p = .019$, partial $\eta^2 = .315$, and significantly lower posttest than pretest in the relaxation response condition $F(1, 15) = 7.155, p = .017$, partial $\eta^2 = .323$. State anxiety scores at pretest and posttest did not significantly differ in the neutral condition ($F < 1$), see Figure 4.1.

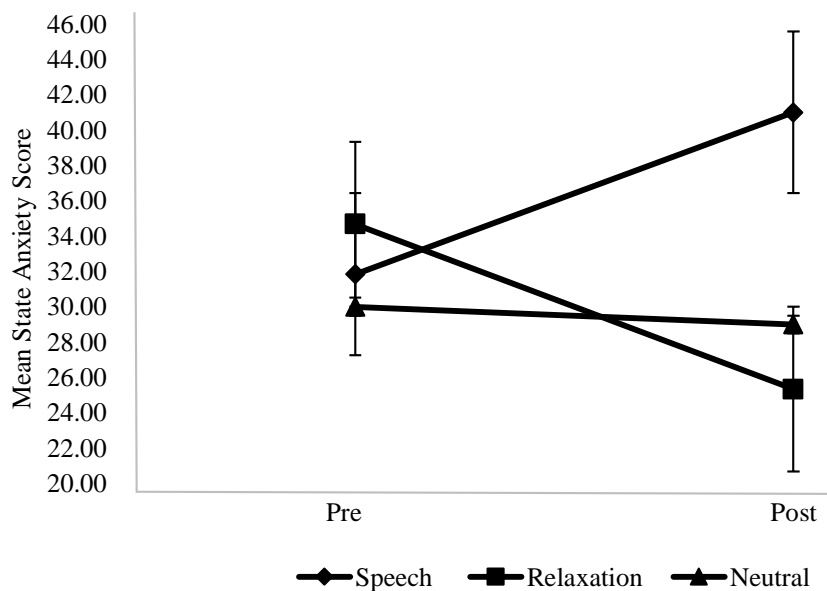


Figure 4.1. Mean state anxiety scores at pre-test and post-test for each mood condition; speech, relaxation and neutral. Error bars are $1 \pm$ between-subject standard error of the mean.

The results of this experiment confirm the ability of the speech and relaxation procedures to induce either a high or low level of state anxiety, respectively. Furthermore, the neutral condition sustained anxiety at its initial, intermediate, level. The primary aim of Experiment 6 was to assess the ability of these mood induction procedures to influence learned variations in attention, using the learned irrelevance paradigm described by Le Pelley et al. (2010b).

4.3 Experiment 6

The first aim of Experiment 6 was to replicate the results from Experiment 5: that the three mood induction procedures; speech, relaxation and neutral tasks serve to increase, decrease or maintain levels of state anxiety, respectively. The second aim was to examine how the varying levels of induced state anxiety influence learned variations in attention, using a learned irrelevance paradigm (see Le Pelley et al., 2010b). Experiment 6 employed the same learned irrelevance paradigm as described in Experiment 4, (see Chapter 3; learned irrelevance and anxiety for further discussion). Assuming that the mood manipulation procedures prove effective in creating three groups of participants who differ in their level of state anxiety (comparable to the pattern of results observed in Experiment 5); comparisons of participant's performance on the learned irrelevance task will enable appraisal of whether high anxiety causes an inability to direct attention, resulting in a disruption of learned irrelevance, relative to low anxious individuals and controls. First the effectiveness of the mood induction task in modulating state anxiety is explored before assessing the ability of these procedures to influence learned variations in attention.

4.3.1 Method

4.3.1.1 Participants

Ninety healthy Nottingham University participants and members of the general public (25 males and 65 females) took part, in exchange for course credit or a £5 inconvenience allowance. The age range was 18-52. The participants were randomly allocated to one of the three mood induction conditions (speech stressor, relaxation response, or neutral reading), with 30 participants in each. A sample size of 90 ensured equal counterbalancing across the 3 mood

conditions and a total sample size in keeping with Experiment 4 (as the current experiment employed the same learned irrelevance paradigm as described in Experiment 4).

4.3.1.2 Materials & Apparatus

4.3.1.2.1 Mood induction tasks

The materials for the speech stressor task and relaxation response task were the same as described in sections 4.2.1.2.1 and 4.2.1.2.2, respectively.

4.3.1.2.2 Mood Assessment Scale

As per previous experiments, the STICSA; both state and trait subscales (Ree et al., 2008) and the O-LIFE (Mason et al., 1995) were administered for participants to complete.

4.3.1.2.3 Learned irrelevance task

The apparatus were the same as described in Chapter 3, Experiment 4: section 3.3.1.2.

4.3.1.3 Procedure

4.3.1.3.1 Mood induction tasks

The procedure for the speech stressor task, relaxation response task and neutral reading task was the same as described in sections 4.2.1.3.1, 4.2.1.3.2 and 4.2.1.3.3, with participants completing only one task condition. The state anxiety subscale of the STICSA (Ree et al., 2008) was completed both before and after the mood induction procedure to measure baseline and post-mood induction level of state anxiety. The STICSA was then completed for a third time following completion of the learned irrelevance task (see section 4.3.1.3.2 below) to assess whether levels of state anxiety following the mood induction procedure, remained consistent at follow-up (after completion of the learned irrelevance task), see Figure 4.2 below.

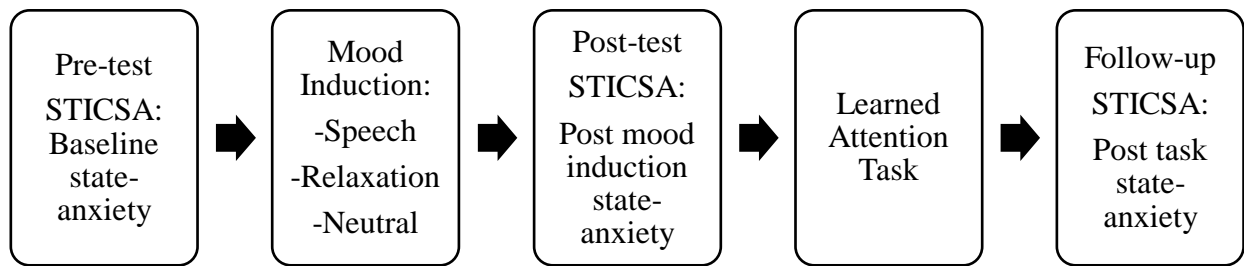


Figure 4.2. A flow diagram to illustrate the order of task completion for Experiment 6.

4.3.1.3.2 Learned irrelevance task

The procedure was the same as described in Chapter 3, Experiment 4: section 3.3.1.3. At the end of the session, all participants were fully debriefed about the true purpose of the study. Again, for participants in the stressor condition, the relaxation exercises, which formed the relaxation condition, were offered as a way to lower individual's level of state anxiety back to baseline before leaving the laboratory. The complete procedure lasted approximately 40 minutes.

4.3.1.3.2.1 Scoring

The scoring was the same as described in Chapter 3, Experiment 4: section 3.3.1.4.

4.3.2 Results and Discussion

First, it is necessary to analyse the mood induction data to determine whether the separate procedures were effective in inducing differential mood states for this group of participants. If this mood induction procedure is found to be effective, then the data collected from the learned irrelevance task can be analysed to reveal the attentional variation as a consequence of inducing either a high, low or neutral state of anxiety.

Figure 4.3 shows the mean pre-test, post-test and follow-up state anxiety scores for each mood induction condition. It is evident from this figure, that prior to any mood induction condition; mean state anxiety scores were similar across all participants. Whereas state anxiety scores post mood induction, show an increase for participants in the speech stressor condition; a decrease for the relaxation condition and little or no change for the neutral condition. State anxiety scores at follow-up show there is a slight convergence towards the mean for the speech and relaxation conditions but mean state anxiety scores remain higher than both neutral and relaxation conditions. This impression was confirmed using a 3 (state anxiety: pre, post, follow-up) x 3 (mood condition: stress, relaxation and neutral) mixed ANOVA which revealed a significant main effect of state anxiety $F(2, 86) = 3.348, p = .040$, partial $\eta^2 = .072$, and a significant state anxiety x mood condition interaction $F(4, 174) = 20.002, p < .001$, partial $\eta^2 = .315$. Simple main effects analysis with applied Bonferroni adjustment⁸ revealed no significant effect of state anxiety between each of the mood conditions at pre-test ($F < 1$), whereas, there was a significant effect of state anxiety between each of the mood conditions at post-test $F(2, 87) = 22.706, p < .001$, partial $\eta^2 = .343$, and at follow-up $F(2, 87) = 6.089, p = .003$, partial $\eta^2 = .123$. At post-test, state anxiety scores for the speech condition were significantly different from both the relaxation condition and the neutral condition. However, with Bonferroni correction in place, there was no significant difference between the state anxiety scores for the relaxation and neutral conditions at post-test. At follow-up, state anxiety scores remained significantly different between the speech condition and the relaxation condition, see Table 4.1.

⁸ Bonferroni adjustment was applied for the current analyses due to multiple comparisons made between the 3 mood conditions which is in contrast to Experiments 3 and 4 that only compared high versus low anxiety.

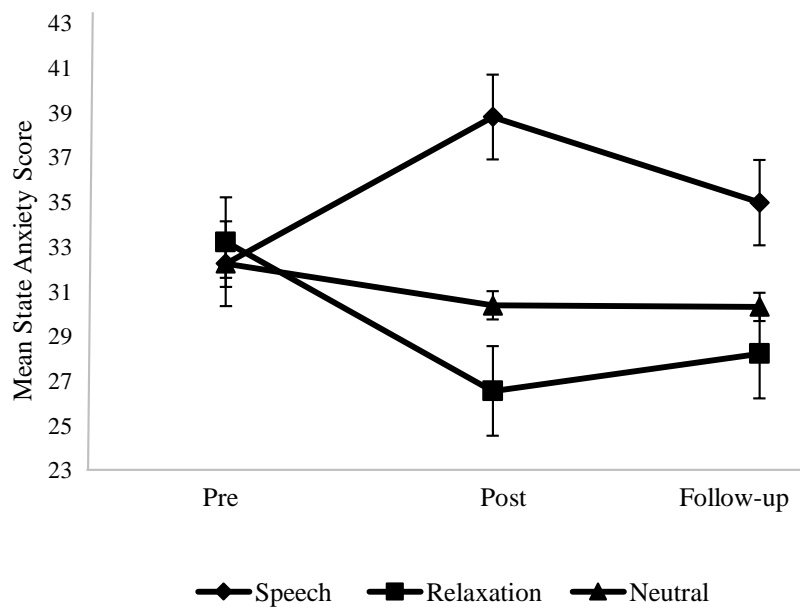


Figure 4.3. Mean state anxiety scores at pre-test, post-test and follow-up for each mood condition; speech, relaxation and neutral. Error bars are 1 +/- between-subject standard error of the mean.

Table 4.1

Pairwise comparisons for state anxiety scores between the different mood condition at pre-test, post-test and follow-up.

	Mean Differences		
	Speech	Relaxation	Neutral
<u>Pre-test</u>			
Speech	-	-.967	5.433E-015
Relaxation	.967	-	.967
Neutral	-5.433E-015	-.967	-
<u>Post-test</u>			
Speech	-	12.267*	8.433*
Relaxation	-12.267*	-	-3.833
Neutral	-8.433*	3.833	-
<u>Follow-up</u>			
Speech	-	6.767*	4.667
Relaxation	-6.767*	-	-2.100
Neutral	-4.667	2.100	-

Note. *. The mean difference is significant at the .05 level.

b. Adjustment for multiple comparisons: Bonferroni.
Significant findings are bolded.

Additional simple main effects analysis revealed state anxiety scores were significantly different at pre-test, post-test and follow-up for individuals in the speech condition $F(2, 86) = 34.530, p < .001$, partial $\eta^2 = .445$, those in the relaxation condition $F(2, 86) = 38.288, p < .001$, partial $\eta^2 = .471$, and the neutral condition $F(2, 86) = 3.567, p = .032$, partial $\eta^2 = .077$. As can be seen in Table 4.2 there was a significant increase in state anxiety scores for the speech condition from pre-test ($M = 32.27, SD = 6.52$) to post-test ($M = 38.83, SD = 9.44$), and a significant decline in state anxiety scores from post-test to follow-up ($M = 35.00, SD = 9.31$). For the relaxation condition, there was a significant decrease in state anxiety scores from pre-

test ($M = 33.23$, $SD = 5.52$) to post-test ($M = 26.57$, $SD = 4.65$), and no significant difference from post-test to follow-up ($M = 28.23$, $SD = 5.30$). For the neutral group, there were no significant changes in state anxiety score between pre-test ($M = 32.27$, $SD = 7.07$), post-test ($M = 30.04$, $SD = 6.73$) and follow-up ($M = 30.33$, $SD = 7.91$) with Bonferroni correction in place.

Table 4.2

Pairwise comparisons for the pre, post and follow-up anxiety scores for each of the mood conditions.

	Mean Differences		
	Pre-test	Post-test	Follow-up
<u>Speech</u>			
Pre-test	-	-6.567*	-2.733*
Post-test	6.567*	-	3.833*
Follow-up	2.733*	-3.833*	-
<u>Relaxation</u>			
Pre-test	-	6.667*	5.000*
Post-test	-6.667*	-	-1.667
Follow-up	-5.000*	1.667	-
<u>Neutral</u>			
Pre-test	-	1.867	1.933
Post-test	-1.867	-	.067
Follow-up	-1.933	-.067	-

Note. *. The mean difference is significant at the .05 level.

b. Adjustment for multiple comparisons: Bonferroni.
Significant findings are bolded.

4.3.2.1 Learned irrelevance

Figure 4.4 shows the mean percentages of correct responses per block across the 6 blocks of stage 1. Accuracy increased rapidly for the relevant cues as the participants learnt the

correct responses, in comparison to the irrelevant cues. The relevant trials were compared with the irrelevant trials using a 2 (cue: relevant-cue, irrelevant-cue) x 6 (block 1-6) repeated measures ANOVA. This analysis revealed a significant main-effect of cue; $F(1,89) = 255.528$, $p < .001$, partial $\eta^2 = .742$, a significant main-effect of trial number; $F(5, 85) = 6.232$, $p < .001$, partial $\eta^2 = .268$, and a significant interaction; $F(5, 85) = 1.782$, $p = .125$.

Figure 4.5 shows the mean discrimination scores across stage 2; the mean discrimination scores for previously relevant-cues appear higher than previously irrelevant-cues during the first few blocks, with equal discrimination scores by the end of stage 2. The relevant trials were compared with the irrelevant trials using a 2 (cue: relevant-cue, irrelevant-cue) x 10 (blocked trials 1-10) repeated measures ANOVA. This analysis revealed a significant main-effect of cue; $F(1,89) = 8.658$, $p = .004$, partial $\eta^2 = .089$, a significant main-effect of trial number; $F(9, 81) = 20.379$, $p < .001$, partial $\eta^2 = .694$, and a significant interaction $F(9, 81) = 2.286$, $p = .024$, partial $\eta^2 = .203$.

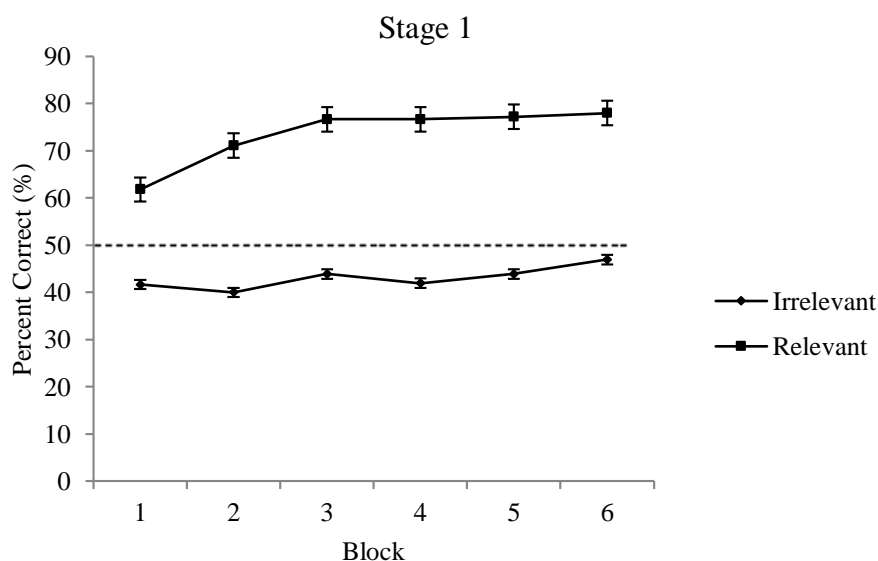


Figure 4.4. Mean percentages of correct responses across the six blocks of stage 1, averaged separately for relevant and irrelevant cues. Dotted line shows theoretical level of chance responding (50%). Error bars are 1+/- between-subject standard error of the mean.

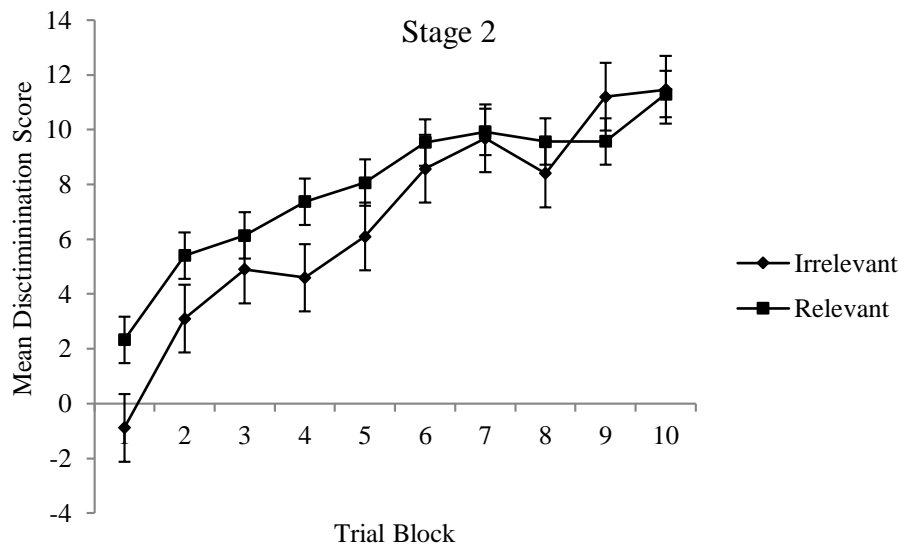


Figure 4.5. Mean discrimination scores for stage 2, averaged separately for relevant and irrelevant cues. Error bars are 1+/- between-subject standard error of the mean.

In contrast to Experiment 4 (see Chapter 3) that used this same task, the current results provide support for an effect of learned irrelevance, similar that reported by Le Pelley et al. (2010b), when taking into account all 10 blocks of stage 2. It is possible that the data presented in Experiment 4, do contain an effect of predictiveness and uncertainty on cue associability, but varying levels of state anxiety are masking this effect (as previously discussed in Chapter 3, see section 3.3.2.1). Due to the nature of the mood induction tasks used in Experiment 6, it would be expected that levels of anxiety would be at the extremes for the speech and relaxation groups, and in the middle for the neutral groups. Therefore, levels of state anxiety are expected to be less variable in experiment 6 (relative to Experiment 4), thus allowing an effect of predictiveness and uncertainty on cue associability to be demonstrated. The statistical power of the current sample may also be increased due to the larger sample size. How these induced levels of state anxiety co-vary with learned irrelevance, is the focus of the following section. In order to make a direct comparison with Experiments 3 and 4, we first calculated a total state anxiety score and dichotomised participants into high and low anxiety groups. This analysis

permitted assessment as to whether a comparable result was observed in the current experiment relative to Experiments 3 and 4 before moving on to investigate the 3 separate mood induced conditions and their relationship with learned irrelevance.

4.3.2.2 Learned irrelevance and anxiety – high vs low state anxiety groups

In order then to make a direct comparison with Experiments 3 and 4, a total state anxiety score was calculated for each participant in the current experiment (average of pre-test, post-test and follow-up state anxiety scores), assigned into a ‘low’ state anxiety group ($N = 48$) if their score lay on or below a mean state anxiety score of 31, and to a ‘high’ state anxiety group ($N = 42$) if their score lay above this mean. Comparable to the previous experiments, this split was determined by the population norm reported for state anxiety in a healthy student population (see Ree et al., 2008). To investigate whether there was a significant effect of high or low state anxiety on attention to relevant and irrelevant-cues, a 2 (state anxiety: high, low) x 2 (cue: relevant cue, irrelevant cue) mixed ANOVA was carried out for stage 1 and a 2 (state anxiety: high, low) x 2 (cue: relevant, irrelevant) x 3 (trial block: 1-3) mixed ANOVA was carried out for stage 2.

Figure 4.6 shows the mean percentages of correct responses to the relevant and irrelevant cues collapsed across the six blocks for high and low anxiety groups in stage 1. It is evident from this figure that the percentage of correct responses was higher to the relevant cues compared to the irrelevant cues for all participants. This impression was confirmed for stage 1 as there was a significant main effect of Cue $F(1, 87) = 246.504, p < .001$, partial $\eta^2 = .739$, no significant main effect of State anxiety ($F < 1$) and no significant Stimulus x State anxiety interaction ($F < 1$).

Figure 4.7 shows the mean discrimination scores for the relevant and irrelevant cues collapsed across the three 3-trial blocks of stage 2, for high and low anxiety groups. Indicating a pattern of results in keeping with Experiments 3 and 4; low anxious individuals show increased accuracy to previously relevant cues, than to previously irrelevant cues. In contrast, high anxious individuals show a reduced influence of prior relevance of the cues on novel learning. Although, analysis of stage 2 did reveal a significant main effect of Cue $F(1, 87) = 8.834, p = .004$, and no significant main effect of State anxiety $F(<1) = 2.787, p = .099$ but no significant State anxiety x Cue interaction; $F < 1$. This non-significant interaction suggests a weaker relationship between anxiety and learning about the previously relevant and irrelevant cues (in comparison to the results of experiments 3 and 4). However, in light of the comparable pattern of results to the previous experiments, and the expected differences between the high and low anxious groups, simple main effects analysis with Bonferroni adjustment were carried out and revealed a significant effect of cue for the low-anxiety group, $F(1, 87) = 7.213, p = .009$, partial $\eta^2 = .077$ but not for the high anxiety group $F(1, 87) = 2.449, p = .121$, partial $\eta^2 = .027$, see Figure 4.7.

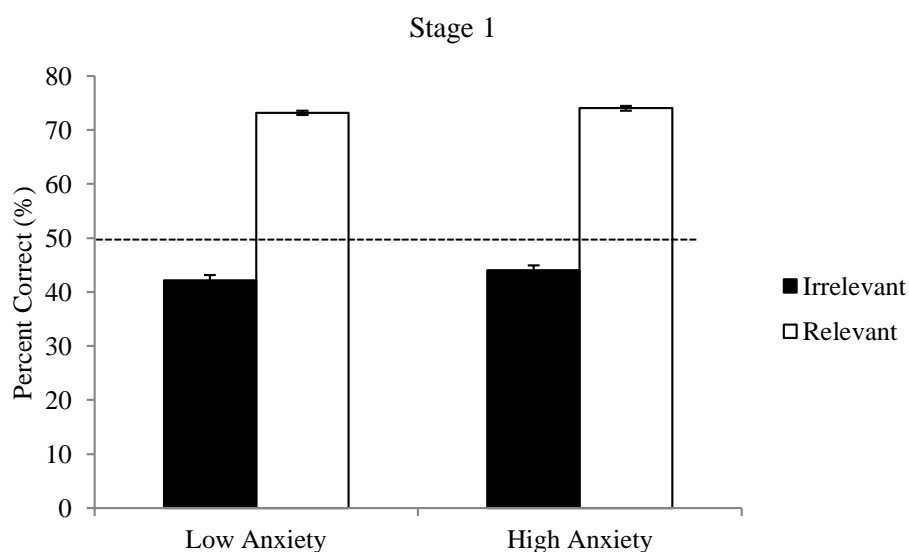


Figure 4.6. Percentage of correct responses to target cued by relevant and irrelevant cues for stage 1. Dotted line shows theoretical levels of chance responding (50%). Error bars are $1 \pm$ between-subject standard error of the mean.

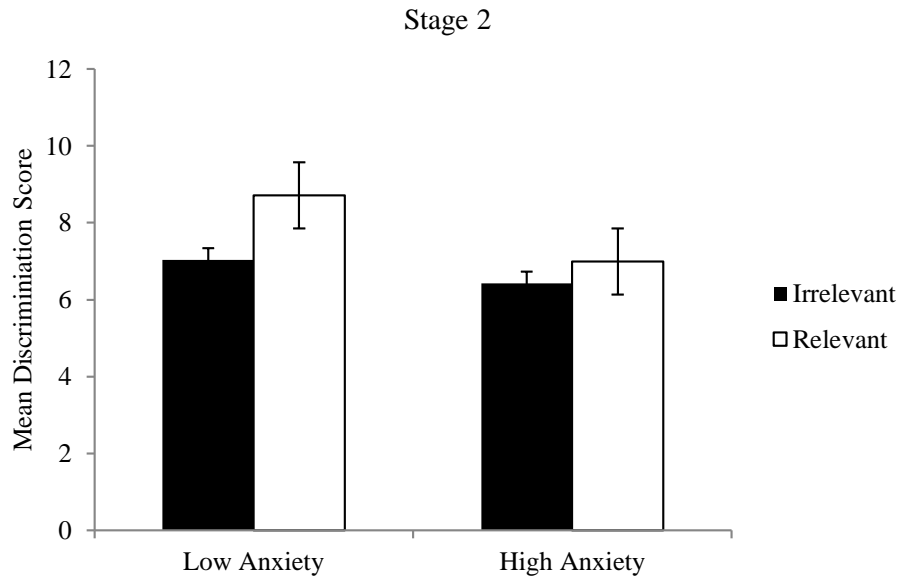


Figure 4.7. Mean discrimination scores for stage 2, averaged separately for relevant and irrelevant cues for the low and high anxious groups. Error bars are 1+/- between-subject standard error of the mean.

4.3.2.3 Learned irrelevance and anxiety – Speech, Relaxation and Neutral conditions

Figure 4.8 shows the mean percentages of correct responses to the relevant and irrelevant cues collapsed across the six blocks for relaxation, neutral and speech groups for stage 1. It is evident from this figure that the percentage of correct responses was higher to the relevant cues compared to the irrelevant cues for all participants. To investigate whether there was a significant effect of mood manipulation condition on attention to relevant and irrelevant-cues, a 3 (mood manipulation: speech, relaxation and neutral) x 2 (cue: relevant cue, irrelevant cue) mixed ANOVA was carried out for stage 1. This analysis revealed a significant main effect of Cue $F(1, 87) = 256.824, p < .001$, partial $\eta^2 = .742$, a significant main effect of Mood manipulation $F(1, 87) = 5.565, p = .005$, partial $\eta^2 = .742$, but no significant Cue x Mood manipulation interaction $F(1, 87) = 1.226, p = .299$. Follow-up simple main effects analysis was ran to explore the significant main effect across mood conditions. This analysis revealed that the percentage of correct responses (collapsed across cue) were higher for participants in the

relaxation condition compared to the speech stressor condition $F(2, 87) = 5.565, p = .005$, partial $\eta^2 = .113$.

Figure 4.9 shows the mean percentages of correct responses to the relevant and irrelevant cues collapsed across the 3 3-trial blocks of stage 2, for relaxation, neutral and speech groups. Similar to the pattern of data from stage 1, it is evident from this figure that all participants show increased accuracy to previously relevant cues, than to previously irrelevant cues. A 3 (mood manipulation: speech, relaxation and neutral) x 2 (cue: relevant, irrelevant) x 3 (trial block: 1-3) mixed ANOVA was carried out for stage 2 which revealed a significant main-effect of Cue $F(1, 87) = 9.686, p = .003$, partial $\eta^2 = .100$, no significant main-effect of Mood manipulation $F < 1$ and no significant Mood manipulation x Cue interaction; $F < 1$.

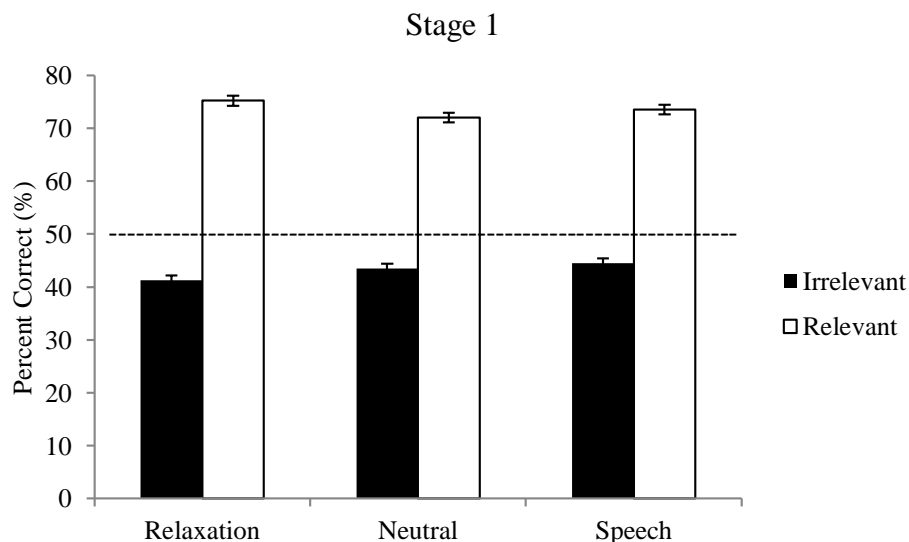


Figure 4.8. Percentage of correct responses to target cued by relevant and irrelevant cues for stage 1. Dotted line shows theoretical levels of chance responding (50%). Error bars are 1+/- between-subject standard error of the mean.

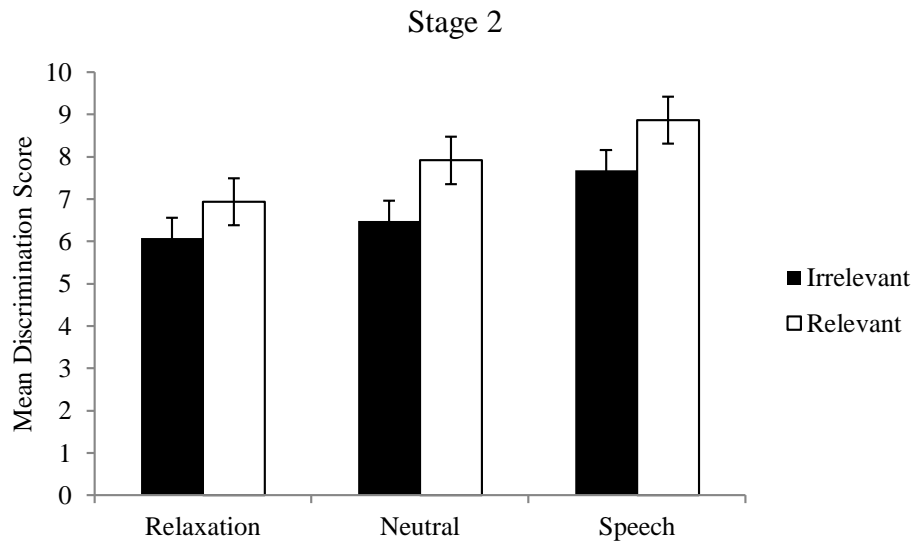


Figure 4.9. Mean discrimination scores for stage 2, averaged separately for relaxation, neutral and control conditions. Error bars are 1+/- between-subject standard error of the mean.

In contrast to Experiments 3 and 4 (see Chapter 3), there was no significant difference in the experimentally induced high and low state anxious individuals (denoted by the speech and relaxation conditions, respectively) and their ability to learn the association between cues with history relevance or irrelevance and a target. The pattern of results however indicates an increase in learning towards both cues in high state anxiety individuals (in the speech condition) compared to low state anxiety individuals (in the relaxation condition). This observation is in the opposite direction to the pattern of results reported in Experiments 3 and 4; the possible reasons for this are discussed later in this section. It is important, however, to determine whether the current non-significant result supports the null hypothesis (that there was no difference between speech and relaxation conditions in learning about the previously relevant and irrelevant cues), or supports no conclusion at all (Dienes, 2011). To determine between these possibilities a Bayes factor was calculated, where values less than .33 indicate support for the null hypothesis, values above 3 indicate support for the alternative hypothesis, and values between .33 and 3 indicate data no support for either hypothesis (Jefferys, 1961; see Dienes, 2008 for a rationale). To calculate a Bayes factor, it is necessary to estimate a plausible

effect size. In order to achieve this, the data from the 88 participants recruited from Experiment 4⁹ were used to calculate the mean difference between high and low anxiety individuals and learning about the previously predictive cue¹⁰; a mean difference of 2.91 was observed. In the current experiment, a mean difference of -2.17 ($SE = 1.48$) was observed between the speech and relaxation conditions for learning about the previously predictive cue. Following Dienes (2011: see also http://www.lifesci.sussex.ac.uk/home/Zoltan_Dienes/inference/Bayes.htm), Experiment 6 was modelled with a 2-tailed distribution with a mean of 0 (indicating no difference in learning about the previously relevant cue between the speech and relaxation conditions) and a SD set to 2.91. This yielded a Bayes factor of 1.06, indicating no support for either hypothesis. However on the basis of the current findings from Experiment 6, which point in the *opposite* direction to both Experiments 3 and 4, suggests that if we were to recruit more participants, we would either sustain or increase the effect being observed here, rather than the reverse effect.

There are two possible reasons why all participants, regardless of their induced level of anxiety, show increased learning towards the previously predictive cue over the non-predictive cue. First, it might be argued that the mood induction procedures fail to manipulate anxiety in the same way in which anxiety is influenced in the real world. For example, some authors suggest that stressful life episodes do not induce stress unless the situation is appraised as threatening. Therefore, the way individuals think about situations determines how they respond emotionally to them (e.g., Lazarus, 1990; See the General Discussion for further exploration of this issue). Second, there might be additional variables that correlate with anxiety, such as

⁹ Data from experiment 4 were used for the Bayes factor analysis as this experiment uses the same learned irrelevance task as that used in the current experiment 6.

¹⁰ Here the predictive cue is used in the analysis as the correlations in Experiment 4 were only significant between state anxiety and learning about the previously predictive cue. A significant SE is required for Bayes analysis to determine whether a comparative non-significant result supports the null hypothesis, or no conclusion at all (see Dienes, 2011).

schizotypy, which subsequently mediate the relationship between state anxiety and disrupted learned irrelevance. The following analyses explore the correlations between the study variables from experiment 6, to enable direct comparisons with experiments 3 and 4 (that instead measured non-induced levels of anxiety). Part 2 of this chapter then moves on to assess potential mediators of the relationship between anxiety and learned irrelevance.

Pearson product-moment correlation coefficients were computed between: relevant and irrelevant cues and the overall discrimination scores (calculated by subtracting the relevant cues from irrelevant cues); state anxiety scores (pre-test, post-test and follow-up); trait anxiety scores; each of the four schizotypy sub-dimensions (Pearson's r , using all participants; see Table 4.3 & 4.4). Given the exploratory nature of this analysis, no adjustments for multiple comparisons were made. For stage 1 there were significant correlations between the discrimination score and unusual experiences; $r = -.212, p = .046$, the irrelevant-cue and unusual experiences; $r = -.213, p = .045$ and the predictive-cue and follow-up state anxiety scores; $r = -.213, p = .044$. For stage 2, correlations were only significant for the relevant-cue and unusual experiences; $r = -.229, p = .032$. Therefore, in contrast to Experiments 3 and 4; Experiment 6 revealed a weaker relationship between state anxiety and learned irrelevance which suggests variations in anxiety that have been generated in the current experiment do not have the same relationship with learning as naturally occurring variations in anxiety, as observed in Experiments 3 and 4 (see general discussion for a more detailed discussion concerning this finding). There were however significant positive correlations between state anxiety, trait anxiety and the four sub-dimensions of schizotypy suggesting that levels of anxiety exist in the schizotypy scales. Whether schizotypy is a mediating factor in the relationship between state anxiety and learned irrelevance is explored in Part 2 of this chapter using a mediation analysis.

Table 4.3

Correlation matrices among study variables for stage 1.

	Stage 1 Relevant Cue	Stage 1 Irrelevant Cue	Pre- Mood State	Post- Mood State	Follow- up Mood State	Trait	UnEx	CogDis	IntrovAn	ImpNon
Stage 1 Discrimination-score	.833**	-.625**	-.074	-.058	-.172	-.031	.212*	-.116	.062	.011
Stage 1 Relevant Cue		-.089	-.041	-.143	-.213*	-.020	.120	-.113	.072	-.118
Stage 1 Irrelevant Cue			.075	-.099	.009	.029	-.213*	.050	-.010	-.186
Pre-Mood State				.621**	.672**	.657**	.228*	.386**	.147	.197
Post-Mood State					.763**	.374**	.164	.241*	.222*	.240*
Follow-up Mood State						.545**	.128	.266*	.143	.177
Trait							.281**	.578**	.180	.209*
UnEx								.340**	.277**	.525**
CogDis									.350**	.192
IntrovAn										.200

Note. Values shown are Pearson's product-moment correlation coefficients.

** Correlation is significant at the 0.01 level.

* Correlation is significant at the 0.05 level.

Significant results are bolded.

Table 4.4

Correlation matrices among study variables for stage 2.

	Stage 2 Relevant Cue	Stage 2 Irrelevant Cue	Pre- Mood State	Post- Mood State	Follow- up Mood State	Trait	UnEx	CogDis	IntrovAn	ImpNon
Stage 2 Discrimination-score	.344**	-.295**	-.118	-.063	-.115	-.015	-.166	-.106	-.023	-.103
Stage 2 Relevant Cue		.796**	-.116	.017	-.129	-.149	-.280**	-.173	.012	-.090
Stage 2 Irrelevant Cue			-.042	.058	-.058	-.142	-.177	-.106	.028	-.024
Pre-Mood State				.621**	.672**	.657**	.228*	.386**	.147	.197
Post-Mood State					.763**	.374**	.164	.241*	.222*	.240*
Follow-up Mood State						.545**	.128	.266*	.143	.177
Trait							.281**	.578**	.180	.209*
UnEx								.340**	.277**	.525**
CogDis									.350**	.192
IntrovAn										.200

Note. Values shown are Pearson's product-moment correlation coefficients.

** Correlation is significant at the 0.01 level.

* Correlation is significant at the 0.05 level.

Significant results are bolded.

Part 2: Learned irrelevance - Experiments 3, 4 and 6 combined

4.4 Experiments 3, 4 & 6 combined

Part 1 of this chapter observed a null result in terms of the relationship between the 3 induced mood conditions (speech, relaxation and neutral) and learned irrelevance. However, follow-up correlation analyses (see Table 4.4) suggests there may be personality variables (i.e., schizotypy) that mediate the relationship between state anxiety and reduced learned irrelevance. This is further supported by the contention that latent inhibition has previously been reported to be the result of high levels of anxiety experienced in high schizotypal individuals (see Braunstein-Bercovitz, 2000; see Chapter 1, section, 1.6.1.2) which begs the question as to whether schizotypy mediates the relationship between anxiety and learned irrelevance. Particularly given the limitations with previous latent inhibition methods and whether these findings actually represent learned irrelevance (see Chapter 2, section 2.1.5). Support for this investigation stems from further inspection of the results from Experiments 3, 4 and 6. Upon observation of the correlation matrices drawn from these experiments (see Tables 3.4, 3.8, 3.9, 4.3 and 4.4), there are significant positive correlations between both state and trait anxiety scores, and the schizotypy sub-dimensions. These significant correlations suggest that schizotypal scales may contain an anxiety factor. Furthermore, the data show a trend for individuals high in unusual experiences displaying reduced learning about both previously predictive and irrelevant cues, and thus a reduced effect of learned irrelevance. This is consistent with existing research findings that show an attenuated effect of learned irrelevance with individuals high in unusual experiences (see Le Pelley, 2010a; see also Chapter 1, section 1.5.2.1.1 and Chapter 3, section 3.1.5 for a discussion). These findings provide a basis for the subsequent analyses to investigate whether unusual experiences mediate

the relationship between state anxiety and learned irrelevance. To increase statistical power, the data from Experiments 3, 4 and 6 were combined in order to carry out a mediation analysis.

4.4.1 Scoring

The dependent variable for Experiment 3 (reaction time to the predictive and irrelevant cues) was inverted using the transformation $1/\text{reaction-time}$. This transformation ensured a comparable dependent variable across all experiments, allowing the data from each to be combined (Total $N = 242$). Z scores were then calculated for the predictive cue, irrelevant cue and the discrimination score (predictive cue minus irrelevant cue) for each experiment, to be used as the dependent variables. The state anxiety scores from Experiment 6, collected at the three separate time points (pre-test, post-test and follow up) were averaged across the 3 mood conditions to calculate an overall state anxiety scores for each participant, comparable to Experiments 3 and 4.

4.4.2 Preliminary analysis

Pearson product-moment correlation coefficients were computed between the discrimination scores, relevant and irrelevant cues for stage 2, and both state and trait anxiety subscales, and the four dimensions of the schizotypy subscale (Pearson's r , using all participants; see Table 4.5). As this initial part of the analysis was preliminary, no adjustments for multiple comparisons were made. Correlations were significant for the relevant-cue with; state anxiety $r = -.146$, $p = .035$; trait anxiety $r = -.136$, $p = .035$ and; unusual experiences $r = -.189$, $p = .033$. The irrelevant cue was also significantly correlated with unusual experiences $r = -.157$, $p = .015$, and the correlations approached significance for discrimination score and state anxiety $r = -.115$, $p = .074$, and unusual experiences $r = -.121$, $p = .060$.

Table 4.5

Correlation matrices among study variables for stage 2.

	Stage 2 Relevant Cue	Stage 2 Irrelevant Cue	State	Trait	UnEx	CogDis	ImpNon	IntrovAn
Discrimination Score	.236**	-.334**	-.115	-.078	-.121	-.084	.064	-.022
Stage 2 Relevant Cue		.761**	-.146*	-.136*	-.189**	-.106	-.048	-.024
Stage 2 Irrelevant Cue			-.069	-.095	-.157*	-.075	-.031	-.015
State				.682**	.369**	.461**	.176**	.280**
Trait					.452**	.675**	.255**	.263**
UnEx						.508**	.295**	.357**
CogDis							.366**	.234**
ImpNon								.124

Note. Values shown are Pearson's product-moment correlation coefficients.

** Correlation is significant at the 0.01 level.

* Correlation is significant at the 0.05 level.

Significant results are bolded.

4.4.3 Mediation analysis

To investigate whether unusual experiences mediates the relationship between state anxiety and learned irrelevance, a mediation analysis was conducted. A mediation analysis allows exploration of whether there is a variable(s), known as the mediator variable, which underlies an observed relationship between an independent and a dependent variable. A mediation model proposes that rather than a direct causal relationship between the independent variable (i.e., anxiety) and dependent variable (learned irrelevance), it is the independent variable which influences the mediator variable (i.e., schizotypy; unusual experiences), which in turn influences the dependent variable. Thus the mediator variable serves to clarify the nature of the relationship between the independent variable, and the dependent variable (Fields, 2008). A real world example is the positive correlation between ice cream sales (independent variable) and people drowning in the sea (dependent variable). The mediating variable is temperature; when it is hot more people go swimming in the sea, and eat ice cream.

The pre-requisite for mediation analysis is that the variables of interest are all significantly correlated; the independent variable and the proposed mediator must correlate, as must the independent variable and the dependent variable (Field, 2008). As can be seen from Table 4.5, both state and trait anxiety significantly correlate with unusual experiences, and each of these personality variables independently correlates with learning about the previously predictive cue (consistent with Experiments 3 and 4). Therefore, the aim of the subsequent analyses was to assess whether unusual experiences and trait anxiety mediate the relationship between state anxiety and learning in stage 2 about the previously predictive cue (Model 1), and whether unusual experiences and state anxiety mediate the relationship between trait anxiety and learning about the previously predictive cue (Model 2). Such findings would contribute and

extend existing knowledge regarding the relationship between schizotypy and anxiety, and their subsequent effects on learned variations in attention.

(1) Model 1: Unusual experiences and trait anxiety as mediators of the relationship between state anxiety and learning about the previously predictive cue

A mediation analysis was performed using bootstrapping analyses (see Preacher & Kelley, 2011) to test the mediation model of unusual experiences and trait anxiety as mediators of the relationship between state anxiety and learning about the previously predictive cue. In these analyses, mediation is significant if the 95% Bias Corrected and accelerated confidence intervals (BCa CI) do not include 0 (Preacher & Kelley). Refer to Figure 4.10 for the path diagram that corresponds to this mediation analysis.

Results based on 1000 bootstrapped samples indicated that whilst the total effect of state anxiety on learning towards the previously predictive cues was significant, $b = -.018$, BCa CI $[-.033, -.002, p = .023]$, the direct effect was not $b = -.010$, BCa CI $[-.031, .011, p = .346]$. There was a significant indirect effect of state anxiety on learning towards the previously predictive cue through unusual experiences, $b = -.007$, BCa CI $[-.014, -.001]$, and through trait anxiety, $b = -.007$, BCa CI $[-.014, -.001]$. Thus, individuals who indicated high levels of state anxiety, through high levels of unusual experiences, and through high levels of trait anxiety, showed reduced learning towards the previously predictive cue. A Sobel test indicated that only the indirect coefficient for state anxiety on learning towards the previously predictive cue through unusual experiences was significant ($z = -1.957, p < .05$, two tailed). However, because zero is not in the 95% CI for either indirect effects, both are considered significantly different

from zero at $p < .05$ (see Field, 2008 for a discussion regarding CI's as a more direct measure of statistical significance over the sobel test).

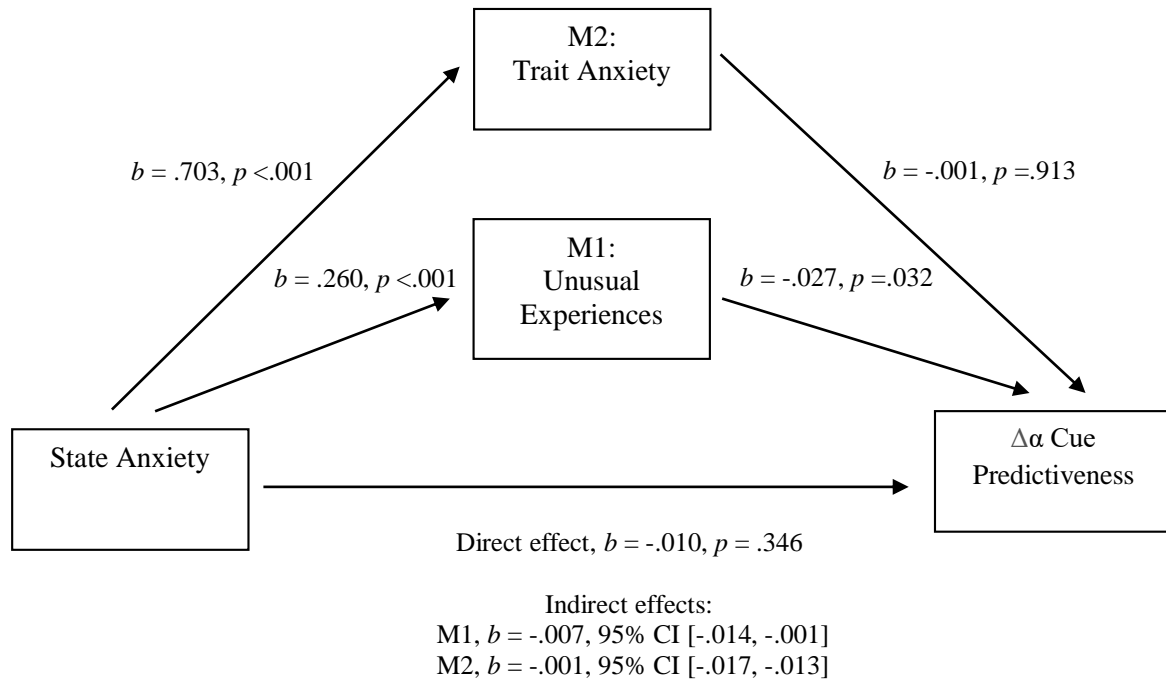


Figure 4.10. Model of state anxiety as a predictor of learned predictiveness, mediated by unusual experiences and trait anxiety. The CI for the indirect effect is a BCa bootstrapped CI based on 1000 samples. Arrow headers and beta coefficients indicate the predictive relationship between variables.

(2) Model 2: Unusual experiences and state anxiety as mediators of the relationship between trait anxiety and learning about the previously predictive cue

A mediation analysis was performed using bootstrapping analyses to test the mediation model of unusual experiences and state anxiety as mediators of the relationship between state anxiety and learning about the previously predictive cue. Comparable to model 1; mediation is significant if the 95% BCa CI's do not include 0 (Preacher & Kelley, 2011). Refer to Figure 4.11 for the path diagram that corresponds to this mediation analysis.

Results based on 1000 bootstrapped samples indicated that whilst the total effect of trait anxiety on learning towards the previously predictive cues was significant, $b = -.016$, BCa CI $[-.031, -.001, p = .035]$, the direct effect was not $b = -.001$, BCa CI $[-.022, .020, p = .913]$. There was a significant indirect effect of trait anxiety on learning towards the previously predictive cue through unusual experiences, $b = -.008$, BCa CI $[-.016, -.001]$, and through state anxiety, $b = -.007$, BCa CI $[-.021, .008]$. Thus, individuals who indicated high levels of trait anxiety, through high levels of unusual experiences, and through high levels of state anxiety, showed reduced learning towards the previously predictive cue. Similar to model 1, a sobel test indicated that only the indirect coefficient for trait anxiety on learning towards the previously predictive cue through unusual experiences was significant ($z = -1.957, p < .05$, two tailed). However, because zero is not in the 95% CI for either indirect effects, both are considered significantly different from zero at $p < .05$.

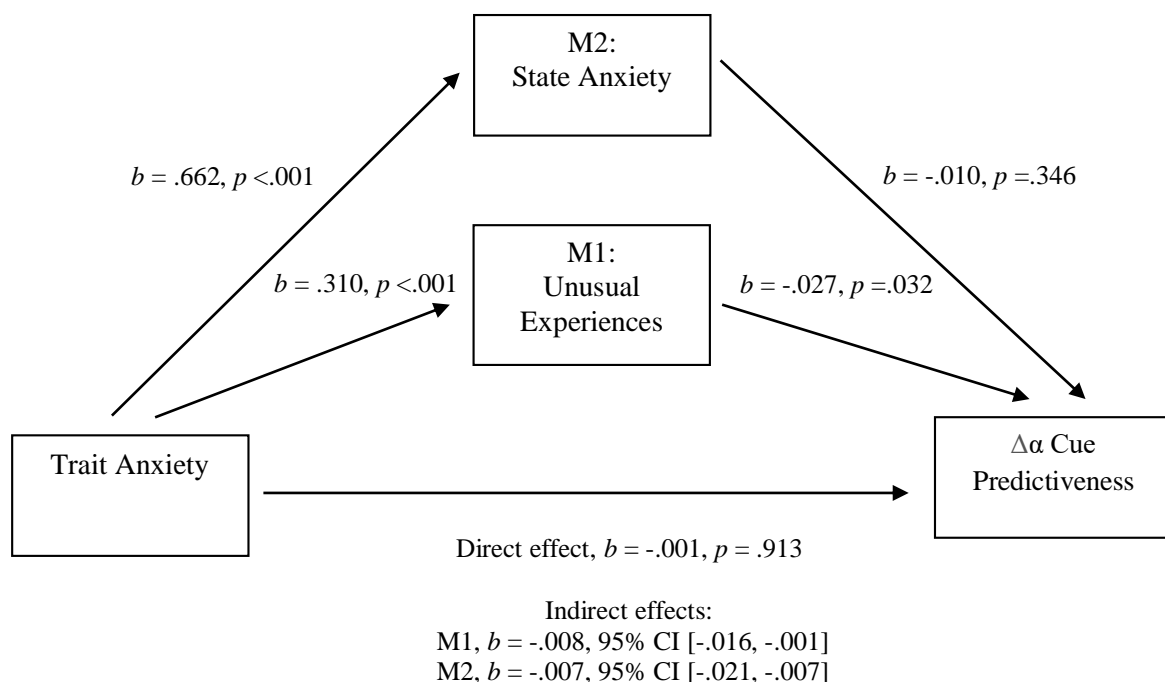


Figure 4.11. Model of trait anxiety as a predictor of learned predictiveness, mediated by unusual experiences and state anxiety. The CI for the indirect effect is a BCa bootstrapped CI based on 1000 samples. Arrow headers and beta coefficients indicate the predictive relationship between variables.

4.5 General Discussion

Across two experiments a mood induction procedure was used to examine the influence of state anxiety on learned attention, using an established learned irrelevance task (Le Pelley et al., 2010b). The mood manipulation procedures were successful in both Experiments 5 and 6 showing an increase in state anxiety from pre to post test in the speech stressor condition, a decrease in state anxiety in the relaxation condition, and little or no change in the neutral condition. A similar pattern of results was also observed at a post-task follow-up in Experiment 6. On the basis that stress elicits anxiety (e.g., Houston, 1987) it can then be assumed that anxiety levels per se, in the speech stressor group, were elevated as compared to the relaxation and neutral control groups.

Experiment 6 successfully demonstrated learned irrelevance: the significant effect of cue (assessed across all experiments) indicates that, overall, participants showed faster learning in stage 2 about cues that were previously relevant, than cues that were previously irrelevant. This finding replicates the effect of learned irrelevance observed by Le Pelley et al (2010b). This result is also anticipated by attentional theories of associative learning (Mackintosh, 1975; Kruschke, 2001) which suggest that the attention allocated to a cue is directly determined by the previously experience relevance of that cue.

Crucially however, the non-significant interaction between cue relevance and the 3 mood conditions indicates that there was no effect of the different mood induction conditions on learning about either the previously relevant cue, or the previously irrelevant cue. Thus, irrespective of whether participants are in either, a low, neutral or high state of anxiety, individuals overall devote more attention to stimuli that are good predictors of subsequent

events than stimuli that are followed by uncertain events. This finding is in contrast to Experiments 3 and 4 but interestingly, when the mood conditions were collapsed across into high and low anxiety groups, the results were comparable to Experiments 3 and 4. Low state anxious individuals showed increased learning towards the previously predictive cue with high anxiety individuals demonstrating a reduced attentional bias towards this cue. The main interaction between cue relevance and state anxiety (high and low groups) did however fail to reach the conventional criterion for statistical significance for Experiment 6. The weaker relationship between state anxiety and learned irrelevance observed here suggests variations in anxiety that have been generated in the current experiment do not have the same relationship with learning as naturally occurring variations in anxiety, as observed in Experiments 3 and 4. In Experiment 6, anxiety is manipulated in an acute manner, but it is unclear whether it is a chronic build-up of stressful life events that results in participant's level of state anxiety which consequently results in disrupted attentional processes. The latter effect of chronic stress might be what we are observing in Experiments 3 and 4. Support for this proposition comes from a study by Chajut and Algom (2003) that used an acute stressor task in healthy participants before presenting them with the Stroop task (Stroop, 1935) of selective attention. Here, the induction of acute stress using noise and impossible psychometric tests, served to improve attentional abilities on the Stroop task. The task irrelevant dimension of threat related words were not processed, and the resources available under stress were devoted in full to the task-relevant dimension of colour. Other studies have also reported a decrease in the Stroop effect (i.e., improved selectivity) under acute stress (e.g. Agnew & Agnew, 1963; Callaway, 1959; Folkard & Greeman, 1974; Glass & Singer, 1972; Houston, 1969; Houston & Jones, 1967; Huguet et al., 1999; O'Malley & Poplawsky, 1971; Tecce & Happ, 1964). On the basis of such results it has been suggested that once a stressor has been identified and appropriately managed, automatic attentional engagement related to threat may be overridden by more controlled,

higher level processes, resulting in attentional disengagement away from threat. Whereas, reduced attentional control due to chronic stress exposure may not be sufficiently overridden by higher level attentional processes, resulting in an enhancement of automatic attentional capture towards threat related stimuli (Chajut & Algom).

The current results present an extension of the above findings (Chajut & Algom, 2003) suggesting that acute levels of induced stress improve attentional selectivity towards the previously relevant cue compared to the previously irrelevant cue. On the other hand, it might be said that chronic stress precipitates the broadening of attention, rendering an individual vulnerable to intrusions from task irrelevant information; as can be seen in Experiments 3 and 4 and existing studies (e.g., Braunstein-Bercovitz, 2001). Regarding these latter findings, it is entirely plausible that participant's reported level of state anxiety is due to a chronic build-up of situational anxiety of which the consequence is disrupted learned attention; a disruption which is not observed with individuals experiencing an acute one off feeling of state anxiousness due to stress induction. The dissociation between acute and chronic anxiety and the subsequent effects of learned variations in attention is for future research to determine (see General Discussion section, Chapter 5 for a further discussion).

Interestingly however, the mediation analysis, which combined Experiments 3, 4 and 6, revealed that whilst there is a total effect of anxiety on learning about the previously predictive cue, indicating an overall relationship between these two variables, there is not a direct, effect of increased anxiety reducing learning towards the predictive cue. It is unusual experiences or trait anxiety that mediates this relationship between state anxiety and reduced learning about the previously predictive cue. Thus, the inability of high anxious individuals to direct attention towards cues with a history of predictiveness or irrelevance is governed by both

their high levels of positive schizotypy and their high levels of trait anxiety. Similarly, state anxiety or unusual experiences also mediate the relationship between trait anxiety and learned irrelevance. This finding is in accord with previous studies that have argued diminished latent inhibition in high schizotypal individuals to be the result of the high levels of anxiety which accompany schizotypy states (Braunstein-Bercovitz, 2000, 2001). The present results extend these findings using a less ambiguous measure of attention and suggest that diminished learned irrelevance in high state anxious individuals' is the result of high levels of schizotypy which accompany anxiety; suggesting a bi-directional relationship between anxiety and schizotypy characteristics. In further support of this finding; both state and trait anxiety sub-scales were correlated with unusual experiences, when collapsing across experiments 3, 4 and 6, which suggests a schizophrenia-like component in the anxiety scales, and vice versa. This is comparable with previous studies that have also found a relationship between schizotypy and anxiety scores (Braunstein-Bercovitz, 2000; Gibbons & Rammsayer, 1999).

As mentioned in the general introduction, the relationship between disrupted latent inhibition, anxiety/stress and schizotypy/schizophrenia has a well-established pharmacological basis (e.g. Gray et al., 1991; Gray, 1998). Studies have shown augmented dopaminergic activity in both schizophrenic (Caplan & Guthrie, 1994; Silver, 1994; Silver, 1995) and anxious (McIvor et al., 1996; Nutt et al., 1998; Peroutka et al., 1998) individuals and furthermore that latent inhibition is modulated by schizophrenia and stress. This evidence, together with the fact that existing latent inhibition paradigms encompass components of learned irrelevance, provides additional support for the present findings that learned irrelevance can be impaired in anxious (state or trait) individuals who are also characterised by high levels of positive schizotypy, and by extension vulnerability to schizophrenia. Although, in order to examine cognitive functioning in the form of learned irrelevance specifically in patient populations; it

is desirable that the neuropsychological, neuroanatomical and psychopharmacological basis of learned irrelevance and its disruption is examined in more detail. Here we can only speculate on the body of pharmacological research that exists for latent inhibition; of which the limitations have been extensively discussed in previous sections.

In summary, whilst the current experiments do not provide evidence that changes in acute induced anxiety have a causal effect on learned variations in attention, they do however provide evidence to suggest that under low anxiety conditions, individuals are able to learn about stimuli with a history of predictiveness and irrelevance. Whereas, individuals encountering high levels of anxiety accompanied by a vulnerability to schizophrenia are unable to direct attention and there is a breakdown in attentional-inhibitory processing. The outcome of such events may result in a relapse too or worsening of a pathological state. Future research suggestions that could explore these findings and propositions are discussed in the following, concluding chapter.

Chapter 5:

General Discussion

5.1 Discussion

5.1.1 Overview

Establishing how cognitive abnormalities result in the signs and symptoms that define schizophrenia and anxiety disorders has become a prominent question in clinically, and sub-clinically, applied research. Moreover, the prevalence of co-morbid anxiety disorders in individuals with schizophrenia has encouraged research to address how schizophrenia and anxiety might interact in relation to the cognitive deficits involved in both disorders. One attempt to understand the origins of these disorders is the study of cognitive endophenotypes, defined as quantifiable traits that can provide an illustrative link between neurological abnormalities and the expressed symptoms of a disorder. The identification of reliable endophenotypes will hopefully lead to improvements for treatments and could possibly be applied as prevention techniques for related disorders. Abnormal performance in schizotypy, schizophrenia and anxiety has been observed in comparison to healthy individuals on a range of cognitive and behavioural tasks.

Latent inhibition has been considered as one promising endophenotype, particularly in the study of schizophrenia. Abnormal attention to irrelevant information has long been recognised by clinicians, which has since encouraged researchers to elucidate the nature of the relationship between schizophrenia, and anxiety more recently, with allocation of attention to stimuli in laboratory studies providing empirical evidence for an attentional view of these disorders. However, there are a number of limitations encompassed within existing research, specifically regarding the nature of the latent inhibition paradigms that have been designed,

and whether they instead reflect the operation of learned irrelevance (see Le Pelley et al., 2010a). The present work has aimed to address some of the limitations with existing research and advance the literature to improve our current understanding of schizotypy and anxiety, and the cognitive abnormalities involved:

- 1) By designing a paradigm that examines a purer effect of latent inhibition, by minimising the contribution of learned irrelevance, and assessing how this latent inhibition task co-varies with both schizotypy and anxiety (Experiments 1 and 2).
- 2) By employing an alternative, less equivocal, learned attentional paradigm (learned irrelevance) and assessing the relationship between this task with both schizotypy and anxiety (Experiments 3 and 4).
- 3) By assessing the causal relationship between induced variations in anxiety (stress, relaxation or neutral mood) and learned variations in attention (Experiments 5 and 6); assessing whether schizotypy level mediates this relationship.

The aim across these experiments and analyses was to separate out the effects of latent inhibition and learned irrelevance, to enable an assessment of the difference/similarities in performance across these tasks in relation to schizotypy (and by extension schizophrenia), and anxiety. Taking converging evidence, from latent inhibition and learned irrelevance tasks, allowed the assessment of learned variations in attention in relation to schizotypy and anxiety. The mood induction study permitted insight into the causal nature of the relationship between anxiety, schizotypy and a less ambiguous measure of attention (compared to latent inhibition): learned irrelevance.

The following conclusions will highlight how this thesis has furthered existing research, by permitting advancement in the current understanding of the mechanisms disrupted in both schizotypy (by extension schizophrenia) and anxiety. How the use of these potentially more viable tools can be used to further investigate how schizotypy/schizophrenia and anxiety interact to produce cognitive abnormalities, is discussed in terms of future research.

5.1.2 Summary of findings

5.1.2.1 Experiments 1 and 2

a) Nature of the relationship between schizotypy and latent inhibition

The first aim was to design a within-participant's latent inhibition task which did not encompass the limitations found in many of the other within-participant latent inhibition tasks that have been reported in the literature (De la Casa & Lubow, 2001; Lubow & De la Casa, 2002; Swerdlow et al., 2003; Evans et al., 2007; Granger et al., 2012). Specifically, it is ambiguous whether they measure latent inhibition or other related learning phenomena. This makes the interpretation of existing findings difficult as we might instead be observing an effect of schizotypy on learned irrelevance or conditioned inhibition; both of which have been reported to vary with schizotypy (Migo et al., 2006; Le Pelley et al., 2010a). It was therefore important to develop a refined latent inhibition task so that future experiments can make clear predictions about the effect of experimental manipulations, based on the large human and animal literature that is available on latent inhibition (for a review see: Lubow & Weiner, 2010). This aim was successfully achieved, particularly with respect to Experiment 2, which minimised the possibility of either conditioned inhibition *or* learned irrelevance being observed in a within-participant latent inhibition design. Performance was nevertheless similar across Experiments 1 and 2, suggesting an effect that is specific to stimulus preexposure (latent inhibition).

The second aim was to determine whether any schizotypy dimensions co-varied with performance on these ‘purer’ latent inhibition tasks, where the contribution of conditioned inhibition and learned irrelevance are minimised. Both Experiments 1 and 2 demonstrated that individuals scoring higher on the unusual experiences dimension of the schizotypy sub-dimension of the O-LIFE showed slower learning of the stimulus-target association for preexposed stimuli throughout the trials, compared to lower scorers on this dimension. This in conjunction with the fact that there was no significant association between unusual experiences and learning about the non-preexposed stimulus suggests an enhancement of latent inhibition in individuals scoring higher on the positive dimension of schizotypy.

The current findings build upon existing research to suggest that the distribution of latent inhibition is not only heterogeneous in patients with schizophrenia; rather, a comparable distribution can also be observed in high schizotypy individuals. Whether the current result was a specific effect of the latent inhibition tasks developed here, or an effect of some other sub-clinical characteristic associated with schizotypy such as anxiety (i.e., Braunstein-Bercovitz, 2000, 2001), formed the basis of the additional analyses. These findings are discussed in the following section.

b) Additional analyses: Nature of the relationship between schizotypy, anxiety and latent inhibition

Existing research draws similarities in cognitive performance between schizotypy and anxiety (see Braunstein-Bercovitz, 2000, 2001, 2002) and demonstrates that co-morbidity rates of anxiety in schizophrenia are relatively high. Consequently, the purpose of the additional analyses was to address the research question posed by Braunstein-Bercovitz (2000); ‘Is the attentional dysfunction in schizotypy related to anxiety?’ In contrast to the results observed by Braunstein-Bercovitz, the current results however showed that neither component of anxiety,

state nor trait, influenced latent inhibition alone, or modulated the ability of schizotypy to modify learning about a preexposed stimulus. Thus the variations observed in latent inhibition are specific effects of schizotypy, as opposed to non-specific effects related to anxiety. The limitations associated with existing latent inhibition paradigms (i.e., the inclusion of a masking task) question the validity of the findings reported by Braunstein-Bercovitz (2000, 2001) which may explain these contradictory findings. Thus, the outcome of enhanced latent inhibition with positive schizotypy (unusual experiences) and an attenuation of latent inhibition with cognitive disorganisation (akin to the negative symptoms of schizophrenia), are the first demonstrations of these phenomena in a sub-clinical population: 1) using a *refined* latent inhibition task and 2) that can account for variations in latent inhibition as *specific* effects of schizotypy, and by extension schizophrenia, which are not underpinned by anxiety. Future research would benefit from the use of factor-analysis to assess the details of this relationship, which currently remains open to debate.

Overall, two within-participant experiments (Experiments 1 and 2) are reported that measure the effect of familiarity on learning without confounds of alternative effects that also retard learning and co-vary with schizotypy (e.g., learned irrelevance and conditioned inhibition). Consistent with some of the clinical literature (i.e., Raschle et al., 2001; Cohen et al., 2004; Gal et al., 2009), a positive association was found between the rate of learning to the familiar, but not the novel, stimulus and the unusual experiences dimension of schizotypy – implying abnormally persistent latent inhibition in high schizotypy individuals. The use of the task described in Experiment 2 is particularly encouraged, as this task successfully minimised the contribution of both conditioned inhibition and learned irrelevance on the preexposure effect. This implies a new procedure that is an efficient tool (taking only 7 minutes to complete) to investigate the anomalous expression of latent inhibition and presents a potentially useful

tool for assessing attentional dysfunction in schizophrenia, as well as other clinical and sub-clinical populations. The aim of Experiments 3 and 4 were to provide complimentary evidence of these findings using an alternative task that also measures an effect of attention on learning; learned irrelevance. If learned irrelevance is underpinned by the same unitary mechanism (e.g. Mackintosh, 1975) as latent inhibition, it would be expected that the effect of schizotypy, and anxiety, observed in a refined latent inhibition paradigm (Experiments 1 and 2) to be comparable in a learned irrelevance paradigm (Experiments 3 and 4).

5.1.2.2 Experiments 3 and 4

c) Nature of the relationship between schizotypy, anxiety and learned irrelevance

In contrast to latent inhibition, the learned irrelevance paradigm provides a less ambiguous measure of the impact of attention on learning (see Le Pelley et al., 2010a). The aim here was to employ a learned irrelevance procedure that could measure the associability of relevant versus irrelevant cues in subsequent learning, and subsequently assess the relationship between this task with measures of schizotypal traits and of anxiety. If differential performance on this task is related to high schizotypy (and by extension schizophrenia) in a similar way to that observed in Experiments 1 and 2, this would provide support for the attentional deficit view of schizophrenia.

Interestingly however, both Experiments 3 and 4 provide findings contrary to predictions. Based on the results from Experiments 1 and 2 (enhanced latent inhibition in high schizotypy individuals), a superior effect of learned irrelevance in high schizotypy individuals was expected. Instead, there were no significant correlations between schizotypy and overall discrimination score, and neither relevant nor irrelevant cues. The results of Experiments 3 and

4 are however comparable, as both sets of results indicate that the associability of the cue that was previously relevant, was higher than the cue that was previously irrelevant, but only in participants who were low in anxiety. Participants who were high in anxiety showed, numerically, the opposite pattern of results (increased learning to irrelevant cues), although the difference in the associability of these cues was not significant. These results indicate that we are observing an insensitivity to the difference between relevant and irrelevant information in high state anxiety individuals. This finding is also in contradiction to our prediction; based on the findings from Experiments 1 and 2, we expected to find no effect of anxiety on learned irrelevance. What these opposing findings mean, from Experiments 1 and 2; and Experiments 3 and 4, in terms of applications of attentional associative models to these sub-clinical traits and by extension, their related pathologies, is discussed in section 5.1.3.

Interestingly, and to the best of knowledge, the present data constitute the first observation of disrupted learned irrelevance in high state anxious individuals. Existing research findings suggest anxiety results in decreased attentional control, characterised by an increase in distractibility by irrelevant information (see Braunstein-Bercovitz et al., 2002; Eysenck et al., 2007, 2009). The current results corroborate this and extend it to circumstances in which attentional biases are acquired during learning. Here, people with high levels of state anxiety failed to show the normal attentional bias towards information that was relevant to the solution of a learning task. This suggests an association between everyday anxiety and a disruption of people's appropriate allocation of attention to stimuli based on their previous experiences. This discovery is important because the natural variation in attention that stems from people's interaction with the environment permits them to tune out irrelevance. If this is disrupted, then the repercussions are substantial, as a diminished ability to tune out irrelevance may slow the solution of complex tasks and perpetuate a focus on unimportant information (see Hullinger et

al., 2014). At this juncture however, the causal status of the relationship between disrupted learned attention and anxiety was unclear. It remained to be determined whether high anxiety caused an inability to direct attention, or alternatively whether the inability to distinguish previously relevant from irrelevant cues induced a state of anxiousness. Experiments 5 and 6, discussed in the following section, aimed to address this research proposition.

5.1.2.3 Experiments 5 and 6

a) Nature of the relationship between induced anxiety and learned irrelevance (PART 1)

The aim here was to introduce a mood induction procedure to examine the relative influence of induced state anxiety on learned attention, using the established learned irrelevance task previously employed in Experiment 4 (see also Le Pelley et al., 2010b). The effectiveness of stress, relaxation and neutral mood conditions to induce variations in levels of state anxiety were explored first before assessing their ability to influence learned variations in attention. Based on the findings from Experiments 3 and 4, a reduced attentional bias towards previously established predictive cues was expected in individuals induced with an acute state of anxiousness, relative to individuals induced with either a relaxed or neutral mood state.

Across both Experiments 5 and 6 mood induction procedures successfully manipulated participants' reported level of state anxiety. From pre-test to post-test state anxiety scores significantly increased for individuals in the speech stressor condition; decreased in the relaxation condition; with no significant difference in the neutral condition. A similar pattern of results across mood conditions was observed at follow-up in Experiment 6; suggesting participants' manipulated level of state anxiety sustained throughout the duration of the study. On the basis that stress elicits anxiety (e.g., Houston, 1987) it was assumed that state anxiety

levels per se, were elevated in the speech stressor condition as compared to the relaxation and neutral control conditions. We first assessed how the results compared to Experiments 3 and 4 by calculating a total state anxiety score and dichotomising participants into high and low anxiety groups, before moving on to investigate the 3 separate mood induced conditions and their relationship with learned irrelevance.

When the data were collapsed across the stress, relaxation and neutral mood conditions and participants scores dichotomised into high and low anxiety groups the pattern of results are comparable to Experiments 3 and 4. Only low state anxious individuals showed increased learning towards the cue that was previously relevant than the cue that was previously irrelevant; whereas high anxious individuals show a reduction of this effect. It is important to note the interaction between cue relevance and state anxiety (high vs low) in Experiment 6 was not significant but follow up analyses revealed a comparable pattern of results. This weaker relationship between state anxiety and learned irrelevance observed by the non-significant interaction suggests that induced variations in anxiety do not have the same relationship with learning as naturally occurring variations in anxiety, as observed in Experiments 3 and 4. This proposition is further supported by the non-significant interaction between cue relevance and the 3 individual mood conditions (stress, relaxation and neutral conditions), indicating no effect of induced variations in anxiety on learning about either the previously relevant or irrelevant cue. Interestingly, the pattern of results denoted by the speech, relaxation and neutral mood induction conditions indicate, if anything, an increase in learning towards the previously predictive cue in high state anxiety individuals (in the speech condition) compared to low state anxiety individuals (in the relaxation and neutral condition), albeit a non-significant result. This observation is in the opposite direction to the pattern of results reported in Experiments 3 and 4, and when these mood conditions are collapsed across and dichotomised into high/low

anxiety groups in Experiment 6. Suggesting that induced levels of acute anxiety have a fundamentally different effect on attentional processes and learning.

One attempt to explain the differing findings across Experiments 3, 4, and 6, is that the mood induction procedures utilised in Experiment 6 were designed to invoke an acute state of anxiety. At this juncture it is unclear whether it is a chronic build-up of stressful life events that push an individual's level of state anxiety to a certain threshold, and it is only when this chronic threshold is reached that the consequence is a disruption of attentional processes, resulting in an inability to tune out irrelevance. Previous research dissociates between acute and chronic stress, suggesting that induced acute stress leads to a narrowing of attention to task-relevant attributes, and thus improves attentional selectivity. Whereas chronic stress, lead to the broadening of attention, rendering the person vulnerable to intrusions from task irrelevant information (for a review see: Chajut & Algom, 2003). The results from Experiment 6 possibly lend support this dissociation as there was a trend for individual in the stress induced condition to demonstrate better learning about the previously relevant cue than individuals in the relaxation condition. Here it would be ideal to make a comparison with individuals who are experiencing a chronic state of anxiety; however, for Experiments 3 and 4 it is only possible to gauge participant's level of current experienced anxiety, not the duration of their symptomatology. Thus it would be of interest for future research to include an additional psychometric measure of symptom duration to assess whether it is symptom chronicity in high anxious individuals that correlates with their impaired attentional inhibition; disrupted learned irrelevance.

a) *Nature of the relationship between anxiety, schizotypy and learned irrelevance (PART 2): Mediation analysis*

The high correlations of schizotypal scale scores with anxiety scale scores suggest that schizotypal scales may contain an anxiety factor; and that anxiety scale scores may contain a schizotypy factor. This, together with data which indicate dopaminergic involvement in schizotypality (Caplan & Guthrie, 1994; Silver, 1995) and anxiety (McIvor et al., 1996; Nutt et al., 1998; Peroutka et al., 1998), and that anxious individuals are distracted by irrelevant stimuli as previously measured by 'latent inhibition' (Braunstein-Bercovitz, 2002; see Chapter 1, section, 1.6.1.2), reinforces the possibility that the co-existence of these states may account for the observed selective attention deficits in these individuals. Using a direct measure of learned irrelevance, the aim here was to assess whether schizotypy mediates the relationship between state anxiety and disrupted learned irrelevance, in a similar way to that previously investigated by Braunstein-Bercovitz (2000) with reference to latent inhibition. This aim was addressed using two mediation models. The first assessed whether unusual experiences and trait anxiety mediated the relationship between state anxiety and learning about the previously predictive cue (Model 1), and the second assessed whether unusual experiences and state anxiety mediated the relationship between trait anxiety and learning about the previously predictive cue (Model 2). In line with our predictions, the results from Model 1 suggest that it is only when unusual experiences and trait anxiety co-vary with state anxiety that individual's experience an inability to demonstrate the normal attentional bias towards information that had previously been relevant the solution of a learning task (disrupted learned irrelevance). Similarly, Model 2 revealed state anxiety and unusual experiences also mediate the relationship between trait anxiety and learned irrelevance.

Overall, these findings provide an important advancement in the current literature that learned irrelevance is impaired in anxious (state or trait) individuals who are also characterised

by high levels of schizotypy, and by extension vulnerability to schizophrenia. The predictive validity of psychometrically assessed positive and negative schizotypy to predict the development of schizophrenia-spectrum disorders has been supported by a 10-year longitudinal study carried out by Kwapil et al. (2013) in a non-clinical sample of University students (mean age = 19.3 years), thus representing a similar sample of participants to those reported in this thesis.

The current findings also support the suggestion that the co-variation between schizotypy, anxiety and latent inhibition observed by Braunstein-Bercovitz (2000, 2001) were actually observing an effect of learned irrelevance. How learned irrelevance co-varies with individuals experiencing clinically co-morbid anxiety with psychosis is a key area of focus for future research.

5.1.3 Implications of findings

Based on single-process models of attentional learning, such as Mackintosh (1975) and Pearce and Hall (1980), the mechanism underlying an effect of latent inhibition should be the same mechanism underling an effect of learned irrelevance. Both of these models assume that latent inhibition is generated by an attention-like mechanism, resulting from a reduction in the processing of the stimulus during non-reinforced preexposure. And, learned irrelevance is viewed as reflecting a change in the processing (in terms of a change in attention or associability) as a result of irrelevance pre-training. Thus Mackintosh (1975) explains latent inhibition and learned irrelevance as the result of a failure to encode the relationship between the preexposed stimulus and the US (see also Le Pelley, 2004; McLaren & Mackintosh, 2000). However, in contradiction to the assumptions of these models that assume there is only one mechanism of associability (α), the results of the current studies demonstrate a double

dissociation. Experiments 1 and 2 showed an enhanced effect of latent inhibition with schizotypy but not with anxiety, whereas Experiments 3 and 4 showed a reduced effect of learned irrelevance with anxiety, but not with schizotypy. The fact that schizotypy and anxiety did not have comparable effects on *both* latent inhibition and learned irrelevance suggests that these sub-clinical personality characteristics (and by extension their clinical counterparts) may influence attention differently and furthermore, that attention is not a unitary system. Thus neither the Mackintosh nor the Pearce-Hall model can provide a full account of the current results as such single-process models would assume that if schizotypy (or anxiety) modulates latent inhibition, it should also modulate learned irrelevance in the same way. The following sections discuss the limitations of single-process models before moving on to describe how the current results provide novel support for dual-process models of attention and learning.

One problem with assuming a single theory of associability is that the single-process models conflict with each other in the *view* of associability that they support. For example, the approach developed in the Mackintosh (1975) model was that good predictors of an outcome maintain high associability, while the associability of poor predictors falls. The results of various extant studies (e.g., Le Pelley and McLaren, 2003; Le Pelley et al., 2010a; Haselgrove et al., 2015) provide support for this view. Contrastingly, the Pearce-Hall model instead suggests that learning proceeds faster with stimuli that are inaccurate predictors of an outcome, and slows with stimuli that are accurate predictors of an outcome (e.g., Kaye & Pearce, 1984). As a consequence of the evidence supporting these two opposing views of associability, dual process models of attention on learning have been proposed (e.g., Le Pelley, 2004; Esber & Haselgrove, 2011). Such models combine the ideas encapsulated in both the Mackintosh and Pearce-Hall models in an attempt to capture the strengths of each and provide a full account of the way in which processing afforded to a stimulus changes as the result of past experience.

Le Pelley (2004) proposed that the simplest way to reconcile the Mackintosh (1975) and Pearce-Hall (1975) models would be to describe them as each measuring different properties of a cue, rather than being rival descriptions of the same property (associability). In this way Le Pelley describes the Mackintosh α as ‘attentional associability’, determining which stimuli should be selected for learning on the basis of their predictive history; and describes the Pearce-Hall α as ‘salience associability’, determining how much should be learnt about those stimuli, given that they have been selected. Given these proposed differences, Le Pelley labelled ‘attentional associability’ of the Mackintosh model as α and the ‘salience associability’ of the Pearce-Hall model as σ and incorporated the two properties as multiplicative factors for associability change, thus creating a dual-process model of associability. Applied to learned irrelevance, this model suggests that during uncorrelated CS/US exposure, the CS is a poorer predictor of the US than is the experimental context, and thus the attentional associability (α_{CS} determined by the Mackintosh, 1975 equations) of the CS will fall. As the CS and the context is a relatively poor predictor of the US, the salience associability of the CS (σ_{CS} determined by the Pearce-Hall, 1980 equations) will be relatively high. However, the low α of the CS following uncorrelated CS/US exposure will ensure that learning between the CS and US during subsequent conditioning will be slower compared to a novel CS. Applied to latent inhibition, this dual process model assumes that preexposure to a CS with no consequence (in the absence of reinforcement) will thus not affect α_{CS} but because the absence of reinforcement following the CS are not surprising, there will be a decline in σ_{CS} . Consequently, non reinforced exposure to the CS will reduce its ability to enter into an association with the US on subsequent conditioning trials, compared to a novel CS that has not been exposed to this decrease in salience associability. As such, this model can account for the independent effects of learned irrelevance by including a variable of attentional associability (following the Mackintosh approach) and of latent inhibition by including a variable of salience associability (following

the Pearce-Hall approach). This model therefore demonstrates that latent inhibition and learned irrelevance can be separated into dissociable components and the current findings provide a novel confirmation of this by demonstrating the modulation of these separable effects and their double dissociation with schizotypy and anxiety. How the current results also provide support for an alternative dual process model of attention on learning (Esber & Haselgrove, 2011) is discussed next.

The preceding discussion has focused on a dual process (hybrid) model which specifies how the components of the Mackintosh model (1975) and the Pearce-Hall model (1980) interact such that the appropriate mechanism dominates under a given set of circumstances (Le Pelley, 2004). Ultimately, suggesting that two different kinds of attentional mechanism are required to account for the effects of predictiveness and uncertainty. A second approach taken by Esber and Haselgrove (2011) however emphasises a single attentional process based on predictiveness (Mackintosh model), but in such a way so that the model can also account for uncertainty effects (Pearce-Hall model). In the spirit of the Mackintosh model, Esber and Haselgrove suggested that a cue acquires salience as a consequence of becoming a good predictor of outcomes, and loses salience as a consequence of being predicted by other events (e.g. the context).

Applied to the results of the current experiments to the Esber-Haselgrove (2011) model then; the finding that attention is increased to good predictors of subsequent events (learned irrelevance; Experiments 3 and 4) and that attention can be reduced as a consequence of an outcome being predicted (latent inhibition; Experiments 1 and 2) can be fully accounted for with the Esber-Haselgrove model. Comparable to the application of the current findings to Le Pelley's (2004) dual process model, the current findings thus present a novel confirmation of

the extant literature by demonstrating the modulation of these separable effects and their double dissociation with schizotypy and anxiety. Aside from associative learning theory, there are other reasons why the current double dissociation between learned irrelevance with schizotypy and anxiety may have been observed; these possibilities are discussed below.

Other possibilities to consider for the observed double dissociation across the current experiments are simply that non-attentional accounts of latent inhibition (e.g. Hall, 1991; Bouton, 1993; 1997) may instead have some role in determining latent inhibition disruptions in schizophrenia. This would suggest the learned irrelevance paradigm to be a more reliable potential endophenotype. Another reason however could be that the current latent inhibition experiments are generating a purer effect of preexposure than has previously been demonstrated in the literature. As discussed in detail previously; many existing latent inhibition paradigms have been confounded by learned irrelevance and thus it is problematic to know whether existing schizotypy-latent inhibition findings (e.g. Evans et al., 2007; Schmidt-Hansen et al., 2009; Granger et al., 2012) are actually showing a relationship between schizotypy and learned irrelevance (Le Pelley et al., 2010a). Thus, by disentangling the effects of latent inhibition and learned irrelevance in the current experiments instead allowed an assessment of their independent effects on schizotypy and anxiety. Whilst schizotypy did not have a direct effect on learned irrelevance in the current experiments, it was found to mediate the relationship between anxiety and learned irrelevance which provides a novel extension of existing research findings in this area (Braunstein-Bercovitz, 2000, 2001; Le Pelley et al., 2010a). The fact that schizotypy did not have a direct effect on learned irrelevance could also have something to do with the inherent difference between single and compound learned irrelevance tasks. The learned irrelevance study by Le Pelley et al. (2010a) used a compound cue task (as opposed to the single cue task used in the current experiments) and reported a reduced learned irrelevance

effect in high positive schizotypy individuals. Within such compound cue paradigms, two cues (one relevant and one irrelevant cue) are presented on each trial. Thus if it is an inability of high schizotypal individuals and by extension schizophrenia, to block out irrelevant information then we can imagine the sensitivity to detect this effect to be higher in a task where participants have to choose between which two cues on the screen to pay attention too, as opposed to one single cue. This idea is explored further in section 5.1.4 for future research considerations.

Nevertheless, the results from Experiments 3 and 4, contribute to existing knowledge regarding an attention deficit in individuals in a transient state of anxiety, when only using single cue training. This finding supports the proposal that anxious individuals not only exhibit a ‘specific’ hyper-vigilance towards threat related stimuli, but also a ‘general’ hyper-vigilance towards any task-irrelevant stimuli, in the absence of threat. In an extension of this finding, the key result from Experiment 6, suggests it is only when an individual experiences either state or trait anxiety accompanied by a vulnerability to psychotic tendencies that the end result is a disrupted learned attentional bias. Given the potential common underlying cognitive processes to both anxiety and schizophrenia, it seems likely that therapies which target the symptoms of anxiety (e.g., ABMT) would also be beneficial to individuals who have also been diagnosed with a psychotic disorder. Primary benefits may not only involve anxiety reduction but also reduced levels of schizophrenic symptomology; something which to the best of current knowledge has not been empirically reported in the literature. The clinical application of harnessing cognitive bias modification therapy developments for co-morbid anxiety and schizophrenia, are discussed in the following section.

5.1.4 Clinical applications and future directions for research

Although clinical application and avenues for future research have been discussed in previous chapters, when the current research is viewed as a whole, a number of particularly promising avenues emerge.

As previously discussed; the mediation analysis suggests that unusual experiences and trait anxiety together mediate the relationship between state anxiety and learned variations in attention; and similarly that unusual experiences together with state anxiety mediates the relationship between trait anxiety and learned variations in attention. The fact that all three variables predict disrupted learned irrelevance provides an extension of the findings reported by Braunstein-Bercovitz (2001, 2002) which also suggest schizotypy, trait anxiety and induced-stress account for the disrupted ability to tune out irrelevance. Braunstein-Bercovitz (2000, 2001) demonstrated these findings using a latent inhibition task but as previously discussed this paradigm encompasses components of learned irrelevance; which provides a parsimonious comparison for the present results.

Additionally, as briefly mentioned in the preceding sections, the identified mediators possibly account for the non-significant interaction observed between mood condition and cue predictiveness in Experiment 6 (see Chapter 4; section 4.3.2.3), as there were unknown co-variates associated with induced state anxiety that were not experimentally manipulated. Thus it would be of interest for future research to not only experimentally manipulate anxiety but to also manipulate levels of schizotypy to fully examine the proposed mediation model. This proposition follows from the evidence that dopamine signalling is associated with normal variation in schizotypal traits. Following dopamine challenge, Woodward et al (2011)

demonstrated that total scores on the schizotypal personality questionnaire (SPQ; Raine, 1991) were correlated with dopamine release in the striatum. This, together with evidence of augmented dopamine release in patients with schizophrenia experiencing an acute phase of the illness; and a transient increase in positive psychotic symptoms in individuals with schizotypal personality disorder (Laruelle et al., 1999), suggests the link between d-amphetamine induced dopamine release and schizophrenia extends to normal variation in schizotypal personality traits. In addition to this, a relationship between increased dopaminergic activity and anxiety has also been established (McIvor et al., 1996; Nutt et al., 1998; Peroutka et al., 1998). Thus, D-amphetamine induced dopamine release may be a useful endophenotype for investigating the pharmacologic effects on cognition in relation to *both* schizophrenia and anxiety disorders. Further understanding of the genetic basis of schizophrenia and anxiety and importantly, how they interact, will allow further insight into how cognition might be pharmacologically improved which represents a major target for novel therapeutics in both clinical conditions.

The implication is that people with diagnosed anxiety and schizophrenia will show reduced learned irrelevance in this task, and this remains for future research with a clinical population to determine. More generally though, this approach has the potential to disambiguate the psychological mechanisms underlying both psychiatric disorders and hence to advance our understanding of the cognitive changes associated with vulnerability to co-morbid anxiety with psychosis. Thus, it would seem that current emerging technologies aimed at changing the cognitive biases underlying anxiety (i.e., Mathews and Macleod, 2000; Hertel, 2002; Mackintosh et al., 2006; Mathews et al., 2007; Koster et al., 2009) require continued development for the high proportion of individuals with schizophrenia who are distressed by co-morbid anxiety. In support of this suggestion, existing findings suggest anxiety processes such as scanning for threat and confirmation bias are also common within psychosis, and it is

these underlying psychological processes which are associated with the onset and maintenance of phenomena associated with both conditions (Garety et al., 2001). Thus, it seems likely that therapies which target these symptoms would also be beneficial to individuals who have also been diagnosed with schizophrenia.

However, there are a number of key questions that remain for future research to determine in order to understand in more detail, the complexity of the interaction between learned attention, anxiety and schizotypy. One question for future research would be to examine whether there are differences between the current results utilising a single cue learned irrelevance task and the development of a compound cue design (as previously used by Le Pelley et al., 2010a). As discussed in the previous section, it is possible that the intrinsic differences between these designs are accountable for why Le Pelley et al (2010a) noted a direct effect of schizotypy on learned irrelevance whereas the current experiences did not. Moreover, it would be of interest to explore the effects of state versus trait anxiety on a compound cue learned irrelevance task as existing studies (e.g. Pacheco-Unguetti, Acosta, Callejas & Lupiáñez, 2010) have demonstrated that different types of anxiety (state or trait) influence attentional processes differently. Trait anxiety for example has been associated with an impoverished attentional control for inhibiting distractor information (i.e., when two stimuli are presented and thus compete for processing resources) (Pacheco-Unguetti et al.). Such findings suggest a reason why we did not observe a direct effect of trait anxiety on learned irrelevance using a single cue task (as only one cue is present and thus there is no competition for processing resources). Such comparisons remain for future research to explore. It is also important to highlight that there is a large literature evaluating gender differences in learned attention tasks, particularly in the latent inhibition and schizotypy literature (see Baruch et al., 1988a; Lubow et al., 2002 for a review). Thus future research may wish to consider exploring

the effects of gender to better understand the relationship between learned attention, schizotypy and anxiety.

Predominantly, future research should endeavour to refine the current understanding of how anxiety and schizotypy disrupt learned attention in the real world environment. Through the use of online data collection, diary studies could be deployed where participants provide measurements of the types and levels of their anxieties, unusual experiences and variations in their attention. Coupled with this, participants could complete the learned irrelevance task outlined in Experiment 4 (and subtly different variations of this task i.e., a compound cue) over a period of 6-7 days to provide an insight into how cognition co-varies with the wax and wane of everyday chronic anxiety and variations in psychotic experiences. The use of focus groups with the general public and relevant stakeholders would provide qualitative data on the influence of anxiety, schizotypy and learned attention and provide an evidence base for the continued development of the relevant interventions discussed (i.e., attentional bias modification treatment). An extension of this idea would be to run a study using wireless activity trackers to collect real time psychophysiological data such as heart rate and galvanic skin response that could be used to corroborate the self-report, psychometric measure of anxiety (STICSA; Ree et al., 2008), and also schizotypy (O-LIFE; Mason et al., 1995) used in the current studies. The learned irrelevance task could be programmed on an App so that completion of the task could take place whilst psychophysiological data is recorded. This type of study could, in real time, assess the co-variation between cognition and symptoms of anxiety and psychotic experiences, which is key research that can appropriately inform future ‘attention based’ interventions for both sub-clinical/at risk populations for anxiety and schizophrenia.

5.1.5 Conclusions

This thesis has aimed to address some of the key questions and limitations with existing research that evaluate latent inhibition and learned irrelevance as potentially useful cognitive endophenotypes for schizophrenia and anxiety disorders. Across 6 experiments, the findings suggest dissociation between schizotypy, anxiety and attention on learning using latent inhibition and learned irrelevance paradigms and urge continued use of the less ambiguous paradigm; learned irrelevance (as described in Experiment 4), as a potential cognitive endophenotype for both clinical disorders.

The evidence presented in Experiments 1 and 2 suggest that a refined measure of latent inhibition generates an enhanced expression of latent inhibition, underpinned by the positive symptom dimension of schizotypy, unusual experiences, and an attenuation of latent inhibition, underpinned by the cognitive disorganisation dimension of schizotypy. These effects are independent of anxiety related symptoms. To the best of knowledge, the current data constitute the first demonstration of an enhanced latent inhibition effect in a non-clinical population, suggesting a heterogeneous latent inhibition distribution exists in both patients with schizophrenia and in high schizotypy individuals.

Across Experiments 3 and 4, learned irrelevance did not provide complementary evidence of the latent inhibition work. Instead, a reduced learned irrelevance effect was observed in high, state anxious individuals, with no direct effect on schizotypy. If anything there was a trend for reduced learned irrelevance on schizotypy – the opposite of that observed in the latent inhibition experiments. This observed double dissociation suggests latent inhibition and learned irrelevance are not governed by the same underlying, attentional

mechanism, which provides a way in which to challenge the single-process model of learning and attention (e.g., Mackintosh, 1975; Pearce & Hall, 1980). Instead, the current results advocate a dual process model of attention on learning that can separate the effects of latent inhibition and learned irrelevance into dissociable components (e.g., Le Pelley, 2004; Esber & Haselgrove, 2011) and furthermore, that these can be modulated independently by schizotypy and anxiety; providing a novel confirmation of the existing literature. At this juncture though, it appears that there is an association between schizotypy and learned irrelevance, and it is this relationship that underlies deficits in selective attention (as previously demonstrated in existing research; Braunstein-Bercovitz et al., 2002) and in extension, learned variations in attention. This effect is only demonstrated however using the learned irrelevance paradigm (which also confounds Braunstein-Bercovitz' findings); as opposed to the latent inhibition paradigm. A developed understanding of the pharmacological basis of learned irrelevance will shed more light on whether the two learning paradigms are similar or different.

This work represents the first attempt to investigate the independent effects of latent inhibition and learned irrelevance on schizotypy and anxiety, using refined tasks that minimised the contribution of either learning phenomenon on each other. How these learning tasks co-vary in patients with schizophrenia and clinically diagnosed anxiety remains for future research to determine. The experiments reported in this thesis are considered the first step in attempting to truly disentangle the attention deficit in schizophrenia and anxiety disorders by considering their degree of overlap and thus their co-morbidity in sub-clinical populations.

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Appendices

Appendix 1: DSM-V Schizophrenia Diagnostic Criteria

Diagnostic Criteria	Schizophrenia 295.90 (F20.9)
<p>A. Two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated). At least one of these must be (1), (2), or (3):</p> <ol style="list-style-type: none"> 1. Delusions. 2. Hallucinations. 3. Disorganized speech (e.g., frequent derailment or incoherence). 4. Grossly disorganized or catatonic behavior. 5. Negative symptoms (i.e., diminished emotional expression or avolition). <p>B. For a significant portion of the time since the onset of the disturbance, level of functioning in one or more major areas, such as work, interpersonal relations, or self-care, is markedly below the level achieved prior to the onset (or when the onset is in childhood or adolescence, there is failure to achieve expected level of interpersonal, academic, or occupational functioning).</p> <p>C. Continuous signs of the disturbance persist for at least 6 months. This 6-month period must include at least 1 month of symptoms (or less if successfully treated) that meet Criterion A (i.e., active-phase symptoms) and may include periods of prodromal or residual symptoms. During these prodromal or residual periods, the signs of the disturbance may be manifested by only negative symptoms or by two or more symptoms listed in Criterion A present in an attenuated form (e.g., odd beliefs, unusual perceptual experiences).</p> <p>D. Schizoaffective disorder and depressive or bipolar disorder with psychotic features have been ruled out because either 1) no major depressive or manic episodes have occurred concurrently with the active-phase symptoms, or 2) if mood episodes have occurred during active-phase symptoms, they have been present for a minority of the total duration of the active and residual periods of the illness.</p> <p>E. The disturbance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition.</p> <p>F. If there is a history of autism spectrum disorder or a communication disorder of childhood onset, the additional diagnosis of schizophrenia is made only if prominent delusions or hallucinations, in addition to the other required symptoms of schizophrenia, are also present for at least 1 month (or less if successfully treated).</p>	

Appendix 2: DSM-V Generalized Anxiety Disorder (GAD) Diagnostic Criteria

Generalized Anxiety Disorder	
Diagnostic Criteria	300.02 (F41.1)
<p>A. Excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least 6 months, about a number of events or activities (such as work or school performance).</p> <p>B. The individual finds it difficult to control the worry.</p> <p>C. The anxiety and worry are associated with three (or more) of the following six symptoms (with at least some symptoms having been present for more days than not for the past 6 months):</p> <p>Note: Only one item is required in children.</p> <ol style="list-style-type: none">1. Restlessness or feeling keyed up or on edge.2. Being easily fatigued.3. Difficulty concentrating or mind going blank.4. Irritability.5. Muscle tension.6. Sleep disturbance (difficulty falling or staying asleep, or restless, unsatisfying sleep). <p>D. The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.</p> <p>E. The disturbance is not attributable to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition (e.g., hyperthyroidism).</p> <p>F. The disturbance is not better explained by another mental disorder (e.g., anxiety or worry about having panic attacks in panic disorder, negative evaluation in social anxiety disorder [social phobia], contamination or other obsessions in obsessive-compulsive disorder, separation from attachment figures in separation anxiety disorder, reminders of traumatic events in posttraumatic stress disorder, gaining weight in anorexia nervosa, physical complaints in somatic symptom disorder, perceived appearance flaws in body dysmorphic disorder, having a serious illness in illness anxiety disorder, or the content of delusional beliefs in schizophrenia or delusional disorder).</p>	

Appendix 3: The O-LIFE (Mason et al., 1995)

[1] Do you prefer reading to meeting people?	YES	NO
[2] Do you often hesitate when you are going to say something in a group of people whom you more or less know?	YES	NO
[3] Are you always willing to admit it when you have made a mistake?	YES	NO
[4] Do you sometimes put off until tomorrow what you ought to do today?	YES	NO
[5] Do you often overindulge in alcohol or food?	YES	NO
[6] Do you often feel that people have it in for you?	YES	NO
[7] Are the sounds you hear in your day-dreams really clear and distinct?	YES	NO
[8] Do you enjoy many different kinds of play and recreation?	YES	NO
[9] Do your thoughts sometimes seem as real as actual events in your life?	YES	NO
[10] Do you have many different hobbies?	YES	NO
[11] Does it often happen that nearly every thought immediately and automatically suggests an enormous number of ideas?	YES	NO
[12] When in a group of people do you usually prefer to let someone else be the centre of attention?	YES	NO
[13] If you say you will do something do you always keep your promise no matter how		

inconvenient it might be?	YES	NO
[14] Do you frequently have difficulty in starting to do things?	YES	NO
[15] Has dancing or the idea of it always seemed dull to you?	YES	NO
[16] When you catch a train do you often arrive at the last minute?	YES	NO
[17] Is trying new foods something you have always enjoyed?	YES	NO
[18] Do you always wash before a meal?	YES	NO
[19] Do you believe in telepathy?	YES	NO
[20] Do you often change between intense liking and disliking of the same person?	YES	NO
[21] Have you ever cheated at a game?	YES	NO
[22] Are there very few things that you have ever really enjoyed doing?	YES	NO
[23] Would you call yourself happy-go-lucky?	YES	NO
[24] Do you at times have an urge to do something harmful or shocking?	YES	NO
[25] Do you often worry about things you should not have done or said?	YES	NO
[26] Are your thoughts sometimes so strong that you can almost hear them?	YES	NO
[27] Do you usually take the initiative in making new friends?	YES	NO
[28] Do your thoughts ever stop suddenly causing you to interrupt what you are saying?	YES	NO
[29] Are you usually in an average sort of mood, not too high and not too low?	YES	NO
[30] Do you often take on more activities than you have time for?	YES	NO
[31] Would you take drugs which may have strange or dangerous effects?	YES	NO

[32] Do you think you could learn to read other s minds if you wanted to?	YES	NO
[33] When in a crowded room, do you often have difficulty in following a conversation?	YES	NO
[34] No matter how hard you try to concentrate do unrelated thoughts always creep into your mind?	YES	NO
[35] Are you easily hurt when people find fault with you or the work you do?	YES	NO
[36] Do you stop to think things over before doing anything?	YES	NO
[37] Have you ever felt that you have special, almost magical powers?	YES	NO
[38] Are you much too independent to really get involved with other people?	YES	NO
[39] Do you ever get nervous when someone is walking behind you?	YES	NO
[40] Do ideas and insights sometimes come to you so fast that you cannot express them all?	YES	NO
[41] Do you easily lose your courage when criticized or failing in something?	YES	NO
[42] Can some people make you aware of them just by thinking about you?	YES	NO
[43] Does a passing thought ever seem so real it frightens you?	YES	NO
[44] Do you always practice what you preach?	YES	NO
[45] Would you dodge paying taxes if you were sure you could never be found out?	YES	NO
[46] Have you ever blamed someone for doing something you know was really your fault?	YES	NO
[47] Are you a person whose mood goes up and down easily?	YES	NO
[48] Does your voice ever seem distant or faraway?	YES	NO
[49] Do you think having close friends is not as important as some people say?	YES	NO
[50] Do you like doing things in which you have to act quickly?	YES	NO

[51] Are you rather lively?	YES	NO
[52] Do you feel at times that people are talking about you?	YES	NO
[53] Are you sometimes so nervous that you are blocked ?	YES	NO
[54] Do you find it difficult to keep interested in the same thing for a long time?	YES	NO
[55] Have you ever insisted on having your own way?	YES	NO
[56] Do you dread going into a room by yourself where other people have already gathered and are talking?	YES	NO
[57] Have you ever felt that you were communicating with someone telepathically?	YES	NO
[58] Does it often feel good to massage your muscles when they are tired or sore?	YES	NO
[59] Do you sometimes feel that your accidents are caused by mysterious forces?	YES	NO
[60] Do you like mixing with people?	YES	NO
[61] On seeing a soft thick carpet have you sometimes had the impulse to take off your shoes and walk barefoot on it?	YES	NO
[62] Can you get a party going?	YES	NO
[63] Do you often have difficulties in controlling your thoughts?	YES	NO
[64] Do you feel that you cannot get close to other people?	YES	NO
[65] Do the people in your daydreams seem so true to life that you sometimes think they are real? YES	NO	
[66] Do other people think of you as being very lively?	YES	NO
[67] Are people usually better off if they stay aloof from emotional involvements with people?	YES	NO

[68] Have you ever broken or lost something belonging to someone else?	YES	NO
[69] Are you mostly quiet when you are with other people?	YES	NO
[70] Can just being with friends make you feel really good?	YES	NO
[71] Do you enjoy meeting new people?	YES	NO
[72] Is your hearing sometimes so sensitive that ordinary sounds become uncomfortable?	YES	NO
[73] Have you often felt uncomfortable when your friends touch you?	YES	NO
[74] When things are bothering you do you like to talk to other people about it?	YES	NO
[75] Do you ever have the sensation that your body or a part of it is changing shape?	YES	NO
[76] Do you have many friends?	YES	NO
[77] Are all your habits good and desirable ones?	YES	NO
[78] Do you tend to keep in the background on social occasions?	YES	NO
[79] Have you ever taken anything (even a pin or a button) that belonged to someone else?	YES	NO
[80] As a child were you ever cheeky to your parents?	YES	NO
[81] Would being in debt worry you?	YES	NO
[82] Have you ever felt when you looked in a mirror that your face seemed different?	YES	NO
[83] Do you think people spend too much time safeguarding their future with savings and insurance?	YES	NO
[84] Do you believe that dreams can come true?	YES	NO
[85] Do you ever have the urge to break or smash things?	YES	NO

[86] Do you often feel that there is no purpose to life?	YES	NO
[87] Do things sometimes feel as though they were not real?	YES	NO
[88] Do you worry about awful things that might happen?	YES	NO
[89] Have you ever felt the urge to injure yourself?	YES	NO
[90] Would it make you nervous to play the clown in front of other people?	YES	NO
[91] Do you prefer watching television to going out with other people?	YES	NO
[92] Have you felt that you might cause something to happen just by thinking too much about it?	YES	NO
[93] Have you had very little fun from physical activities like walking, swimming, or sports?	YES	NO
[94] Have you ever been late for an appointment or work?	YES	NO
[95] Have you ever said anything bad or nasty about anyone?	YES	NO
[96] Do you feel so good at controlling others that it sometimes scares you?	YES	NO
[97] Are you easily distracted from work by daydreams?	YES	NO
[98] Are you easily confused if too much happens at the same time?	YES	NO
[99] Do you ever have a sense of vague danger or sudden dread for reasons that you do not understand?	YES	NO
[100] Is it true that your relationships with other people never get very intense?	YES	NO
[101] Do you feel that you have to be on your guard even with your friends?	YES	NO
[102] Have you sometimes had the feeling of gaining or losing energy when certain people look at you or touch you?	YES	NO

[103] When coming into a new situation have you ever felt strongly that it was a repeat of something that had happened before?	YES	NO
[104] Do you worry too long after an embarrassing experience?	YES	NO
[105] Do you love having your back massaged?	YES	NO
[106] Do you consider yourself to be pretty much an average kind of person?	YES	NO
[107] Have you ever taken advantage of someone?	YES	NO
[108] Would you like other people to be afraid of you?	YES	NO
[109] Have you ever thought you heard people talking only to discover that it was in fact some nondescript noise?	YES	NO
[110] Have you occasionally felt as though your body did not exist?	YES	NO
[111] Do you often feel lonely?	YES	NO
[112] Do you often have an urge to hit someone?	YES	NO
[113] Do you often experience an overwhelming sense of emptiness?	YES	NO
[114] On occasions, have you seen a person s face in front of you when no one was in fact there?	YES	NO
[115] Do you feel it is safer to trust nobody?	YES	NO
[116] Is it fun to sing with other people?	YES	NO
[117] Do you often have days when indoor lights seem so bright that they bother your eyes?	YES	NO
[118] Have you wondered whether the spirits of the dead can influence the living?	YES	NO
[119] Do people who try to get to know you better usually give up after a while?	YES	NO

[120] Do you often feel fed up ?	YES	NO
[121] Have you felt as though your head or limbs were somehow not your own?	YES	NO
[122] Do you ever become oversensitive to light or noise?	YES	NO
[123] When you look in the mirror does your face sometimes seem quite different from usual?	YES	NO
[124] Do you nearly always have a ready answer when people talk to you?	YES	NO
[125] Do people who drive carefully annoy you?	YES	NO
[126] Do you like telling jokes and funny stories to your friends?	YES	NO
[127] Do you sometimes boast a little?	YES	NO
[128] Are you very hurt by criticism?	YES	NO
[129] Do you feel lonely most of the time, even when you are with people?	YES	NO
[130] Would you call yourself a nervous person?	YES	NO
[131] Can you usually let yourself go and enjoy yourself at a lively party?	YES	NO
[132] Do you ever feel that your thoughts don't belong to you?	YES	NO
[133] Do you ever suddenly feel distracted by distant sounds that you are not normally aware of?	YES	NO
[134] As a child, did you do as you were told immediately and without grumbling?	YES	NO
[135] Do you sometimes talk about things you know nothing about?	YES	NO
[136] When you are worried or anxious do you have trouble with your bowels?	YES	NO
[137] When in the dark do you often see shapes and forms even though there's nothing there?	YES	NO
[138] Can you easily get some life into a rather dull party?	YES	NO

[139] Do you often have vivid dreams that disturb your sleep?	YES	NO
[140] Do you like plenty of bustle and excitement around you?	YES	NO
[141] Have you sometimes sensed an evil presence around you, even though you could not see it?	YES	NO
[142] Is it hard for you to make decisions?	YES	NO
[143] Do you find the bright lights of a city exciting to look at?	YES	NO
[144] Does your sense of smell sometimes become unusually strong?	YES	NO
[145] Do you usually have very little desire to buy new kinds of food?	YES	NO
[146] Are you often bothered by the feeling that people are watching you?	YES	NO
[147] 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
[148] Do you often feel like doing the opposite of what other people suggest, even though you know they are right?	YES	NO
[149] Do you like going out a lot?	YES	NO
[150] Do you feel very close to your friends?	YES	NO
[151] Are you sometimes sure that other people can tell what you're thinking?	YES	NO
[152] 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
[153] Do you often feel the impulse to spend money which you know you can't afford?	YES	NO
[154] Are you easily distracted when you read or talk to someone?	YES	NO

[155]	Are you a talkative person?	YES	NO
[156]	Were you ever greedy by helping yourself to more than your share of anything?	YES	NO
[157]	Do everyday things sometimes seem unusually large or small?	YES	NO
[158]	Do you feel that making new friends isn't worth the energy it takes?	YES	NO
[159]	Have you ever taken the praise for something you knew someone else had really done?	YES	NO

Appendix 4: STICSA State Subscale (Ree et al., 2008)

Instructions				
Below is a list of statements which can be used to describe how people feel. Beside each statement are four numbers which indicate the degree with which each statement is self-descriptive of mood at this moment (e.g., 1 = <i>not at all</i> , 4 = <i>very much so</i>). Please read each statement carefully and circle the number which best indicates how you feel right now, at this very moment, even if this is not how you usually feel.				
	Not at All	A Little	Moderately	Very Much So
1. My heart beats fast.	1	2	3	4
2. My muscles are tense.	1	2	3	4
3. I feel agonized over my problems.	1	2	3	4
4. I think that others won't approve of me.	1	2	3	4
5. I feel like I'm missing out on things because I can't make up my mind soon enough.	1	2	3	4
6. I feel dizzy.	1	2	3	4
7. My muscles feel weak.	1	2	3	4
8. I feel trembly and shaky	1	2	3	4
9. I picture some future misfortune.	1	2	3	4
10. I can't get some thought out of my mind.	1	2	3	4
11. I have trouble remembering things.	1	2	3	4
12. My face feels hot.	1	2	3	4
13. I think that the worst will happen.	1	2	3	4
14. My arms and legs feel stiff.	1	2	3	4
15. My throat feels dry.	1	2	3	4
16. I keep busy to avoid uncomfortable thoughts.	1	2	3	4
17. I cannot concentrate without irrelevant thoughts intruding.	1	2	3	4
18. My breathing is fast and shallow.	1	2	3	4
19. I worry that I cannot control my thoughts as well as I would like to.	1	2	3	4
20. I have butterflies in the stomach.	1	2	3	4
21. My palms feel clammy.	1	2	3	4

Appendix 5: STICSA Trait Subscale (Ree et al., 2008)

Instructions				
Below is a list of statements which can be used to describe how people feel. Beside each statement are four numbers which indicate how often each statement is true of you (e.g., 1 = <i>not at all</i> , 4 = <i>very much so</i>). Please read each statement carefully and circle the number which best indicates how you often, in general, the statement is true of you.				
	Not at All	A Little	Moderately	Very Much So
1. My heart beats fast.	1	2	3	4
2. My muscles are tense.	1	2	3	4
3. I feel agonized over my problems.	1	2	3	4
4. I think that others won't approve of me.	1	2	3	4
5. I feel like I'm missing out on things because I can't make up my mind soon enough.	1	2	3	4
6. I feel dizzy.	1	2	3	4
7. My muscles feel weak.	1	2	3	4
8. I feel trembly and shaky	1	2	3	4
9. I picture some future misfortune.	1	2	3	4
10. I can't get some thought out of my mind.	1	2	3	4
11. I have trouble remembering things.	1	2	3	4
12. My face feels hot.	1	2	3	4
13. I think that the worst will happen.	1	2	3	4
14. My arms and legs feel stiff.	1	2	3	4
15. My throat feels dry.	1	2	3	4
16. I keep busy to avoid uncomfortable thoughts.	1	2	3	4
17. I cannot concentrate without irrelevant thoughts intruding.	1	2	3	4
18. My breathing is fast and shallow.	1	2	3	4
19. I worry that I cannot control my thoughts as well as I would like to.	1	2	3	4
20. I have butterflies in the stomach.	1	2	3	4
21. My palms feel clammy.	1	2	3	4