UNIVERSITY OF SOUTHAMPTON

FACULTY OF SOCIAL, HUMAN, AND MATHEMATICAL SCIENCES

Psychology

Electrophysiological, pupillary, and oculomotor correlates of inhibitory control and cognitive effort in anxiety

by

Piril Hepsomali

Thesis for the degree of Doctor of Philosophy

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ABSTRACT

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ELECTROPHYSIOLOGICAL, PUPILLARY, AND OCULOMOTOR CORRELATES OF INHIBITORY CONTROL AND COGNITIVE EFFORT IN ANXIETY

Piril Hepsomali

Neurocognitive models of anxiety highlight the importance of attentional control and prefrontal control mechanisms and posit that anxiety is characterised by impaired effectiveness and efficiency during inhibition, especially under high cognitive load and in the presence of threat-related stimuli (Eysenck, Derakshan, Santos, & Calvo, 2007). The current thesis utilised behavioural, oculomotor, pupillary, and neurophysiological measures to examine the inefficient/ineffective inhibitory control and increased cognitive effort in high (vs. low) anxious individuals in the presence and absence of threat under high and low cognitive load conditions. Across three experiments, the results demonstrated that, high (vs. low) trait anxious individuals exert increased effort (as evidenced by increased pupillary responses) and invest more attentional resources during response preparation (as evidenced by decreased negative frontal neurophysiological responses), yet they have impaired inhibitory control (as evidenced by slower and erroneous oculomotor responses and less negative inhibition-related neurophysiological responses), especially under high cognitive load. These findings indicate inefficient inhibitory processing and ineffective inhibitory performance in high trait anxious individuals, especially when the task demands are high.

Table of Contents

List of Tables

List of Figures

DECLARATION OF AUTHORSHIP

I, *Piril Hepsomali*, declare that this thesis entitled **Electrophysiological, Pupillary, and Oculomotor Correlates of Inhibitory Control and Cognitive Effort in Anxiety** and the work presented in it are my own and has been generated by me as the result of my own original research.

I confirm that:

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3. Where I have consulted the published work of others, this is always clearly attributed;
4. Where I have quoted from the work of others, the source is always given. With the exception of such quotations, this thesis is entirely my own work;
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Definitions and Abbreviations

°	Degree (angle)
µV	Microvolt
ACC	Anterior Cingulate Cortex
ACT	Attentional Control Theory
ADM	Affective Decision Mechanism
Ag/AgCl	Silver/Silver Chloride
ANOVA	Analysis of Variance
ANT	Attentional Network Task
B	Blue
BA	Broadmann Area
BOLD	Blood-oxygen-level-dependent
CE	Central Executive
cm	Centimetre
CNV	Contingent Negative Variation
DC	Direct Current
DLPFC	Dorsolateral Prefrontal Cortex
DSM	Diagnostic and Statistical Manual of Mental Disorders
EEG	Electroencephalography
ERP	Event-related Potentials
F	Test Statistic for ANOVA
fMRI	Functional Magnetic Resonance Imaging
G	Green
GAD	Generalised Anxiety Disorder
GES	Goal Engagement System
GTES	Guided Threat Evaluation System
HA	High Anxious
HEOG	Horizontal Electrooculography
Hz	Hertz

IFG	Inferior Frontal Gyrus
ITI	Inter-trial Interval
kHz	Kilo-hertz
kΩ	Kilo-ohm
LA	Low Anxious
LC	Locus Coeruleus
LPFC	Lateral Prefrontal Cortex
M	Mean
MM	Metacognitive Mode
ms	Millisecond
NE	Norepinephrine
ODR	Oculomotor Delayed Response
OM	Orienting Mode
p	Probability, significance of a test statistic
PET	Processing Efficiency Theory
PM	Primal Mode
PTES	Preattentive Threat Evaluation System
R	Red
RAM	Resource Allocation Mechanism
RAS	Resource Allocation System
RT	Reaction Time
S	Second
S.D.	Standard Deviation
S.E.	Standard Error
SC	Superior Colliculus
SCP	Slow-wave Cortical Potentials
STAI	State-Trait Anxiety Inventory
t	Test statistic for t-test
TES	Threat Evaluation System

VEOG	Vertical Electrooculography
VES	Valence Evaluation System
VLPFC	Ventrolateral Prefrontal Cortex

1 General Introduction

1.1 Theoretical Overview: Anxiety

Beck and Clark (1997) proposed that fear and anxiety are adaptive mechanisms that help to detect a potential danger. Fear affects the sympathetic nervous system and causes fight or flight response in which individuals are prepared to generate an appropriate response (i.e. fight) or escape from a threatening situation (i.e. flight). Clinical levels of anxiety, are regarded to occur when objective danger in the environment is smaller than the individuals subjective evaluation of threat and there is significant functional impact of anxious effect on daily life (Beck & Clark, 1997).

The Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM-5; American Psychiatric Association, 2013) describes 12 anxiety disorders that can occur across development, including generalised anxiety disorder (GAD), social anxiety disorder and specific phobia. Core symptoms of anxiety in each disorder include physiological (e.g. muscle tension, sweating, heart palpitations), psychological (e.g. worry, concentration problems, irritability), and behavioural (e.g. escape and avoidance) characteristics. According to *DSM-5*, these symptoms should persist for a minimum of 6 months and cause significant distress and interfere with day-to-day life. Trait anxiety is conceptualised as a stable personality dimension (Eysenck & Calvo, 1992). Some researchers have linked heightened levels of trait anxiety to GAD and argue that boundaries between high anxiety and GAD are "fluid" (Rapee, 2001, p. 496). Individuals with elevated levels of trait anxiety are suggested to experience more state anxiety (in the moment) when faced with actual or perceived threat. State anxiety is defined as "a state in which an individual is unable to instigate a clear pattern of behaviour to remove or alter the event/

object/interpretation that is threatening an existing goal" (Power & Dalgleish, 1997, pp. 206-207).

Several theoretical frameworks aim to understand individual differences in anxiety via attentional control deficiencies, both in the context of processing threat-related information as well as poor attentional control more generally.

1.1.1 Theoretical Models of Attentional Bias in Anxiety in the Presence and Absence of Threat

Theoretical frameworks highlight that individuals with elevated or clinical levels of anxiety show increased distractibility in the presence of threat and impaired response inhibition to threat stimuli (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007). While some (*valence-specific*) models posit that attentional bias is the result of selective attention to threat-related stimuli, other (*attentional control and neurocognitive*) models suggest that attentional bias is caused by reduced attentional control and poor recruitment of prefrontal cortex when completing tasks (Heeren, De Raedt, Koster, & Philippot, 2013). The current review will focus on the mechanisms of attentional bias in valence-specific and attentional control models (Bar-Haim et al., 2007; Beck & Clark, 1997; Bishop, 2007; Eysenck et al., 2007; Mathews, Mackintosh, & Fulcher, 1997; Mogg & Bradley, 1998, 2016; Williams, Watts, Macleod, & Mathews, 1988)

1.1.1.1 Valence-Specific Models

One of the early valence-specific models was proposed by Williams et al. (1988) is composed of two components/mechanisms. The first mechanism, the *Affective Decision Mechanism* (ADM) is suggested to evaluate the threat value of environmental stimuli as high or low threat value, and where this evaluation is influenced by (elevated) state

anxiety. High threat-related stimuli are proposed to activate the second mechanism, the *Resource Allocation Mechanism* (RAM) which allocates attentional resources. RAM is moderated by trait anxiety (i.e. individuals with high trait anxiety allocate attention to threat whereas individuals with low trait anxiety shift their attention away from the threat). Although this model has given rise to development of different models of attentional bias to threat, Williams et al. (1988)'s model does not explain empirical findings when individuals with low trait anxiety display attentional biases for severely threatening, but not mildly threatening stimuli (e.g. Wilson & MacLeod, 2003).

Another model that focuses on threat evaluation and cognitive source allocation in anxiety was proposed by Beck and Clark (1997). Their three-stage model includes (1) initial registration of the stimulus, (2) immediate preparation, and (3) secondary elaboration. Similar to Williams et al. (1988)'s model, this model identifies stimuli and provides processing priority for threat-related stimuli or situations. Threat-related stimuli are argued to be processed rapidly and automatically and the *orienting mode (OM)* is activated. The OM is stimulus driven and doesn't include strategic and elaborative processing. After recognition of personally relevant negative stimulus by the OM, the *primal mode* (PM) is activated, leading to primal response activation to maximise safety and minimise danger. Primal responses are suggested to include autonomic arousal, behavioural mobilisation and inhibition, primal thinking, a feeling of fear, and hypervigilance for threat-related cues. Once the PM is activated, it captures most of the attentional sources and blocks secondary reflexive modes of thinking. Unlike the OM, the PM includes both automatic and strategic/elaborative processing. At the final stage, the *metacognitive mode* (MM) is activated. Although threat processing is involuntary because of the activation of the PM, the MM is argued to include slow, effortful, and schema-driven strategic/elaborative processing.

While previous models outline a sequential pattern of information processing in anxiety, Mathews and Mackintosh's (Mathews et al., 1997) cognitive model highlights the role of competition associated with stimuli or task demands. In addition, it considers mild threat-related stimuli and assumes that low anxious individuals prioritise only severe (and not mild) threat-related input. They posit that attentional bias to threat is possible only if there is a competition between stimuli or task demands. In addition, these stimuli or demands are processed in parallel and outside conscious awareness. After the automatic evaluation of stimulus input, the *Threat Evaluation System* (TES) receives output which is modulated by anxiety level and activates distractor representation, whereas effortful task demand activates target representation. Only low level anxiety levels from the TES decreases attention to threat-related distractor and increases attention to target. However, if the TES sends outputs affected by high anxiety levels, orientation to the threat-related distractor will increase.

Mogg and Bradley's cognitive-motivational model (Mogg & Bradley, 1998) similarly includes a threat evaluation system. This framework includes a *Valence Evaluation System* (VES) (see Figure 1.1) that is argued to be responsible for preconscious assessment of threat value of the stimulus input and is influenced by a number of features including trait anxiety, the situational context, current arousal level, prior experience and state anxiety level. High anxious individuals are argued to have a sensitive VES, resulting in increased appraisals of stimuli as more threating, compared to low anxious individuals. The VES sends its output to the Goal Engagement System (GES) which regulates the allocation of resources for further processing and action. If a stimulus is identified as high threatening, the GES will interrupt current goal-related activities and allocate processing resources to threat-related stimuli. However, if a stimulus is identified as low threatening, it will inhibit processing of that stimulus and focus on goals. According to this model, the

relationship between VES (i.e. subjective stimulus threat value) and GES may not be linear. Similar to Mathews and Mackintosh's (Mathews et al., 1997) cognitive model, the authors note that even mild threat captures attention, and over time leads to avoidance.

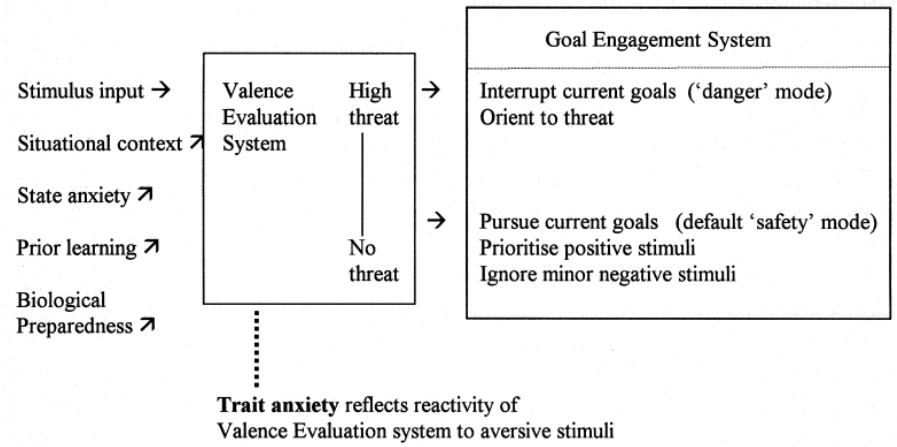


Figure 1.1 Mogg and Bradley's cognitive-motivational model (Mogg & Bradley, 1998, Figure 2, pg.817).

A more recent review of research on anxiety and attention led to the development of a further hierarchical system that aims to capture factors underpinning threat evaluation in anxiety (Bar-Haim et al., 2007). This model is composed of four interdependent systems including Preattentive Threat Evaluation System (PTES), Resource Allocation System (RAS), Guided Threat Evaluation System (GTES), and Goal Engagement System (GES) (Figure 1.2). The PTES is suggested to determine the threat level of environmental stimulus. If this system tags stimulus with a high treat value, the RAS elicits physiological alert state and orients to threat by interrupting ongoing task-related activity. The GTES then assesses the context of the threat-related stimulus, compares it with memory and prior learning and evaluates the available coping resources. If the GTES considers the threat low in importance, (1) feedback is sent to the PTES and the RAS by overriding threat evaluation of the PTES and relaxing the physiological alert state imposed by the RAS and (2) the individual can then continue to pursue goal-oriented activities. Conversely, if the

GTES considers the threat high in importance, the GES interrupts goal-related activities and attention is directed to the threat-related stimulus.

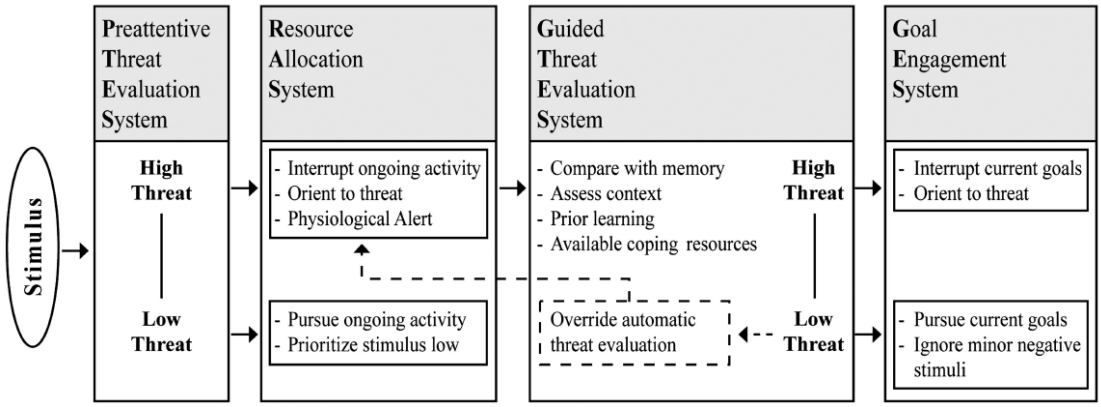


Figure 1.2 Multidimensional model of attentional biases (Bar-Haim et al., 2007, Figure 1, pg. 17).

Although previous models provide a good explanation for threat bias in anxiety, recent research has aimed to understand the relationship between anxiety and attentional control in the absence of threat-related stimuli.

1.1.1.2 Executive Functions, Attentional Control and Neurocognitive Models of Anxiety

This section will briefly mention executive functions and the effect of cognitive load and effort on inhibitory control system and focus on attentional control and neurocognitive models of anxiety.

Executive Functions

In the early stages of research on executive functions, central executive was proposed to be unitary (see Miyake et al., 2000, for a review). However, results from clinical observations, behavioural tasks, and neuropsychological studies have since fractionated executive function into component processes. Miyake et al. (2000) identified three executive functions: (1) shifting (i.e. between multiple tasks or mental sets), (2)

updating (i.e. monitoring new working memory representations and replacing irrelevant information with the new ones), and (3) inhibition (i.e. intentionally inhibiting automatic and proponent responses).

The shifting function involves moving back and forth between tasks or mental sets (Monsell, 1996) and involves the frontal lobes, as well as the bioccipital and parietal cortices (Moulden, Picton, Meiran, Stuss, & Riera, 1998). The updating function is responsible for monitoring memory representations and activates the frontal lobe, especially the dorsolateral prefrontal cortex (DLPFC) and the parietal cortex (Goldman-Rakic, 1996). The inhibition function reflects the ability to inhibit dominant and prepotent responses. Similar to shifting and updating functions, inhibitory control is linked to the frontal cortex.

The Influence of Load and Effort on Inhibitory Control

Increased cognitive load is known to disrupt task performance, however, it also increases the amount of effort participants exert for successful task completion. Cognitive load can be manipulated in various ways including (1) increasing the number items to be remembered (i.e. remembering fewer or more items) (e.g., Leung, Gore, & Goldman-Rakic, 2002), (2) increasing the durability (i.e. remembering the same number of items but retaining them for shorter or longer periods of time) (e.g., Jha & McCarthy, 2000), (3) adding a secondary task (i.e. performing two tasks at the same time) (e.g., Berggren, Richards, Taylor, & Derakshan, 2013), or (4) increasing the number of task distractors (i.e. interfering performance by presenting fewer or more distractor items) (e.g., Lavie, 2005).

These examples act to increase working memory to affect the executive system as a whole. Alternatively, each function of the executive system could be loaded in different ways, such as decreasing the number of trials to be inhibited, thus making inhibition more

difficult (inhibitory load), increasing the number of shifts required (shifting load), and increasing the number of items to be updated (updating load). Increasing delay duration during information maintenance is known to increase reaction time and decrease accuracy. Since delay period activity reflects the stored representation, increased brain activations in the prefrontal cortex of humans and non-human animals are observed throughout delay periods while completing cognitive tasks (see Curtis & D'Esposito, 2003 for a review). However, as well as passive information maintenance, active response selection processes take place in the frontal areas (see Curtis & D'Esposito, 2003 for a review).

In their review, it was concluded that the frontal areas have a role in (1) maintenance by directing attention to internal representations, and (2) motor plans. It has been suggested that delay period activity reflects both (1) prospective motor code (i.e. motor intention, preparation activities; e.g. representations of saccade intentions) or (2) retrospective sensory code (i.e. spatial attention; e.g. representation of space/location) (Curtis, Rao, & D'Esposito, 2004; D'Esposito, Ballard, Zarahn, & Aguirre, 2000; Funahashi, Bruce, & Goldman-Rakic, 1993). However, there is still no consensus about what is being represented and/or remembered during delay periods.

Inhibitory load can be manipulated by increasing the probability of to-be-inhibited stimulus. Some studies have shown performance impairments in inhibitory control paradigms by decreasing the probability of No-Go or Stop stimulus (Bruin & Wijers, 2002b; Dimoska & Johnstone, 2008; Ramautar, Kok, & Ridderinkhof, 2004; Van De Voorde, Roeyers, Verte, & Wiersema, 2011). A tendency to respond is created by presenting No-Go stimuli infrequently. In other words, decreasing the probability of No-Go trials creates high inhibitory load and effort and makes it harder to inhibit the proponent response.

Regardless of load type (i.e. loading the executive system by increasing delay duration or loading inhibition function of the executive system by decreasing the probability of to be inhibited response), decrements in the performance occurs when load increases.

Attentional Control Theory

The first theoretical framework to focus on attentional control in anxiety (Attentional Control Theory; ACT) was proposed by Eysenck et al. (2007). The framework stemmed from and developed Eysenck and Calvo (1992)'s Processing Efficiency Theory (PET). In the original conceptualisation, PET drew a distinction between *effectiveness* and *efficiency*, referring to the quality of performance and the relationship between performance effectiveness in meeting task goals and the efficiency (effort or sources) used to achieve them. PET assumes that performance effectiveness and efficiency are affected by the worry component of anxiety and this negative emotional states impacts on the central executive (CE) of working memory (Baddeley, 2000). Though it lacks explanation as to which function of the CE is most affected by anxiety.

ACT was developed more recently to address the limitations of PET and specifically to more clearly delineate the impact of anxiety and CE functioning. In addition, ACT suggests that anxiety disrupts top-down and bottom-up attentional systems balance. It proposes that anxiety weakens top-down attentional control and strengthens bottom-up (stimulus/data)-driven systems control, affecting to the greatest extent the shifting and switching functions of the CE (i.e., to inhibit task-irrelevant stimuli and pursue goal-oriented behaviour, and to shift from one task to another). Moreover, this effect is argued to increase when the task-irrelevant stimulus is threat-related. Additionally, overall

increased demands on the CE are suggested to reduce processing efficiency in the updating function especially under conditions of situational stress (i.e. state anxiey).

ACT suggests that anxiety affects processing efficiency more than performance effectiveness. High anxious individuals may show comparable performance in terms of accuracy (i.e. performance effectiveness), lowered efficiency can be evident in terms of increased reaction time to complete tasks. Different measures (e.g., self-report, physiological, incentive) have also been used to show that reduced efficiency is linked to increased on-task effort (Eysenck et al., 2007). Furthermore, according to ACT, high anxious individuals are more vulnerable to the effects of tasks with increased cognitive load reflecting that the effect of anxiety on attentional control is most evident when the task demands are high.

A recent model by Mogg and Bradley (2016) is guided by evidence based bottom-up salience evaluation process and executive control models and is both a valence-specific and attentional control model. Similar to ACT, this model focuses on the imbalance between bottom-up mechanisms that is responsible from threat detection and evaluation (such as alerting, bottom-up orienting, evaluating of salience, and perceptual processing) and top-down mechanisms that support goal-directed behaviour (such as top-down orienting, inhibitory control, cognitive flexibility, working memory functions, and reason-based evaluation). According to this model, bottom-up evaluation of salience is crucial in order to (1) assess the motivational importance and threat value of stimuli, and (2) modulate activity in other bottom-up and top-down processes. Also, top-down inhibitory control is important in (1) suppressing/inhibiting/withholding a response/behaviour, (2) and prioritising goal-directed responses/behaviours.

Neurocognitive Models of Anxiety

Similar to Mathews and Mackintosh's model (Mathews et al., 1997), Bishop's neuro-cognitive model (Bishop, 2007) focuses on the effect of perceptual competition on performance. This model suggests that, decreased prefrontal cortex (ACC: Anterior Cingulate Cortex and LPFC: Lateral Prefrontal Cortex) and increased amygdala activation can lead to attentional bias to threat-related stimuli. According to Lavie (2005) attentional competition involves two stages including (1) early perceptual competition and (2) active recruitment of control mechanisms. In the first stage, under high load conditions, distractor processing is prevented for further action, whereas in the second stage, under low load conditions, salient distractors are prevented from competing for processing resources. Bishop (2007) postulated that a common amygdala-prefrontal circuitry underlies attentional biases to threat, with state anxiety modulating early perceptual competition and trait anxiety modulating prefrontal recruitment (Figure 1.3).

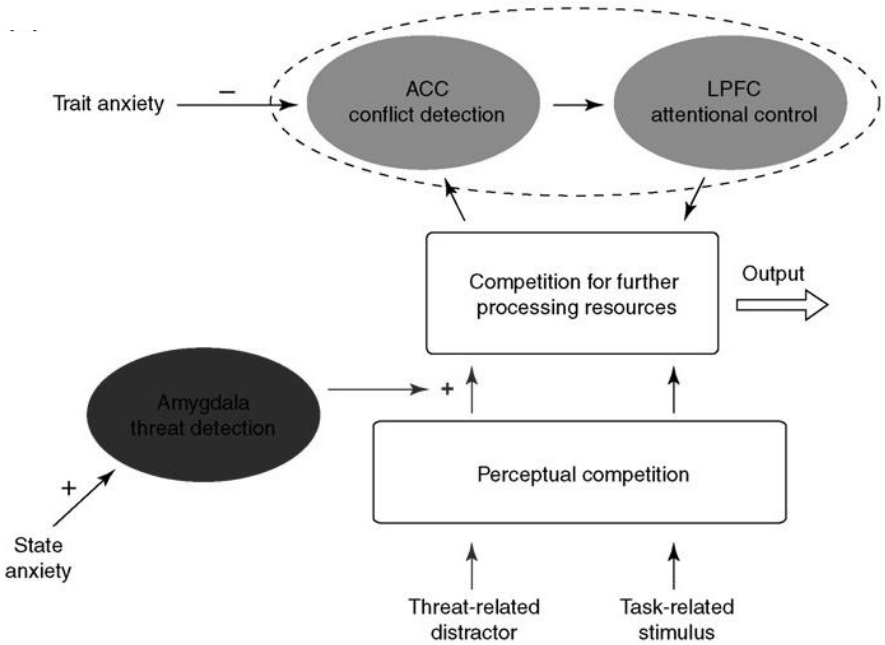


Figure 1.3 Neuro-cognitive model of attentional biases in anxiety to threat (Bishop, 2007, Figure 2, pg. 311).

Summary

The models reviewed above propose that facilitated attention to threat-related stimuli reflects a threat detection mechanism (e.g. the ADM, the OM, the TES, the VES and the PTES) which automatically processes stimuli. Theoretical frameworks suggest that high anxiety impairs executive and emotional processes. In addition, this impairment is proposed to be worsened when the task difficulty is increased.

1.1.1.3 Behavioural and Oculomotor Tasks of Inhibitory Control that Used to Test Predictions of Theoretical Models of Anxiety

Several paradigms have been developed to examine attentional bias during inhibitory control both on the presence of absence of threat-related stimuli (e.g., the Stroop, Go/No-Go, antisaccade, and Stop-Signal tasks (Curtis & D'Esposito, 2008). These tasks rely on the inhibitory control of the executive system and they require participants to withhold their automatic and prepotent responses and generate task-relevant responses.

In the *Stroop* task (Stroop, 1935), participants are presented with lists of coloured names of colours and they are asked to read the word or name the colour of the word. When the colour name and colour of the word are different, it takes more time for participants to read the word or name the colour.

The *Go/No-Go* task (Donders, 1969) requires participants to respond to Go (i.e. target) stimuli and withhold their responses to No-Go (i.e. distractor) stimulus. Main findings from this task show that participants find it harder to inhibit their responses to target stimulus resulting in increased errors.

The *Stop-Signal* task (Logan, Cowan, & Davis, 1984) requires participants to respond to a particular stimulus as quickly as possible. However, in some of the trials this

stimulus presentation is followed by a signal (visual or auditory) where participants are required to withhold their responses. Similar to Go/No-Go paradigm, participants make erroneous responses following a signal.

In the *Antisaccade* task (Hallett, 1978),a visual cue is presented either on the left or right visual field and participants are required to look at the mirror (i.e. opposite) location of the previously presented cue. Participants make more erroneous and slower eye movements in the antisaccade task (compared to the prosaccade task in which participants are required to look at the visual cue).

Summary

Aforementioned tasks require individuals to withholding a prepotent response in the pursuit of task goals. Inhibitory control is an important function in routine tasks as task-appropriate responding is a crucial component various psychological constructs. Since anxiety is associated with impaired inhibitory control and switching to a greater extent than updating function of the CE (Eysenck & Derakshan, 2011; Eysenck et al., 2007), the focus of interest in the programme of research presented here is individual differences on the inhibitory control of attention. Especially, the current thesis utilised antisaccade and Go/No-Go tasks as a measure of inhibitory control as they have strong inhibition demands, and they have been widely used to study inhibitory control in anxiety. The central nervous, pupillary, and oculomotor systems are sensitive to the effects of task demands, cognitive load and emotion processing and are effective indices of the amount of mental effort individuals exert when they complete a task.

1.2 Methodological Approach: Measuring Attentional and Emotional Processing

Recent research has shown that neurophysiological, pupillary and oculomotor responses are valid measures of the amount of mental effort exerted during attentional and emotional processing tasks. This section will focus on how neurophysiological, pupillary, and oculomotor systems work and how they are affected by task demands.

1.2.1 The Neural Substrates of Load/Effort and Inhibitory Control

1.2.1.1 Neural Basis of Inhibitory Control

Brain imaging and lesion studies have been conducted in human and non-human animals to identify the neural mechanisms of response inhibition. Some inhibition paradigms engage the hyper-direct, faster pathway (from prefrontal cortex to subthalamic nucleus), whereas others include the indirect pathway through the basal ganglia to activate prefrontal cortex in response to inhibition (Bunge & Souza, 2009). For example, non-human animal lesion studies have shown that that inhibitory control is associated with increased activation in the DLPFC (Mishkin, 1964) and ventrolateral prefrontal cortex (VLPFC; Iversen & Mishkin, 1970). Similarly, recent fMRI studies with human participants found increased activation in the inferior frontal gyrus (IFG) in the ventral premotor/prefrontal cortex during response inhibition (Aron, Robbins, & Poldrack, 2004). During inhibitory control paradigms, neuroimaging studies found dorsomedial prefrontal cortex (Garavan, Ross, Murphy, Roche, & Stein, 2002; Garavan, Ross, & Stein, 1999), caudal DLPFC (de Zubicaray, Andrew, Zelaya, Williams, & Dumanoir, 2000) and VLPFC (Bunge, Dudukovic, Thomason, Vaidya, & Gabrieli, 2002; Konishi, Kawazu, et al., 1999; Rubia, Smith, Brammer, & Taylor, 2003) activation in humans.

fMRI studies involving the Go/No-Go paradigm showed increased right VLPFC activations. Moreover, both human and non-human neuroimaging studies revealed increased right IFG activity for No-Go than Go trials (Liddle, Kiehl, & Smith, 2001; Morita, Nakahara, & Hayashi, 2004b) suggesting this activity supports inhibition of motor responses. Stop-Signal studies similarly show increased right IFG activity through excitation of the basal ganglia for Stop trials compared to Go trials (Aron & Poldrack, 2006). The authors concluded that larger activation differences between Stop and Go trials might reflect more effective inhibitory control.

Lesion studies provide further evidence for the role of the prefrontal cortex in inhibitory control. Performance impairments during No-Go trials were observed with monkeys with inferior prefrontal convexity (BA45) (i.e., a homologue of VLPFC in humans) lesions (Iversen & Mishkin, 1970). Furthermore, damage to the right IFG (an area in the VLPFC) in humans impaired response inhibition and increased reaction times in a Stop-Signal task (Aron, Fletcher, Bullmore, Sahakian, & Robbins, 2003). Additionally, single cell studies in monkeys showed firing of cells in the central sulcus (monkey homologue of DLPFC; Sakagami et al., 2001) following No-Go stimuli.

1.2.1.2 Electrophysiological Indices of Load/Effort and Inhibitory Control

Previous studies have shown that distinctive electrophysiological responses are affected by increased load/cognitive effort and inhibitory control. Slow-wave cortical potentials (SCPs) are sustained electrophysiological responses that are sensitive to the amount of effort exerted on a task. On the other hand, peak N2 and P3 ERP amplitudes are linked to inhibitory control. This section will focus on SCPs and inhibition-related N2 and P3 components and their temporal and spatial (i.e. cortical) characteristics.

Slow-wave Cortical Potentials

Cognitive effort has been assessed by examination of slow-wave cortical potentials (SCPs; Kotchoubey, 2006; Rosler & Heil, 1991). SCPs are long-lasting potentials that last for several seconds. They are proposed to reflect allocation and consumption of cognitive resources for an anticipated activity. It has been proposed that negative SCPs are related to the preparation of cortical resources for a forthcoming action, whereas positive SCPs reflect the consumption of these resources in actual activity (Kotchoubey, 2006). Among these SCPs, Contingent Negative Variation (CNV; Walter, Cooper, Aldridge, McCallum, & Winter, 1964) has been used as a marker of cognitive effort across several studies and results have shown that it is maximal over frontal sites (Gomez, Flores, & Ledesma, 2007; Rosahl & Knight, 1995). A CNV is a slowly changing negative potential elicited in response to a warning cue that induces preparation for an anticipated activity. It is assumed to reflect preparation and activation of cortical resources that are required for the expected stimulus or response. The CNV amplitude depends on the degree of cognitive effort due to the motivation, task complexity, and subjective expectation of an anticipated event (Khader, Schicke, Roder, & Rosler, 2008).

Inhibition-related ERPs: N2 and P3

Two fronto-central event-related potentials (ERPs) have been associated with response inhibition (see Harper, Malone, & Bernat, 2014, for a review). The *N2* is a negative component at midline frontal sites that appears 250-350 ms after the presentation to-be-inhibited stimuli (*No-Go N2*) (Eimer, 1993). It is assumed to reflect both response inhibition (mediated by the VLPFC and DLPFC) and conflict monitoring (mediated by the ACC) (Lavric, Pizzagalli, & Forstmeier, 2004). The *P3* is a positive component at midline fronto-central areas that peaks between 300-500 ms after the presentation of to-be-inhibited stimuli (*No-Go P3*), and it is associated with motor inhibition and (due to its long

latency) evaluation of inhibition (Bruin & Wijers, 2002a; Falkenstein, Hoormann, & Hohnsbein, 1999; Righi, Mecacci, & Viggiano, 2009). However, the parietal P3 is also observed after target stimuli presentation (*Go P3*) (Fallgatter, Brandeis, & Strik, 1997). Research has reliably shown that No-Go (vs Go) stimuli elicited more negative N2 and more positive P3 components at fronto-central areas and Go (vs No-Go) stimuli produced more positive P3 component at parietal sites (Falkenstein et al., 1999; Fallgatter et al., 1997; Harper et al., 2014; Lavric et al., 2004).

1.2.2 Pupillary System and Pupillary Responses

Pupillary size changes are controlled by two muscles of the iris: *sphincter pupillae* (circular) and *dilator pupillae* (radial). The sphincter pupillae and dilator pupillae muscles control the constriction (*miosis*) and the dilation (*mydriasis*) of the pupil, respectively (see Figure 1.4). The sphincter pupillae is located in the stromal layer of the cornea, mediated by parasympathetic nervous system and controlled by cholinergic system. The dilator pupillae is located posteriorly to sphincter muscle and is mediated by sympathetic nervous system and controlled by adrenergic system.

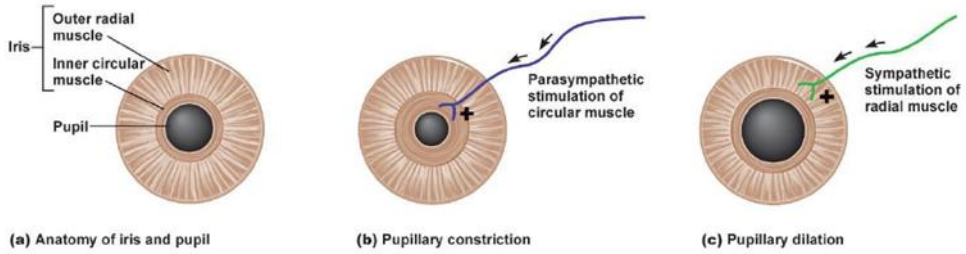


Figure 1.4 **(Left Panel)** Anatomy of iris and pupil. Outer radial and inner circular muscles of the iris are responsible from pupillary responses. **(Middle Panel)** Pupillary constriction. Excitation of parasympathetic nervous system constricts the pupil. **(Right Panel)** Pupillary dilation. Inhibition of the parasympathetic nervous system and excitation of sympathetic nervous system causes pupil dilation.

Both divisions of the autonomic nervous system are responsible for pupillary response changes. Inhibition of the parasympathetic nervous system and excitation of sympathetic nervous system causes pupil dilation by minimising the activity in sphincter pupillae and maximising the activity in dilator pupillae, respectively. In contrast, excitation of parasympathetic nervous system results in pupillary constriction by maximising the sphincter pupillae activity. Sympathetic innervation begins in the hypothalamus, travels through the spinal cord and reaches the superior cervical ganglion and ultimately ends in dilator pupillae. Parasympathetic innervation begins in the Edinger-Westphal oculomotor complex/nucleus which is located in the midbrain, it travels to third cranial nerve (i.e. oculomotor nerve), reaches the ciliary ganglion and finally ends in the sphincter pupillae (see Figure 1.5). Although all sensory stimuli (i.e. visual, tactile, auditory, gustatory, olfactory) conduce pupillary responses (Beatty & Lucero-Wagoner, 2000), they are also observed in response to light and accommodation reflexes (Andreassi, 2000); dim light causes pupils to dilate whereas intense light conditions leads pupils to constrict. Also, while focusing on an object, pupil constricts in order to increase the depth of focusing. In addition, the pupil reacts to light and stimuli at 0.2 seconds and peaks at 0.5 to 1 seconds (Beatty & Lucero-Wagoner, 2000; Lowenstein & Loewenfeld, 1962).

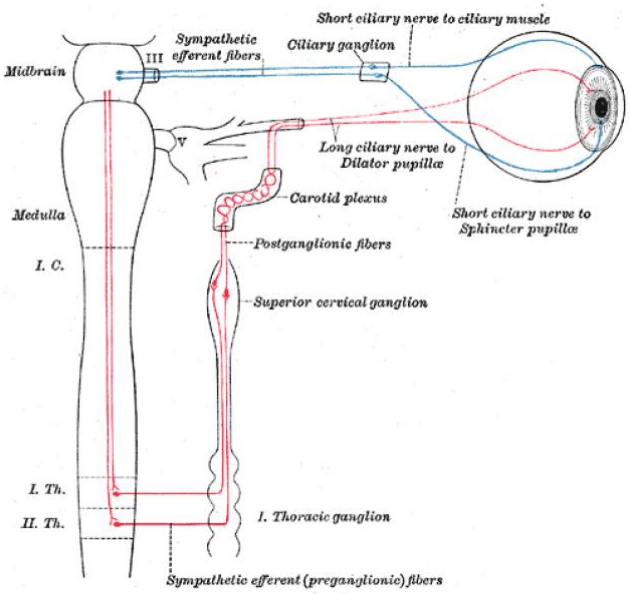


Figure 1.5 Neural structures and pathways that control pupillary responses.

In stable lighting conditions, the pupil size reflects both tonic and phasic modes of the locus coeruleus–norepinephrine (LC-NE) system (Aston-Jones & Cohen, 2005) and is influenced by level of arousal, anxiety and stress and is time locked to stimuli or response for tonic and phasic systems, respectively. Pupillary responses (i.e. the magnitude of dilation and constriction) are species-specific in so much as, in humans pupillary responses range between 1.5 mm and 8-9 mm, (Beatty & Lucero-Wagoner, 2000).

Although pupillary responses are controlled by both divisions to the autonomic nervous system, the connection of pupillary movements to cognitive and behavioural processes must occur at higher levels within the human nervous system. Recent research supports this view and shows that the DLPFC and amygdala are related to pupillary responses in response to cognitive and emotional processing (Siegle, Steinhauer, Stenger, Konecky, & Carter, 2003; Siegle, Ingram, & Matt, 2002).

1.2.2.1 The Pupillary System and Executive Processes

Pupillary responses of executive functions are mediated by the parasympathetic nervous system and reflect ongoing neurological activity in the brain (i.e. information processing, mental effort, and processing load Hess, 1972). Early models suggested Kahneman and Beatty (1966) that pupil dilation is an indirect measure of rehearsal activity during retention intervals (i.e. delay periods), reflecting the intensity of mental effort (Kahneman & Beatty, 1966) and recruitment of cognitive resources to meet task demands (Beatty & Lucero-Wagoner, 2000). In support, Karatekin (2004) showed a positive correlation between moment by moment changes in mental effort and pupil dilation. Likewise, various studies showed that pupillary responses increased in response to task difficulty and memory load reflecting the effect of mental effort and source recruitment (see Karatekin, 2007 for a review).

In addition, according to Siegle et al. (2003), the Edinger-Westphal oculomotor nucleus inhibition in the midbrain causes association of pupillary dilation and executive control with the DLPFC activity. Thus, cognitive content of a stimulus might elicit pupillary responses as the DLPFC has a critical role in working memory (Barbey, Koenigs, & Grafman, 2013).

1.2.2.2 The Pupillary System and Affective Processes

The sympathetic nervous system mediates pupillary responses in response to emotion-laden stimuli (Bradley, Miccoli, Escrig, & Lang, 2008) and emotion-laden stimuli of different modalities elicit bigger pupillary diameters for both pleasant and unpleasant stimuli (see Bradley et al., 2008 for visual; Partala & Surakka, 2003 for auditory stimuli) (but see Hess & Polt, 1960; Libby, Lacey, & Lacey, 1973), suggesting that instead of

emotional valence, emotional arousal is associated with increased sympathetic nervous system activity.

Emotional arousal is known to be an indicator of an alerting self-regulatory mechanism (Hoehl & Striano, 2010) and it is related to hindbrain noradrenergic mechanisms (Rajkowski, Kubiak, & Aston-Jones, 1994) through the LC, which is the main substrate of arousal and alerting response via the activation of the thalamus, parietal, and frontal cortices (Tracy, Faro, Mohamed, Pinsk, & Pinus, 2000). According to Geva, Zivan, Warsha, and Olchik (2013), pupillary responses in reaction to an alerting cue reflect the activation of the autonomic nervous system, typically evoked around 360 ms after the stimulus presentation. Additionally, since the amygdala sends inputs to (1) the medulla and (2) the posterior hypothalamus in order to start excitation of the sympathetic pathway, pupillary responses are known to be affected by amygdala activity (Siegle, Steinhauer, Thase, Stenger, & Carter, 2002). Because the amygdala is known to have a crucial role in emotion processing, the emotional arousal of a stimulus may elicit pupillary responses (Pessoa & Adolphs, 2010; Phelps & LeDoux, 2005).

1.1.2.3 Pupillary Responses, the Locus-Coeruleus Norepinephrine (LC-NE) Release, and Anxiety

As well as the autonomic and central nervous system, a small nucleus in the dorsal pons, Locus coeruleus (LC) which supplies norepinephrine (NE) throughout the central nervous system, affects pupillary responses. According to Aston-Jones and Cohen (2005) pupil dilation is a reliable and non-invasive measure of LC-NE activity during both *tonic* (baseline) and *phasic* (task-related) modes. Tonic LC activity correlates with pupillary responses and is influenced by general factors such as anxiety and level of emotional arousal. On the other hand, phasic LC activity is influenced by a task-specific stimulus onset or response. Although the empirical relationship between LC-NE and pupillary

system is lacking, a recent study showed an association between continuous pupil diameter and BOLD activity in a dorsal pontine cluster overlapping with the LC (Murphy, O'Connell, O'Sullivan, Robertson, & Balsters, 2014).

Researchers have proposed that he LC-NE function is disrupted in high anxious individuals, suggesting that high anxious individuals have increased baseline NE secretion and increased reactivity to challenges of the LC-NE system (see Kalk, Nutt, & Lingford-Hughes, 2011, for a review). According to Howells, Stein, and Russell (2012), high anxious individuals have increased cortical arousal, but impaired performance and attentional control due to increased tonic firing of the LC-NE system. In other words, when phasic firing occurs, individuals with elevated anxiety cannot discriminate between response and distractor (i.e. signal and noise) as a result of high tonic levels of the LC-NE system. In order to perform optimally, both tonic and phasic firing of the LC-NE system have to be balanced. Given the relationship between the LC-NE system and anxiety, anxious affect has been found to influence pupillary responses during both executive and affective processing. Section 1.3.1 and Section 1.3.2 provide evidence of the association of pupillary responses and anxiety.

Eye movements have also been used (in addition to the use of pupillary responses) as a marker of executive and affective processing. Moreover, eye movement research has been utilised in research as an index of attentional and emotional processing to a great extent due to the ease of calibration and increased evidence base linked the validity of results.

1.2.3 The Oculomotor Control System

Eyes are controlled by six extra-ocular muscles that are responsible for sideways (the medial and lateral recti), up-down (the superior and inferior recti), and twist (the superior

and inferior obliques) movements. Eye movement control signals are controlled by cortical and sub-cortical regions, including the occipital cortex, semi-circular canals and superior colliculus.

Saccades are fast rotations of the eye and occur 3 or 4 times per second. Fixations occur in between saccades and eyes remain still during fixations in order to gain information about a visual scene. There is increased activity in the burst and omnipause cells in the brainstem during saccades, and fixations, respectively, which may be related to oculomotor muscles that cause eye movements (Findlay & Walker, 1999). The superior colliculus is one of the most important areas in the midbrain, receiving inputs from both cortical and subcortical areas and triggering saccadic eye movements (Trappenberg, Dorris, Munoz, & Klein, 2001). There are not only fixation-related omnipause cells, but also saccade related burst and buildup cells in the superior colliculus. Burst and buildup cells can be found in all regions of the superior colliculus except the rostral pole, where the fixations cells are located. During visual fixation, activity of omnipause cells inhibit the activity of burst and buildup cells, thus inhibiting the saccadic movement. The balance between omnipause and burst/buildup cells has a significant role in determination of whether to generate a saccadic eye movement or not (Findlay & Walker, 1999).

Oculomotor responses are also affected by executive and affective procesing and they are argued to provide more sensitive measures compared to behavioural responses (Roberts, Fillmore, & Milich, 2011).

1.1.3.1 The Oculomotor Control System and Executive Processes

Neuroimaging studies have shown that executive functions and oculomotor control system are connected and activate overlapping brain areas. The oculomotor system includes the frontal eye fields, posterior parietal cortex, supplementary eye fields, pre-

supplementary motor area, DLPFC, superior colliculus, basal ganglia, thalamus, and cerebellum (Munoz & Everling, 2004). The DLPFC and basal ganglia are especially well known to have a relationship with executive functions and the oculomotor control system (Munoz & Everling, 2004). The frontal eye fields affect the oculomotor control system and the executive functions through the projection to the superior colliculus and brainstem. Both frontal eye fields and the DLPFC also have connections with premotor and cingulate areas (Barbas, 2000).

1.1.3.2 The Oculomotor Control System and Affective Processes

In a visual environment, individuals cannot attend to all the details simultaneously due to capacity limits of the brain. After a prioritization process, the brain selects information for further processing. Emotions, especially those related to threat (i.e., anger and fear), are prioritised since they have evolutionary significance to minimize danger and maximise safety (see Mather & Sutherland, 2011 for a review). Perceptual thresholds (i.e. the lowest level of a stimulus that an individual perceives) for emotional stimuli are lower and perception of emotional (compared to neutral) stimuli is faster (West, Anderson, & Pratt, 2009), providing evidence for this prioritization process (Calvo & Esteves, 2005). Various studies have shown that extrastriate cortex activity could be enhanced by the perception of emotional visual stimuli because of the direct projections from the amygdala to retinotopically aligned regions in the visual cortex (Rudrauf et al., 2008). Biased perception of emotion-laden stimuli is known to be modulated by this amygdala-extrastriate relationship (Fox, Russo, Bowles, & Dutton, 2001; West et al., 2009). A subcortical pathway from magnocellular retinal inputs is known to underlie this emotion prioritization process, and includes reciprocal connections between the superior colliculus (SC), pulvinar, and the amygdala (LeDoux, 2009; Linke, De Lima, Schwegler, & Pape, 1998). The pulvinar has connections with the caudate (Leh, Chakravarty, & Ptito, 2008)

and the caudate has an inhibitory connection with the substantia nigra; a structure which has an inhibitory connection with the intermediate layer of the SC (i.e. the layer which is responsible for the speed, but not the spatial component of saccade generation; see Hikosaka and Sakamoto (1986). This subcortical pathway is not only affected by emotional stimuli due to the amygdala connection, but also aids generation of saccadic motor response with pulvinar and SC activations(Munoz & Everling, 2004). Since the amygdala extracts information about emotions in a visual environment (Anderson & Phelps, 2001; Rudrauf et al., 2008; Whalen et al., 1998), projections from the amygdala to the SC can affect oculomotor behaviour. In sum, emotional stimuli are not only prioritised in perception but also affect oculomotor behaviour via the activation of brain centres that have a role in saccade generation.

1.1.3.3 The Oculomotor Control System and Anxiety

Previous research has shown that frontal cortical areas associated with saccade generation overlap with anxiety circuitry (Bishop, 2007, 2009; Sehlmeyer et al., 2009). Neuroimaging studies suggest that high anxious individuals have reduced DLPFC activation, resulting in impaired attentional control and thus saccade generation. Section 3 provides neural and oculomotor evidence for the relationship between the oculomotor system and anxiety by reviewing pro- and antisaccade studies in the presence and absence of threat-related distractors.

Summary

Executive and affective processing not only affect pupillary and oculomotor systems, but they also influence behavioural and neural systems. In addition, these processes are known to be impacted by elevated anxiety. The next section will consider how these measurements have been used to test theoretical models of anxiety to show increased effort

and arousal and an attentional bias to threat-related stimuli. The next section will outline behavioural, oculomotor, pupillary, and neural evidence of impaired effectiveness and efficiency in anxiety (in the absence and presence of threat-related stimuli).

1.3 The Relationship between Anxiety, Inhibitory Control, and Cognitive Effort

1.3.1 Evidence of Impaired Inhibition and Increased Effort in Anxiety

Individuals with clinical and subclinical anxiety are known to have impaired inhibitory control in the presence of prepotent responses. Empirical research has utilised different experimental paradigms and levels of analysis to provide converging evidence to demonstrate a relationship between anxiety and impaired attentional control. This section provides a summary of behavioural (RTs), oculomotor (eye movements), neural (event-related potentials; ERPs and functional magnetic resonance imaging; fMRI) and pupillary evidence of impaired inhibition function in anxiety.

Behavioural Responses to Inhibition

Early studies in anxiety showed impaired response inhibition in high anxious individuals using a paired-associate learning task. (see Spence, Taylor, & Ketchel, 1956; Standish & Champion, 1960). This task includes a competitional word list, where stimulus and response words are paired more than once to create stronger associations of one stimulus word with a different word. Anxiety was found to impair the performance in these competitional lists due to impairments in inhibition of proponent response.

The Stroop task has also been used to examine the effect of anxiety on response inhibition. In the original version of this task, participants are presented with lists of coloured names of colours and they are asked to read the word or name the colour of the

word (Stroop, 1935). When the colour name and colour of the word are different, it takes more time for participants to read the word or name the colour. Pallak, Pittman, Heller, and Munson (1975) showed that anxiety increased reaction time while naming the colour of colour words (i.e. when a prepotent response inhibition is needed).

One of the main tasks used to examine inhibitory control (i.e. response inhibition) is Go/No-Go paradigm which involves continuous presentation of series of stimuli associated with frequent "Go" and rare "No-Go" cues. In response to Go cues, participants are expected to respond as quickly as possible and when presented with No-Go cues, participants should withhold their responses. More frequent Go cues makes it increasingly difficult to inhibit No-Go cues due to habituation. Using this task, Pacheco-Unguetti, Acosta, Lupianez, Roman, and Derakshan (2012) found that high state anxious individuals showed impairment (i.e., increased errors) in No-Go trials due to impairment of inhibition.

Oculomotor Responses to Inhibition

The most commonly used oculomotor response inhibition paradigm is the antisaccade task (Hallett, 1978). In this task, participants are presented visual cues either on the left or the right visual field and then they are instructed to look away from the visual cue as quickly as possible. The main indicator of performance is saccade onset latency (i.e., the time taken to generate a correct saccade). Considering anxiety, several studies have shown that high anxious individuals make slower antisaccades compared to low anxious individuals (Ansari & Derakshan, 2011b; Ansari, Derakshan, & Richards, 2008; Derakshan, Ansari, Hansard, Shoker, & Eysenck, 2009).

Neural Responses to Inhibition

Two theoretical frameworks explain the impaired inhibition function in anxiety. According to ACT, high anxious individuals have greater activation in the brain areas

linked to attentional control as a result of increased compensatory cognitive effort for successful task completion. On the other hand, Bishop (2009) argued that attentional impairment in high anxious individuals is reflected in impoverished activation of the brain areas associated with attentional control.

Consistent with ACT, ERP studies have shown greater negativity of frontal cortical networks in high anxiety, reflecting impaired inhibitory control mechanisms. For example, using the Go/No-Go task, Righi et al. (2009) found that high anxious individuals showed increased anterior negativity at around 200-300 ms (N2) due to increased activation of the frontal networks in order to compensate for task performance. Similar results were found by using stop-signal paradigm (Savostyanov et al., 2009). Research showed that high anxious individuals had more EEG desynchronization (a marker of cognitive effort and increased use of resources) before and after the warning signal suggesting active preparatory and control mechanisms before, and after the warning signal, respectively.

During the antisaccade task, Ansari and Derakshan (2011b) similarly found lower ERP activity at frontal and central areas prior to the onset of correct antisaccade (i.e. prior to inhibitory response), but only in high anxious individuals. Similarly, individuals with social anxiety showed greater CNV activity before pro- and antisaccades, suggesting increased response preparation in anxiety (Judah, Grant, Lechner, & Mills, 2013).

Unlike previous ERP research that found increased frontal activity in high anxious individuals, by using an fMRI, Bishop (2009) found that high (vs low) anxious individuals have reduced recruitment of prefrontal cortex. The author argued that high anxious individuals have impoverished recruitment of prefrontal attentional control under low load conditions (i.e. when task demands are low). It is important to note that, although fMRI

has greater spatial resolution, it has poor temporal resolution compared to EEG (Vanveen & Carter, 2002).

Pupillary Responses to Inhibition

Several studies have examined the effect of anxiety on the inhibition function using behavioural, oculomotor and neural paradigms. However, no research has explored the relationship between anxiety and pupillary responses during an inhibition task and previous research has found that anxious (versus non-anxious) individuals are known to have low pupillary motility (Oathes, Siegle, & Ray, 2011) and bigger than average pupil diameters (Bertrand, Garcia, Viera, Santos, & Bertrand, 2013). As pupillary responses are associated with increased effort and use of cognitive resources, measurement of pupillary responses might extend our understanding of inefficiency and ineffectiveness of high anxious individuals during inhibitory control.

1.3.2 Evidence of Impaired Inhibition Function in the Presence of Threat in Anxiety

Previous research has shown that anxiety impairs the inhibition function to a greater extent in the context of inhibiting attention to a threat-related stimulus or distractor. This section considers studies which have found impaired inhibition function in the presence of threat in anxiety, as indexed by behavioural (RTs), oculomotor (eye movements), neural (event-related potentials; ERPs and functional magnetic resonance imaging; fMRI) and pupillary response.

Behavioural Responses to Threat

An emotional version of the Stroop task has been used to examine the threat bias in anxiety. In this task, neutral (e.g. house, glass) and threat-related (e.g. angry, cancer) words are presented in colour and participants are asked to name the colour as quickly as

possible. There is overwhelming evidence that anxiety is associated with increased colour naming when the word is threat-related, supporting the proposition that anxious individuals are hypervigilant for threat-related distractors. For example, some studies showed that individuals with elevated anxiety took longer to name the threat-related words (Richards & French, 1990). Consistently, anxiety was found to slow Stroop performance during subliminal (Mogg, Bradley, Williams, & Mathews, 1993) and supraliminal (Vandenhout, Tenney, Huygens, Merckelbach, & Kindt, 1995) presentation of words. However, some studies highlight that regardless of emotional valence, anxious individuals were slower than low anxious individuals to colour name words (Fox, 1993; Mogg & Marden, 1990; Reinholdt-Dunne et al., 2012), suggesting that trait anxiety may reflect attentional impairments more broadly, rather than threat words specifically.

The effect of anxiety on the inhibitory system in presence of threat has also been studied by using emotional version of Go/No-Go task. Putman, van Peer, Maimari, and van der Werff (2010), for example, found significant correlations between trait anxiety and inhibitory response bias for fearful than happy facial expressions.

Oculomotor Responses to Threat

Emotional pro-and antisaccade paradigm has been used to investigate oculomotor correlates of threat-bias in anxiety. For example, Garner, Attwood, Baldwin, James, and Munafo (2011) reported increased error rates for antisaccade trials during inhalation of 7.5 % CO_2 (i.e. high state anxiety) compared to air inhalation (i.e. low state anxiety) group, while processing threat-related faces. On the other hand, Derakshan et al. (2009) presented facial expressions of emotions to participants (on the right or left visual field) and asked them to execute a pro- or antisaccade towards or away from that face (from the central fixation cross). They found that high trait anxiety was associated with impaired

antisaccades (i.e., increased latencies to make a saccade away from the face) when the cue was an angry face. There was no relationship between anxiety and prosaccade latencies or saccadic error rates (regardless of saccade type or emotion). The authors concluded that individuals with high levels of anxiety have problems in inhibitory control while processing threat-related stimuli. Wieser, Pauli, and Muhlberger (2009) used a similar emotional pro- and antisaccade paradigm, however, they found that, regardless of emotion, high anxious individuals made more antisaccade errors. Also, unlike Derakshan et al. (2009), they did not find the effect of anxiety on saccade onset latencies. They concluded that high anxious individuals might have a general attentional control impairment, rather than attentional bias to threat-related stimuli.

Neural Responses to Threat

Miller and Cohen (2001) argued that the function of the prefrontal cortex is to prioritise the correct sensory input (i.e. top-down biasing) to meet current goals. Reduced activation in the prefrontal cortex (i.e. reduced top-down biasing) and increased amygdala activation has been observed in individuals with elevated anxiety symptoms. For example, Bishop and colleagues presented pairs of houses and neutral/fearful faces and asked participants to attend to either the faces or the houses (Bishop, Duncan, Brett, & Lawrence, 2004). The results showed decreased activation of the lateral prefrontal cortex (associated with attentional control) and increased amygdala activation to both attended and unattended threat-related stimuli in participants who reported high anxiety. In contrast, low anxious individuals showed increased amygdala activation only when they were attending to threat-related stimuli, indicating that anxiety interacts with attention to affect amygdalic responses.

Pupillary Responses to Threat

Although pupillometry has been used as a method to study executive functions and emotional processing, few studies have explored associations between pupillary responses and anxiety. Price et al. (2013) asked participants to complete a visual-probe task in which target stimuli replaced a fearful or neutral face. Anxious (vs healthy) individuals showed increased pupil diameters to fearful (compared with neutral) stimuli, suggesting threat-related stimulus increased pupillary responses. Similarly, using an emotion recognition task, Kret, Stekelenburg, Roelofs, and de Gelder (2013) found that there was a positive correlation between pupil dilation and anxiety only when viewing angry facial expressions (versus fearful and happy faces). In contrast, using a valence categorization task with emotional stimuli with interleaved Stroop colour word trials, Oathes et al. (2011) found that negative emotional stimuli (i.e. personally relevant negative words) elicited decreased pupillary dilations. Taken together, the effects of threat-bias on pupillary responses are still not precise.

Further research has found that the association between anxiety and ineffectiveness/inefficiency during inhibitory control is most evident with increased cognitive load.

1.3.3 Effects of Load/Effort on Anxiety

According to ACT, a task that places high demands on cognitive resources affects high anxious individuals more than non or low anxious individuals. Moreover, this effect is suggested to have greatest impact when the task includes an inhibitory control element. ACT also recognises that high anxious individuals will exert greater amounts of cognitive effort to compensate task performance under high load. This section focuses on the effects

of only load and effort on inhibitory control and includes behavioural and oculomotor evidence.

Berggren, Koster, and Derakshan (2012) examined the effect of cognitive load during a visual search task by showing different facial expressions (i.e. angry, happy, and neutral faces) as targets or distractors. They asked participants to search for a target face amongst the same distractor faces. Cognitive load was manipulated by administering a secondary task in which participants were required to count back from a presented number in intervals of three. The results showed that the high cognitive load condition increased reaction times for visual search performance for high (vs low) anxious individuals. The authors concluded that the negative impact of anxiety on task performance is most evident under conditions of high cognitive load.

By using an emotional version of the antisaccade task with a secondary task, (Berggren et al., 2013) were able to further demonstrate the performance cost of increased cognitive load for high anxious individuals. They used tone recognition in a low load condition and specific tone pitch recognition in a high load condition. They found that high cognitive load increased antisaccade latencies (to face stimuli) especially for high anxious individuals.

Summary

Previous research in anxiety has started to build an evidence base to focus on attentional control deficits in anxiety and across different methodologies. However, findings demonstrating the role of increased effort (via pupillary responses) on the processing of emotional stimuli across tasks that have high and low and how these processes are linked to electrophysiological brain activities is sparse. The current thesis

aims to combine behavioural, oculomotor, pupillary, and electrocortical measures of inefficiency and ineffectiveness during inhibitory control in anxious individuals.

1.4 Summary and Research Questions

Anxiety is negative emotional state associated with elevated physiological arousal, worry and behavioural avoidance (American Psychiatric Association, 2013) that can have a significant impairment on an individual's daily functioning. Several theoretical models have proposed that anxiety is associated with impaired cognitive control (Eysenck et al., 2007); it impacts on executive attention processes and specifically tasks requiring inhibition (of salient stimuli), updating information in working memory and shifting attention between different stimuli. Moreover, poor attentional control in anxiety is proposed to be most evident in the presence of threat-related stimuli and in tasks that have high (versus low) cognitive load (Berggren et al., 2013).

The aim of the current thesis was to explore associations between anxiety and inhibitory control in the context of tasks that require more versus less effort and in the presence of threat-related emotional stimuli. Research has reliably shown that electrophysiological, pupillary and oculomotor responses are associated with increased cognitive control, effort, and emotional processing in cognitive tasks. These core constructs map on to theoretical frameworks in anxiety that focus on the role of executive and affective processing as a mechanism that causes or serves to maintain heightened states of anxiety. Executive and affective processing in the current study was therefore investigated using diverse methodologies including electroencephalography, pupillography and eye-tracking.

Research Aims

The current thesis reports data from a series of studies in subclinical anxious individuals that systematically examined the effects of compensatory cognitive effort and inhibitory control when processing emotional and non-emotional stimuli.

Experiment 1. Pupillometric and Saccadic Measures of Affective and Executive Processing in Anxiety. This study examined the effect of emotion and increased load and effort on pupillary and oculomotor responses by using oculomotor delayed response task with different delay durations.

Experiment 2. Electrocortical, pupillometric, and eye-movement evidence of impaired processing efficiency and performance effectiveness in anxiety. This study extends evidence from pupillometric measures in Experiment 1 to examine the effect of increased load/effort on electrophysiological responses (mean CNV amplitudes) by using delayed pro- and antisaccade tasks that manipulated delay duration.

Experiment 3. Effects of anxiety and inhibitory load on pupillary responses and prefrontal function during inhibitory control. The final study examines the effect of inhibitory load on inhibitory control (peak N2 and P3 amplitudes) by using a Go/No-Go task that manipulated stimulus probability.

2 Pupillometric and Saccadic Measures of Affective and Executive Processing in Anxiety

2.1 Introduction

Anxiety is characterised by hyperactivity in physiological, cognitive and behavioural mechanisms in anticipation of threat and in response to threat cues (Bar-Haim et al., 2007). Neuropsychological models of anxiety highlight maladaptive biases in threat appraisal and attention in the aetiology and maintenance of core symptoms that include distractibility, poor concentration, nervous apprehension and worry (Sylvester et al., 2012). Hyperactivity in bottom-up stimulus-driven mechanisms (i.e. increased amygdala activation) increase threat appraisal, autonomic arousal, and attentional bias to threat (Bishop, 2009). In addition hypo-activity in goal-directed control processes (i.e., reduced activity in the dorsolateral prefrontal cortex) reduce attentional control and exacerbate attentional biases to threat distractors, particularly when task demands are high (Bishop, 2009). Recent methodological advances provide more sensitive indices of attention and related processes (e.g., pupillometry and eye-movement measures) to examine anxiety-related biases in emotional reactivity to emotional stimuli, and the impact of low and high cognitive load on attention biases and attentional control more broadly.

Pupillary responses of the human eye are modulated by affective and executive processes via central and peripheral sympathetic and parasympathetic divisions of the nervous system (see Andreassi, 2000, for a review), see Chapter 1, Section 1.2.2. Pupil diameter increases in response to emotional stimuli (both visual and auditory) and correlates with subjective ratings of emotional arousal and skin-conductance responses

(Bradley et al., 2008; Partala & Surakka, 2003; Rosa, Esteves, & Arriaga, 2015). Recent evidence suggests that pupillary responses are sensitive to individual differences in threat processing, as reflected in increased pupil responses to angry faces in anxious individuals (Kret et al., 2013), fearful faces in anxious youths (Price et al., 2013) and to angry faces in children of anxious mothers (Burkhouse, Siegle, & Gibb, 2014).

Behavioural studies provide evidence of selective attention and 'hypervigilance' for threat in anxiety. For example, individuals with clinical and sub-clinical anxiety make speeded reaction times (RTs) to visual targets that appear in the location of threat stimuli (e.g. negative pictures and facial expressions; review by Bar-Haim et al., 2007). Likewise eye-tracking methods reveal preferential and faster eye-movements towards threat cues in anxiety (Chen, Clarke, Watson, Macleod, & Guastella, 2014; Mogg, Garner, & Bradley, 2007) or increased hypervigilance for threat that interferes with task goals (review by Richards, Benson, Donnelly, & Hadwin, 2014). Biases in selective attention have been observed in a range of anxiety groups, including generalized anxiety, social phobia, specific phobias and high trait anxious 'sub-clinical' populations (review by Bar-Haim et al., 2007) and are increased further in individuals who concurrently report poor attentional control (Derryberry & Reed, 2002)

Attentional control theory (Eysenck & Derakshan, 2011; Eysenck et al., 2007) and related models (e.g. Processing Efficiency Theory; Eysenck & Calvo, 1992) propose that anxiety reduces "top-down" attentional resources that are required to maintain goal- focus and inhibit task-irrelevant (negative) distractors, with anxious individuals required to recruit more resources to complete tasks effectively. Consequently, anxiety is thought to be associated with substantial impairment in processing efficiency (reflected in increased

effort or time) alongside modest impairment in performance effectiveness, particularly when task demands are high. Anxiety-related deficits in attention control and executive function have been observed across several behavioural measures. Trait anxious individuals, for example, perform less well on the executive attention subtest of the attention network task (ANT; Pacheco-Unguetti, Acosta, Callejas, & Lupianez, 2010), and show deficits when required to inhibit task-irrelevant distractors or inhibit prepotent behavioural responses (review by Mobini & Grant, 2007). In addition, studies have demonstrated the negative impact of elevated anxiety on reduced processing efficiency in child (Hadwin, Brogan, & Stevenson, 2005) and adult populations (see Eysenck et al., 2007).

Similarly, pupil diameter increases during periods of resource recruitment and mental effort (Beatty, 1982; Beatty & Lucero-Wagoner, 2000; Hess, 1975; Kahneman & Beatty, 1966; Karatekin, Marcus, & Couperus, 2007). Trait anxious individuals show larger pupillary responses (vs. low anxious individuals) during tasks that require sustained attention (e.g. simulated driving tasks; Wilson, Smith, Chattington, Ford, and Marple-Horvat (2006), and pupillary responses are sensitive to anxiety-related deficits in other behavioural tasks such as learning paradigms (e.g. two-arm bandit learning task; Browning, Behrens, Jocham, O'Reilly, & Bishop, 2015).

The antisaccade task is a simple inhibitory control task that utilises eye movement measures to investigate individual differences in attention control across anxiety and mood disorders (review by Ainsworth & Garner, 2013). Participants are instructed to look away from a visual cue (i.e. to its mirror location) as quickly and accurately as possible. Attentional control is indicated in the: (1) inhibition of reflexive saccades, and the (2) generation of volitional saccades (Hutton & Ettinger, 2006). Consistent with predictions

from Attentional Control Theory, anxious individuals are more likely to make erroneous eye-movements on antisaccade trials, and are slower (less efficient) at executing antisaccades (Ansari & Derakshan, 2011b; Garner et al., 2011). Furthermore, anxiety-related deficits in antisaccade performance are greater in response to threat distractors (e.g. angry facial expressions; Derakshan et al., 2009; Reinholdt-Dunne et al., 2012) and when processing demands increase (Berggren et al., 2013).

The effects of task demand/load have been examined in studies that manipulate the time between which a stimulus is presented and an eye-movement response is required. For example, participants make more errors and are slower to make accurate antisaccades when asked to respond immediately after stimulus onset (no-delay) compared to after a short delay, which is argued to facilitate response preparation (e.g. 600 ms - 1500 ms; Ansari & Derakshan, 2010, 2011a; Reuter, Jager, Bottlender, & Kathmann, 2007). Conversely, in an oculomotor delayed response (ODR) task a longer delay is introduced to increase demand on working memory. In this task, participants are required to encode the spatial location of a briefly presented visual cue and store information in working memory during a delay period (e.g. 5-10 secs), while maintaining a central fixation before generating a memory-guided saccade (Curtis & D'Esposito, 2003; Luna & Velanova, 2011). Consequently, the ODR task might be particularly sensitive to anxiety-related deficits in processing efficiency due to increased demands on the dorsolateral prefrontal cortex under high load conditions (i.e., with increased delay periods) (Curtis & D'Esposito, 2003). Furthermore this task can incorporate concurrent online pupillometry measures that can profile the time-course of 'effort' expended throughout periods of high and low load (long and short delay respectively).

In the current task, high and low anxious individuals' pupillary responses to centrally presented emotional (angry, fearful, happy, neutral) facial expressions and subsequent attention to faces presented in a memory-guided pro- and antisaccade ODR task under conditions of high and low cognitive load (following 10s or 5s delay respectively) were compared. It was hypothesised that individuals with elevated levels of trait anxiety (trait anxious individuals) would show (1) larger pupillary responses to negative (angry, fearful) facial expressions (consistent with increased threat appraisal), (2) larger pupil responses during oculomotor delay, particularly during the long delay (consistent with greater effort/poor processing efficiency), and (3) impaired task performance characterised by fewer and slower accurate eye-movements, particularly on antisaccade trials in response to negative faces following a long delay (consistent with reduced ability to orient away from/inhibit threat distractors under conditions of high load).

2.2 Method

2.2.1 Participants

Forty participants (*mean* age=22.65, min= 18, max=34, *SD*=4.47) were recruited from the University of Southampton. Some of the participants were recruited via posters and an online advertisement. Remaining participants were selected amongst five hundred and one university students that completed the screening questionnaire (the trait version of Spielberger State-Trait Anxiety Inventory (STAI-T; Spielberger, Gorusch, Lushene, Vagg, & Jacobs, 1983); see Appendix A).

Participants had normal or corrected-to-normal vision and wore glasses or contact lenses if necessary. Participants confirmed that they had not taken drugs, alcohol, or medication on the day preceding testing. They received either course credits or £6 for

participation. All participants provided informed consent. The research protocol was approved by the University of Southampton Ethics and Research Governance committees. (Please see Appendix D Section 1 for Experiment 1 forms).

2.2.2 Apparatus

Eye movements and pupillary responses were recorded using SR Research EyeLink 1000 desktop-mounted eye tracking system (SR Research Ltd., Ontario, Canada) with a sampling rate of 1 kHz. Pupillary responses were recorded using Centroid model based on pupil diameter in millimetres. The presentation was controlled by Experiment Builder v1.10.1025 software (SR Research Ltd., Ontario, Canada) on a 19-inch ViewSonic (P227f) monitor.

2.2.3 Stimuli

Sixty-four face stimuli were selected from the NimStim Face Stimulus Set (Tottenham et al., 2009) including angry, fearful, happy, and neutral expressions posed by 8 female and 8 male models (models were 02f, 03f, 05f, 06f, 07f, 08f, 09f, 18f, 24m, 25m, 26m, 28m, 30m, 33m, 34m, 37m; see Appendix E). Faces were standardized for size (M_{width}= 303 px, M_{height}= 449 px), aspect ratio (height/width; 1.48) and converted to grayscale with mean luminosity set to 22 lux. In order to adjust for head orientation and to centre the stimuli, the endocanthion (i.e. the point where the inner commissures of the lower and upper eyelid meet) line was rotated to become horizontal and the midpoint of this line was set to a stable coordinate of 253x325 pixels. In addition, a mask was applied to all face stimuli to cover hair and other external features and visual artefacts (e.g. scars, spots) were removed.

2.2.4 Experimental Task and Procedure

As seen in the Figure 2.1, each trial started with a drift correction phase. After participants fixated on the central fixation point, a face stimulus cue was presented in the centre of the screen for 1000 ms, subtending 2º 27' x 3º 31' of visual angle (viewing distance of 65 cm). Following the presentation of the cue, the same face stimulus target (the eccentricity of each face, when fixating the central cross was 7º 21') were presented at one of 8 compass points (0º, 45º, 90º, 135º, 180º, 225º, 270º, 315º) (as per Ichihara-Takeda & Funahashi, 2007; Park, 1997) for 150 ms. After either a short (5 seconds) or long (10 seconds) delay, participants were instructed to look 'TOWARDS' (prosaccade) or 'AWAY' from (antisaccade) the location of the target (instruction SOA = 300 ms). The maximum time available to execute a pro- or antisaccade was 1500 ms. A blank inter-trial interval (ITI) was presented for 1000 ms. All stimuli were presented on a grey background (R = 117, G = 116, B = 116) and all trial screen displays had a mean luminosity of 116.

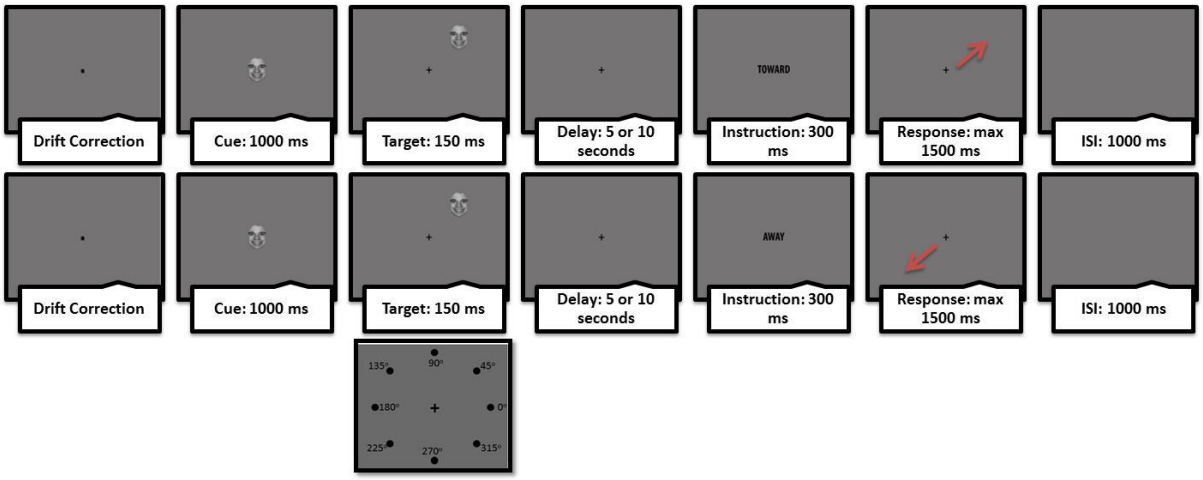


Figure 2.1 Flowchart of prosaccade and antisaccade trials with short and long delay. After a successful drift correction, participants were presented a cue (i.e. facial expressions of emotions: angry, fearful, happy, and neutral). Then, the same face was presented as a target for just a period of time at one of the eight compass points. After 5 (low load) or 10 (high load) seconds of delay, participants generated a prosaccade or antisaccade according to previously presented instructions indicating the type of trial (Toward: Prosaccade, Away: Antisaccade)

Participants were seated in front of the computer and eye-tracking system, with their chin and head supported at a viewing distance of 65 cm. Participants were calibrated (9-point display) before completing 4 practice trials and the experimental task. The task consisted of 256 trials presented across 4 blocks of 64 trials (each with 32 prosaccade, 32 antisaccade, presented randomly). Participants could take a small break between blocks and were re-calibrated when appropriate.

2.2.5 Data Preparation

Pupillary Responses. Pupillary responses were pre-processed using previous standard procedures (cf. Beatty & Lucero-Wagoner, 2000; Bradley et al., 2008; Granholm, Morris, Asarnow, Chock, & Jeste, 2000) by using MATLAB R2013a (The Math-Work, Inc., MA, USA). Firstly, blinks and artefacts (very short increases or decreases of at least

0.375 mm within 20 ms (Partala & Surakka, 2003) were removed. Then, missing values were corrected by linear interpolation resulting in 5.87 % and 11.88 % of data interpolation in face cue and delay periods respectively. Thirdly, continuous pupil data were epoched during each face cue (1000 ms), and during each delay period (5000 ms for short delay and 10000 ms for long delay). Then, baseline correction (relative to the start of epoch) was applied. Peak pupillary responses (maximum pupil diameter) and latency to peak (ms) were calculated during each face cue (1000 ms), during the 5000 ms delay period (A), and during the first (B) and second (C) 5000 ms of the 10000 ms delay period. Responses during short delay (A+B/2) were compared against responses during the long delay (C). Distributions of amplitude and latency of peak pupillary responses were examined and met assumptions of normality using Shapiro-Wilk's test, p's > .05.

Saccades. Mean saccade accuracies (%) and latencies (ms) (from offset of instruction) were extracted for the first valid saccade on each trial (i.e. latencies > 80 ms, velocities > 30°/s, and amplitudes > 3°) (Ansari & Derakshan, 2010). This resulted in the loss of 8.56 % of trials. An erroneous saccade was defined as the first saccade landing outside the relevant interest area for that trial type –i.e. 90° quadrant around the face for prosaccade trials, and the 90° quadrant in the opposite location for antisaccade trials. Distributions of saccadic error rates and latencies were examined and met assumptions of normality using Shapiro-Wilk's test, p's > .05.

2.3 Results [1]

2.3.1 Participants

Mean trait anxiety score as measured by the trait version of Spielberger State-Trait Anxiety Inventory (STAI-T; Spielberger et al., 1983) (see Appendix A) for the sample (*N*=40) was 42.83 (*SD*= 12.75, *min*=20, *max*=66). Anxiety scores were normally distributed (Shapiro Wilk= .93, p=.21). In order to test the effects of anxiety, participants were divided into high and low anxiety groups based on a tercile split on the trait anxiety score. Consistent with previous research (see Ansari et al., 2008) participants who scored ≤ 35 were categorised as low anxious (LA; *n* = 13, *mean* STAI-T = 27.92, *S.D.* = 4.11, *min* = 20, *max* = 34, *mean* age = 21.92; 10 females) and those scoring ≥ 50 as high anxious (HA; *n* = 14, *mean* STAI-T = 56.79, *S.D.* = 5.02, *min* = 50, *max* = 66, *mean* age = 23.45; 12 females). Anxiety scores were normally distributed (LA; Shapiro Wilk= .94, p=.56; HA; Shapiro Wilk= .92, p=.23)

2.3.2 Pupillary Responses

2.3.2.1 Emotion Facial Expressions

Amplitude and latency of peak pupil responses were entered into separate 2 x 4 repeated measures ANOVA with Group (low-anxious, high-anxious) as the between subject factor and Emotion (angry, fearful, happy, neutral) as the within subject factor. Where assumptions of sphericity were violated, Greenhouse-Geisser corrections were applied. Significant effects were followed by paired and independent samples t-tests where appropriate. Level of significance accepted was $p < .05$. Supplementary time-series

[1] See Appendix F Section 1 for descriptive statistics.

analyses of pupil diameter examined effects of emotion and anxiety over-time across 50 consecutive 20 ms epochs as per Geva et al. (2013).

Peak pupillary responses to facial expressions were larger but slower in high-anxious relative to low-anxious individuals, (Amplitude: High-anxious (M = 0.16, $S.E.$ =0.03) vs low-anxious (M = 0.10, $S.E.$ =0.01), $F_{(1,21)}$ = 5.21, p = .03, η^2 = .19; Latency: High-anxious (M = 239.42, $S.E.$ =24.00) vs low-anxious (M = 172.12, $S.E.$ =21.05), $F_{(1,21)}$ = 4.44, p = .04, η^2 = .17).

The time series analyses suggested that differences in pupil dilation between high and low anxiety groups were most pronounced from 300-400 ms after stimulus onset (see Figure 2.2). A main effect of emotion [$F_{(3,63)}$ = 6.08, p = .001, η^2 = .22] was characterised by larger peak responses to angry (M = 0.17, $S.E.$ =0.02) relative to happy (M = 0.10, $S.E.$ =0.01) expressions – time-series analysis suggests this effect was most pronounced from 200-300 ms (Figure 2.3). There was no effect of anxiety x emotion on peak response, nor latency (Fs < 1 *ps* > .1).

Table 2.1

Means (standard deviations) of peak pupillary responses (mm) in high anxious (HA) and low anxious (LA) groups for each emotion.

	HA (*n*=14)	LA (*n*=13)
Angry	.17 (.13)	.16 (.09)
Fearful	.18 (.14)	.10 (.06)
Happy	.13 (.10)	.06 (.04)
Neutral	.17 (.12)	.12 (.05)

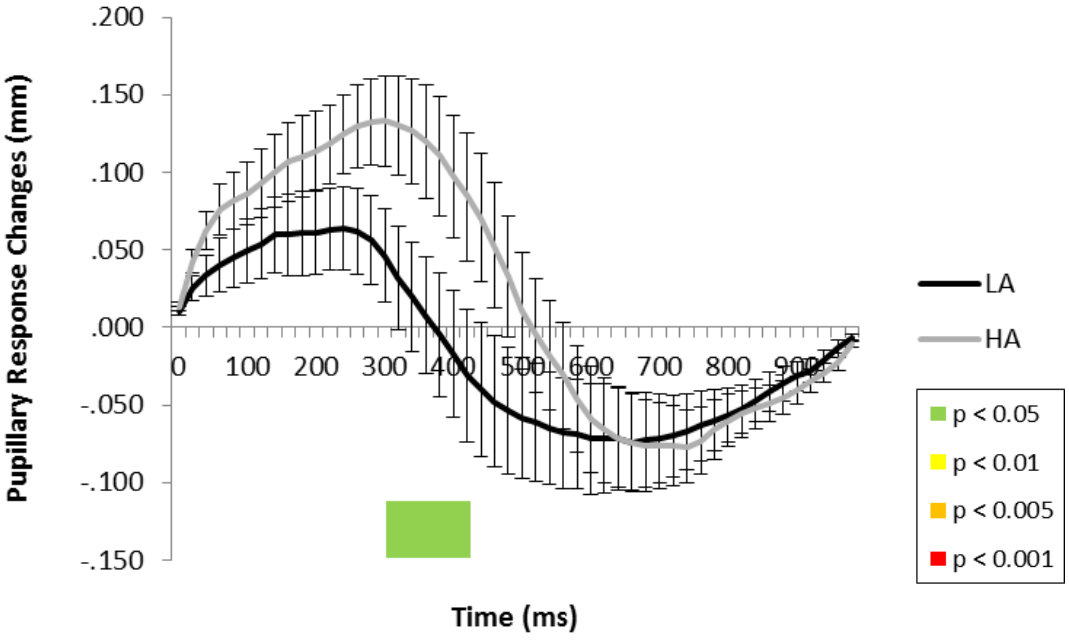


Figure 2.2 Pupillary response time series to face cues in high-anxious (HA) and low-anxious (LA) groups (bars represent standard errors). Pupillary responses of HA individuals are bigger but larger compared to LA individuals, especially between 300-400 ms.

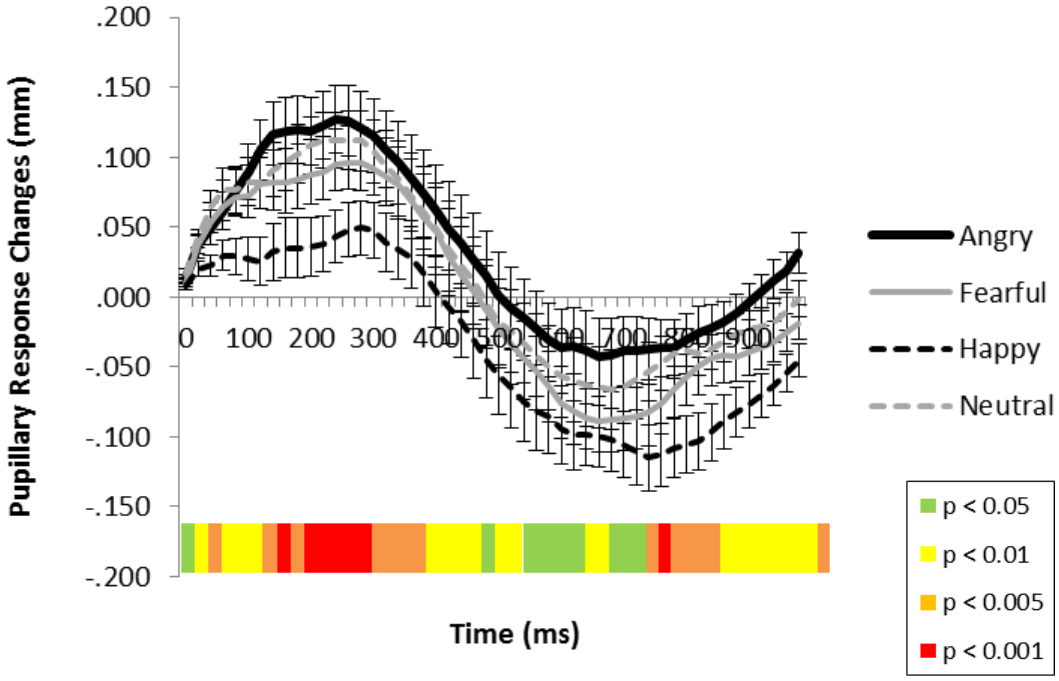


Figure 2.3 Pupillary response time series to face cues (bars represent standard errors). Angry faces elicited increased pupillary responses compared to happy faces. This difference was more pronounced between 200-300 ms.

2.3.2.2 Short and Long Delays

Amplitude and latency of peak pupil responses were entered into a 2 x 2 x 4 repeated measures ANOVA with Group (low-anxious, high-anxious) as the between subject factor and Delay Type (short, long) and Emotion (angry, happy, fear, neutral) as the within subject factors. Where assumptions of sphericity were violated, Greenhouse-Geisser corrections were applied. Significant effects were followed by paired and independent samples t-tests where appropriate. Level of significance accepted was $p < .05$. Follow-up supplementary time-series analyses of pupil diameter examined effects of delay and anxiety over-time across 250 consecutive 20 ms epochs.

A Group x Delay interaction [$F_{(1,22)} = 4.68$, $p = .04$, $\eta^2 = .17$] was characterised by smaller peak pupil amplitude in low anxious individuals during short delay compared to i)

long delay in low anxious individuals ($t(13)$= .2.97, p=.006), and ii) peak responses in high anxious individuals during long ($t(13)$= .2.06, p=.04) and short ($t(13)$= .2.67, p=.01) delay (see Figure 2.4). Peak amplitudes in high anxious individuals were unaffected by delay, and were comparable to the elevated peak amplitude in low anxious individuals during long delay. No other peak amplitude effects were significant (Fs < 1 *ps* > .1). Comparable analyses of peak latency did not reveal significant effects of group, delay, emotion nor their interaction, Fs < 1 *ps* > .1. Supplementary time-series analyses suggested the difference between short and long delay in low anxious individuals reflects an increase in pupil diameter towards the end of the long delay period (> 8500 ms,) (see Figure 2.5 and Figure 2.6). Consistent with peak analyses, time-series analysis did not reveal significant effects in the high anxious participants.

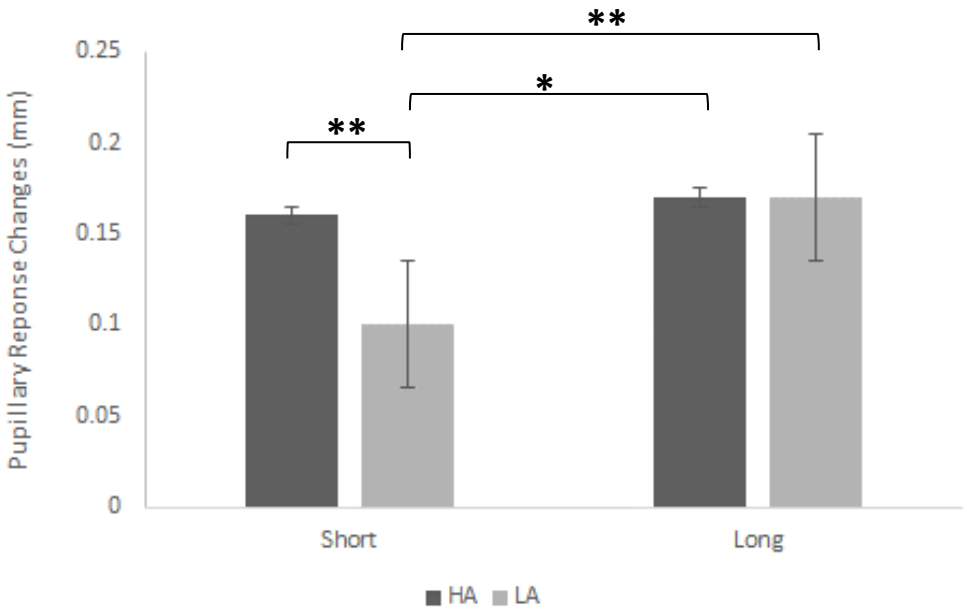


Figure 2.4 Peak pupillary responses during long and short delay trials in high-anxious (HA) and low-anxious (LA) groups (bars represent standard errors). LA individuals produced smaller pupillary responses during short delay compared to long delay. LA individuals also produced smaller pupillary responses than HA individuals during short and long delay.

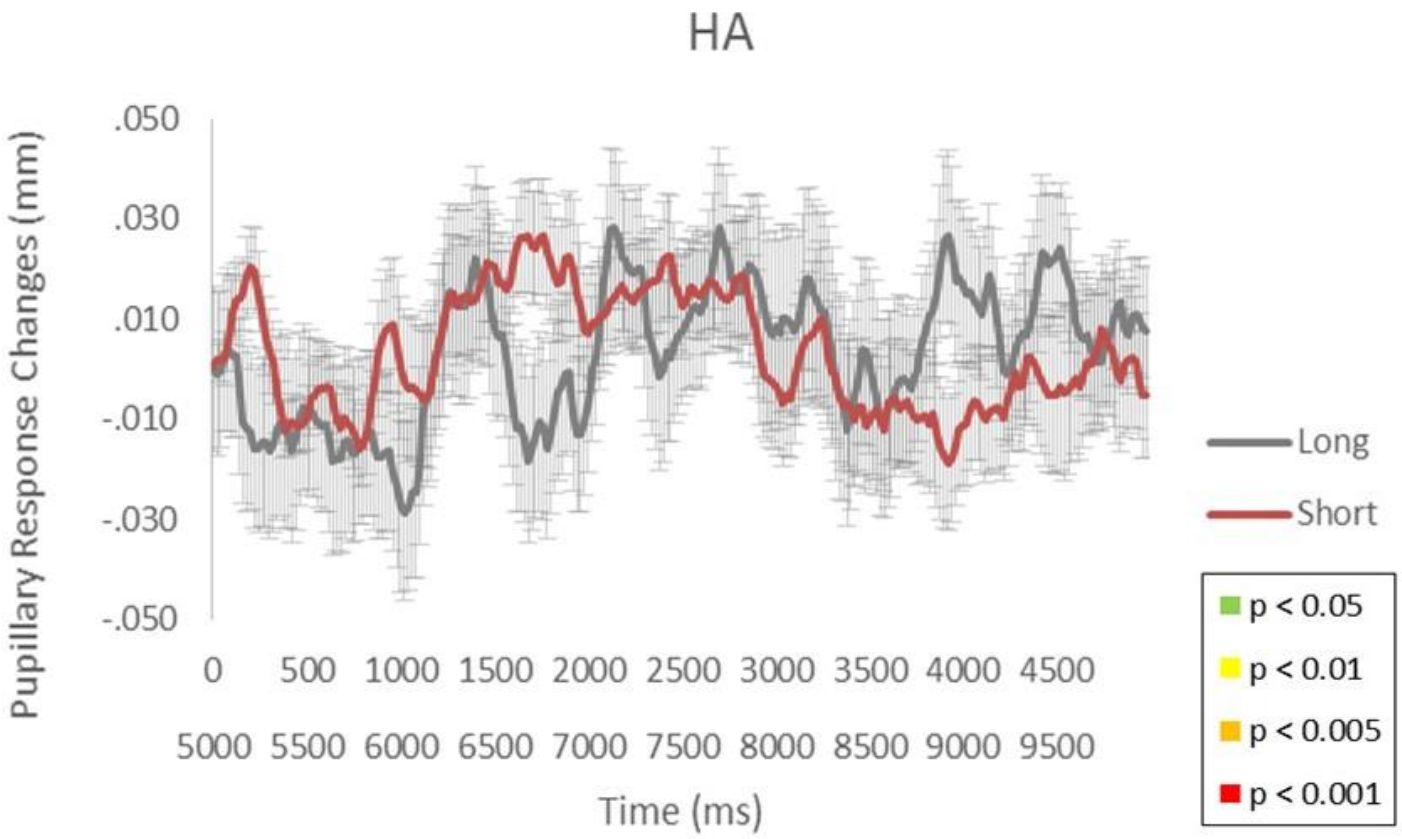


Figure 2.5 Pupillary response time series for long and short delay trials in high-anxious (HA) group (bars represent standard errors) (Upper and lower x-axes represent time points during short and long delay, respectively). Pupillary responses of HA were comparable during short and long delay.

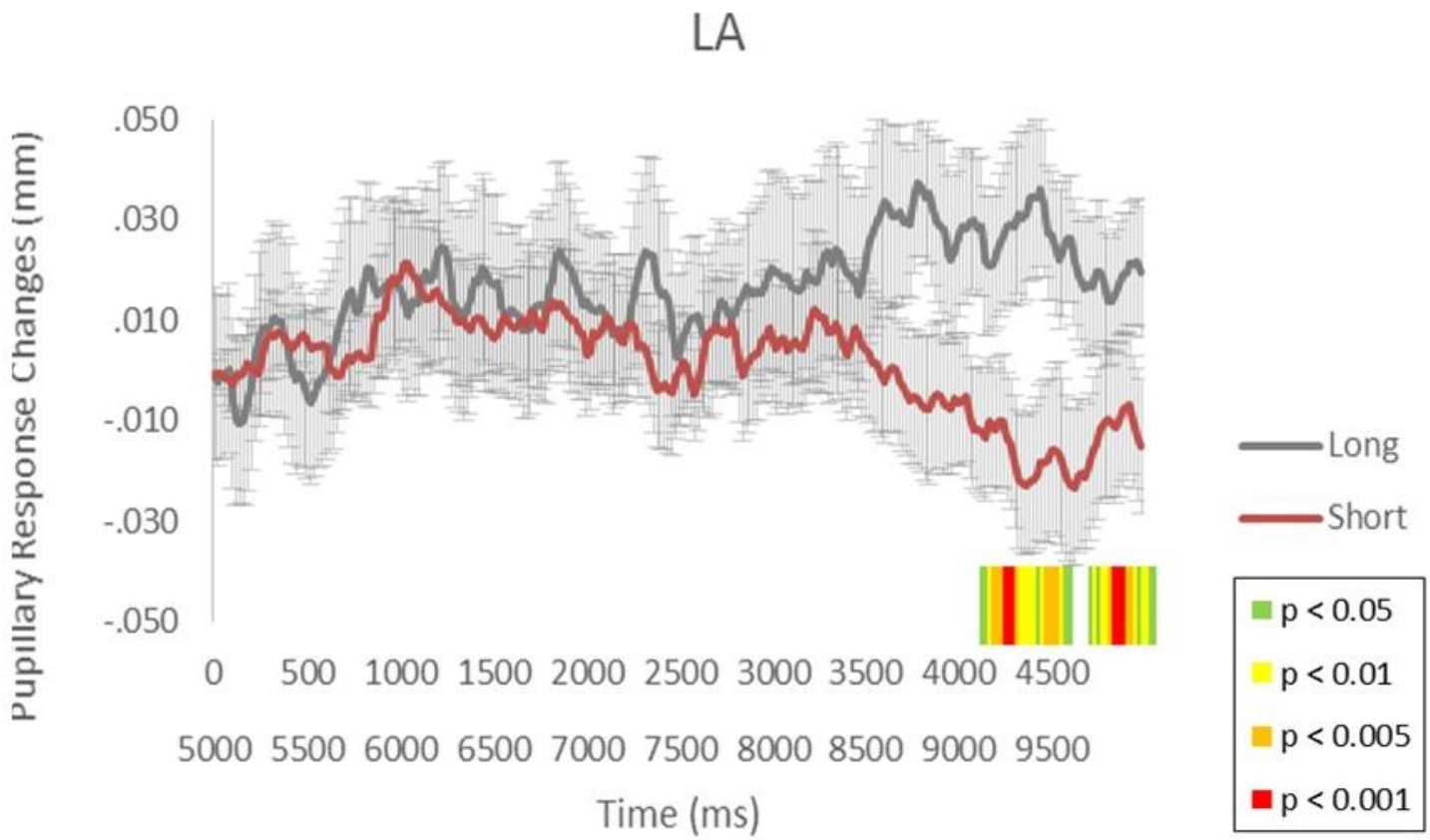


Figure 2.6 Pupillary response time series for long and short delay trials in low-anxious (LA) group (bars represent standard errors) (Upper and lower x-axes represent time points during short and long delay, respectively). Long delay elicited increased pupillary responses in LA individuals.

2.3.3 Eye-movement Saccade Error and Latency

Saccade error and latency were analysed in two separate 2 x 2 x 2 x 4 repeated measures ANOVAs with Group (low-anxious, high-anxious) as the between subject factor and Saccade Type (antisaccade, prosaccade), Delay Type (short, long) and Emotion (angry, fearful, happy, neutral) as the within subject factors. As before, Greenhouse-Geisser corrections were applied where sphericity was violated, paired and independent samples t-tests were used in order to explore interactions (reliable at $p < .05$) where appropriate.

Participants made more errors on antisaccade trials (M = 19.43, $S.E.$ =2.19) than prosaccade trials (M = 16.28, $S.E.$ =1.59), [$F_{(1,25)}$ = 4.09, p = .05, η^2 = .14], irrespective of delay, emotion and anxiety group, Fs < 1 ps > .1. A significant anxiety Group x Delay interaction [$F_{(1,25)}$ = 9.22, p = .001, η^2 = .26] was characterised by an increased number of eye-movement errors in high (vs. low) anxious individuals following long delays $t(13)$= -3.28, p=.005) (see Figure 2.7). Also see Table 2.2.

Table 2.2

Means (standard deviations) of saccadic error rates (%) in high anxious (HA) and low anxious (LA) groups during long and short delay.

	HA (*n*=14)		**LA (*n*=13)**	
	Pro	*Anti*	*Pro*	*Anti*
Long Delay	20.78 (11.07)	24.21 (13.90)	11.72 (5.78)	16.19 (9.35)
Short Delay	19.08 (9.96)	19.30 (11.44)	13.56 (7.94)	10.93 (11.74)

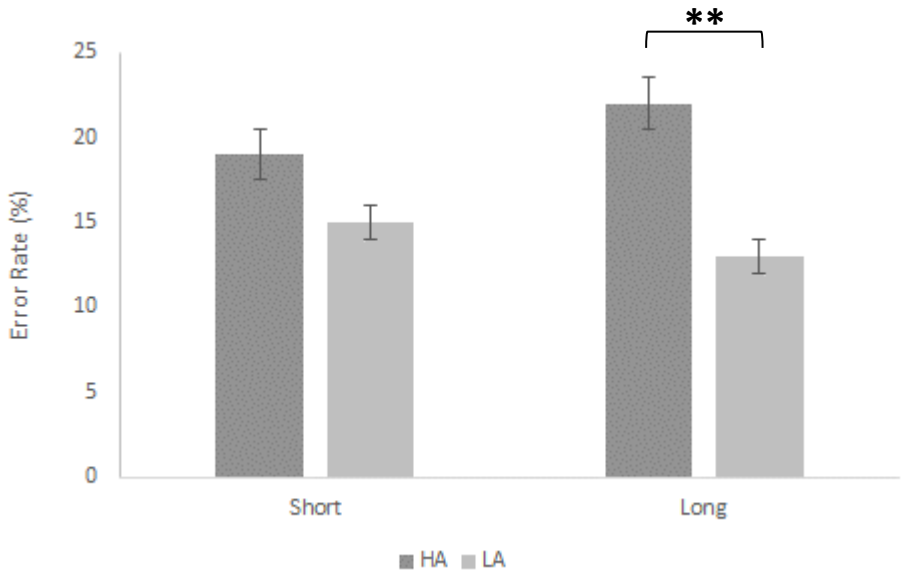


Figure 2.7 Percentage of saccade error in high-anxious (HA) and low-anxious (LA) groups on each of the long and short delay trials (bars represent standard errors). HA individuals made more saccadic errors compared to LA individuals after long delay.

A corresponding analysis of eye-movement latencies indicated that participants were slower to make correct saccades on antisaccade (M = 246.67, *S.E.* =11.50) vs. prosaccade trials (M = 233.66, *S.E.* =10.20), [$F_{(1,25)}$ = 4.77, p = .03, η^2 = .16], and following short delay (M = 250.39, *S.E.* =10.01) compared to long delay (M = 229.94, *S.E.* =11.35), [$F_{(1,25)}$ = 19.91, p = .05, η^2 = .44]. Also see Table 2.3.

Table 2.3

Means (standard deviations) of saccade onset latencies (ms) in high anxious (HA) and low anxious (LA) groups during long and short delay.

	HA (*n*=14)		**LA (*n*=13)**	
	Pro	*Anti*	*Pro*	*Anti*
Long Delay	232.89 (52.33)	247.55 (59.61)	216.96 (66.77)	222.37 (65.64)
Short Delay	250.00 (44.93)	273.91 (63.36)	234.80 (56.32)	242.86 (57.35)

2.3.4 Supplementary Analyses

2.3.4.1. Participant Characteristics

Before the experimental session, participants completed Cognitive Failures Questionnaire (Broadbent, Cooper, FitzGerald, & Parkes, 1982), Generalised Anxiety Disorder Scale (Spitzer, Kroenke, Williams, & Lowe, 2006), Social Phobia Inventory (Connor et al., 2000), Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983), and Attentional Control Scale (Derryberry & Reed, 2002) (see Appendix C). These questionnaires were used as descriptive measures (see Table 2.4) and were not used in relation to pupillary and saccadic data analyses.

Table 2.4*

Means (standard deviations) of participant characteristics questionnaires.

	HA (*n*=14)	**LA (*n*=13)**	**Total (*n*=27)**
CFQ	49.33 (11.74)	34.90 (9.11)	40.00 (12.06)
GAD-7	7.33 (2.65)	2.09 (2.38)	3.94 (3.52)
SPIN	16.83 (8.72)	6.63 (4.36)	10.23 (7.80)
HADS	-	-	-
Anxiety	13.16 (3.76)	8.09 (3.91)	9.88 (4.49)
Depression	13.33 (2.25)	10.45 (3.32)	11.47 (3.24)
ACS	23.50 (5.99)	31.18 (6.36)	28.47 (7.13)
Focusing	7.00 (3.28)	11.27 (4.14)	9.76 (4.30)
Shifting	16.50 (4.76)	19.90 (3.88)	18.70 (4.39)

*CFQ: Cognitive Failures Questionnaire, GAD-7: Generalised Anxiety Disorder Scale, SPIN: Social Phobia Inventory, HADS: Hospital Anxiety and Depression Scale, ACS: Attentional Control Scale

2.3.4.2. Pupillometric and Saccadic Analyses across the Sample

We also analysed amplitude and latency of peak pupillary responses in response to emotion and cognitive load, and mean saccadic errors and latencies across the sample (n=40).

Pupillary Responses. Amplitude and latency of peak pupillary responses to emotion were analysed by separate t-tests. Angry (M = 0.16, *S.E.* =2.32), [$t(37)$= 3.50, p=. 001] and fearful (M = 0.15, *S.E.* =1.01), [$t(37)$= 3.80, p=. 05] faces elicited larger pupillary responses compared to happy (M = 0.11, *S.E.* =1.20) faces. Latency and other amplitude effects were insignificant (Fs < 1 *ps* > .1).

Amplitude and latency of peak pupil responses to delay were entered into a 2 x 4 repeated measures ANOVA with Delay Type (short, long) and Emotion (angry, happy, fear, neutral) as the within subject factors. Long delay (M = 0.18, *S.E.* =2.18) elicited increased pupillary responses than short delay (M = 0.13, *S.E.* =1.67), [$F_{(1,35)}$ = 13.05, p = .001, η^2 = .28]. Latency and other amplitude effects were insignificant (Fs < 1 *ps* > .1).

Saccadic Responses. Saccade error and latency were analysed in two separate 2 x 2 x 4 repeated measures ANOVAs with Saccade Type (antisaccade, prosaccade), Delay Type (short, long) and Emotion (angry, fearful, happy, neutral) as the within subject factors. As before, Greenhouse-Geisser corrections were applied where sphericity was violated, paired and independent samples t-tests were used in order to explore interactions (reliable at p < .05) where appropriate.

Participants made more errors (1) in antisaccade (M = 29.71, *S.E.* =4.01) than prosaccade trials (M = 24.01, *S.E.* =2.59) [$F_{(1,35)}$ = 6.97, p = .01, η^2 = .17] and (2) during long (M = 27.71, *S.E.* =2.51) compared to short delay (M = 26.01, *S.E.* =1.79) [$F_{(1,35)}$ = 4.53, p = .04, η^2 = .12]. Supplementary latency analyses showed that participants were

slower to make correct saccades following short delay (M = 243.65, $S.E.$ =9.05) compared to long delay (M = 220.49, $S.E.$ =14.75), [$F_{(1,35)}$ = 30.93, p = .001, η^2 = .49]. No other effects were significant (Fs < 1 ps > .1).

2.4 Discussion

We examined pupillometric and saccadic measures of affective and attentional processing in high and low anxious groups in an ODR task. High (vs low) anxious individuals showed larger and slower pupillary responses to face stimuli, larger pupillary responses during the short delay, equally larger pupillary responses during the long delay, and more erroneous eye-movements (across pro and antisaccade trials), particularly following long delay. Across groups, pupillary responses were larger to angry compared to happy faces.

Evidence of large and sustained pupil responses to face stimuli in anxiety extends evidence of pupil increases to angry faces in anxious individuals (Kret et al., 2013) and children of anxious mothers (Burkhouse et al., 2014). Contrary to predictions, anxiety was not characterised by larger pupil responses to negative (angry or fearful) facial expressions. Rather, across participants there was evidence of larger pupil responses to angry faces, consistent with previous studies in unselected samples (Bradley et al., 2008; Partala & Surakka, 2003; Rosa et al., 2015). Pupil responses were not greater to other negative faces in our study (i.e. fear faces), consistent with see Kret et al. (2013), but contrary to the effects of fear faces on other autonomic measures (heart-rate, skin conductance) and neural activity in brain regions implicated in threat appraisal (i.e. the amygdala, Adolphs, Tranel, Damasio, & Damasio, 1995; Öhman, 2005). Previous studies have either not examined or not found strong effects of fear faces on pupil diameter, and future studies are required to directly compare pupil response to a range of emotional expressions and other stimuli (e.g.,

emotional sounds and images) to determine the specificity of pupil responses to negative or broadly emotional stimuli in anxiety.

In the current study, anxiety-group differences were most pronounced between 300-400 ms after the face onset and were slower to return to baseline, consistent with relatively early effects of appraisal and attention to face stimuli in anxiety (see the review by Cisler & Koster, 2010). Sustained pupil responses in anxious individuals have been observed in other face-viewing paradigms. Price et al. (2013) observed large and sustained pupil responses 2-10 seconds after attention had been cued to the location of fear faces in a visual probe task. The authors argued that this effect reflected inflexible pupil reactivity during sustained cognitive-affective load (Price et al., 2013; Figure 2A). Interestingly, similarly large pupil responses were observed in anxious individuals during both 5 and 10 second delay periods, whereas low anxious individuals exhibited smaller pupil responses during the short compared to the long delay. This result might reflect increased effort in anxious individuals during short delay alongside low anxious individuals' capacity to reduce effort in low-load/short-delay trials, consistent with flexible resource allocation in low-anxious individuals. Convergent evidence comes from learning paradigms (e.g. two-arm bandit learning task with stable and unstable shock) in which low anxious individuals' pupil responses are more sensitive to changes in environmental contingencies across stable vs. unstable (i.e. volatile) blocks in learning paradigms (Browning et al., 2015).

Together these findings reflect sustained but inflexible patterns of pupil responding during affective stimulus processing and cognitive load in anxious individuals that contrast with adaptive responding to task demands in low anxious individuals. As noted by others, elevated, sustained and inflexible pupil responding in anxiety might reflect individual differences in central arousal mechanisms including the locus-coeruleus-norepinephrine

(LC-NE) system (Browning et al., 2015). For example, the present findings might indicate elevations in tonic LC-NE activity in high trait anxious individuals (Howells et al., 2012) that increase and sustain phasic responses to salient stimuli (i.e. centrally presented face stimuli in our study). Phasic responses may then become more inflexible and resistant to affective/cognitive processing as anxiety or task demands increase.

High trait anxious individuals made more eye-movement errors across prosaccade and antisaccade trials, particularly following a long delay period that in the current task increased working memory load. This general deficit in performance accuracy (effectiveness) was not increased in response to threat faces, nor was it linked to impaired processing efficiency, that is, latencies to make accurate saccades were unaffected by anxiety. This might reflect several features of the task used; notably (1) the affective salience of threat faces may have reduced following their repeated presentation within each trial (first at central fixation and then in the periphery) (see Van Dam, Earleywine, & Altarriba, 2012) and (2) the delay period may have further reduced the affective salience of face cues and placed sufficient demands on working memory (see Berggren et al., 2013) to elicit pronounced anxiety-related deficits in performance effectiveness/accuracy rather than on efficiency.

It is important to note that, unlike pupillary responses, saccade data did not reflect cognitive effort differences between short and long delay conditions across high and low anxiety groups. However, this effect was apparent when the mid-anxiety group was included in the supplementary analyses, showing increased errors following long delay. It is possible that more preparation time during long delay might have deteriorated performance effectiveness/accuracy. On the other hand, we also observed increased latencies following short delay trials. As delay facilitates inhibition (Ansari & Derakshan, 2010; Reuter et al., 2007), shorter preparatory time during short delay might have

worsened processing efficiency/latency. In sum, saccadic error data (including mid anxiety group) and pupillary response data confirmed that long delay is associated with increased cognitive load and effort. However, one should be cautious with manipulating load, as long delay during preparation might increase load and effort (as evidenced by pupillary responses) but facilitate/help eye-movements (as evidenced by error rates and latencies).

The present findings should be interpreted in the light of various limitations. First of all, majority of the participants were female. In order to generalize the findings, future studies should be gender matched. Secondly, although performance of clinical and subclinical anxiety groups is comparable (see Chapter 5, Section 5.4), the current results await replication within a clinical sample. Thirdly, although face stimuli were carefully selected and processed (for pupillary responses), one could argue that processed faces have no ecological validity. Further studies should use unprocessed faces and implement behavioural measures. Finally, the current study utilised 5 and 10 seconds of delay in order to manipulate cognitive load. It is of interest to examine the effects of different delay durations on the performance and pupillary responses.

Our findings suggest that pupil diameter can provide a comparatively simple and objective measure of dynamic changes in emotion processing and cognitive effort in anxiety, to extend studies of subjective effort (Hadwin et al., 2005). Evidence of increased and sustained pupil responses in trait anxious individuals across experimental conditions of low and high cognitive load warrants replication in larger samples and clinical groups (e.g. generalized anxiety disorder). To this end future pupillometry and ERP studies could be used in experimental designs that can dissociate individual differences in early appraisal

mechanisms, refractory and preparatory behavioural responses in complex cognitive tasks. This is addressed in the next chapter.

3 Electrocortical, Pupillometric, and Eye-Movement Evidence of Impaired Processing Efficiency and Performance Effectiveness in Anxiety

3.1 Introduction

Anxiety is typically characterised by a range of biases in selective attention and attention control that increase distractibility and reduce processing efficiency and performance effectiveness on goal-directed tasks (Eysenck et al., 2007). In addition, anxious individuals are motivated to perform tasks to a high standard and to invest additional cognitive resources and effort to try and achieve performance goals (Berggren & Derakshan, 2013). Neuropsychological models of anxiety highlight a range of maladaptive biases in top-down attention and cognitive control processes that increase hypervigilance and impair inhibitory control, cognitive flexibility and working memory (see Mogg & Bradley, 2016 for recent theoretical synthesis). Anxiety-related deficits in attention control and executive function have been observed across several behavioural measures including poor performance on the executive attention subtest of the attention network task (ANT; Pacheco-Unguetti et al., 2010), and slower and less accurate eye-movements in the antisaccade task, particularly when task demand/cognitive load is high (review by Ainsworth & Garner, 2013). Subsequent studies have found larger pupil responses in anxious individuals under load reflecting increased arousal and effortful processing (see Chapter 2). Also, neuroimaging studies have shown that the activation of amygdala-medial frontal structures is associated with affective bias and impaired attentional control in anxiety (Robinson et al., 2016). Here measures of electrocortical activity, pupil diameter and antisaccade performance were combined to examine processing efficiency and effectiveness in individuals with high versus low symptoms of trait anxiety.

The antisaccade task is a simple inhibitory control task that utilises eye movement measures to investigate individual differences in attention control across anxiety and mood disorders. Participants are instructed to look away from a visual cue (i.e. to its mirror location) as quickly and accurately as possible. Consistent with predictions from Attentional Control Theory (Eysenck et al., 2007), anxious individuals are more likely to make erroneous eye-movements on antisaccade trials, and are slower (less efficient) at executing antisaccades (Ansari & Derakshan, 2011b; Garner et al., 2011). Furthermore, anxiety-related deficits in antisaccade performance are greater when processing demands increase (Berggren et al., 2013).

Slow-wave cortical potentials (SCP; Kotchoubey, 2006; Rosler & Heil, 1991) are long-lasting potentials that sustain from 300 ms to several seconds and reflect the depolarization (reduced firing threshold) and corresponding increased excitability of cortical neuronal networks. Contingent Negative Variation (CNV; Walter et al., 1964) is a SCP that is maximal over midline frontal sites in the period between a warning cue and action (Gomez et al., 2007; Rosahl & Knight, 1995). CNV amplitudes (Khader et al., 2008) increase with cognitive effort, task difficulty and response preparation and may be sensitive to changes in effort expended by high trait anxious individuals throughout cognitive tasks. To date, electrophysiological correlates of effort in anxiety have not been widely examined. Consistent with models that propose poorer efficiency/greater effort in anxious individuals when task demands are high, Ansari and Derakshan (2011a) observed larger (less positive) CNV in high vs. low anxious individuals at frontal sites during medium (400 ms) and long (1500 ms) delay in a pro/anti-saccade task.

In addition to CNV, pupillary responses also vary with effort. Previous studies have shown larger pupillary responses is associated with resource recruitment and task difficulty

(Beatty, 1982; Beatty & Lucero-Wagoner, 2000; Hess, 1975; Kahneman & Beatty, 1966; Karatekin et al., 2007) (also see Chapter 1 and Chapter 2). Initial studies suggest that high trait anxious individuals elicit larger pupillary responses during tasks that require sustained attention (e.g. simulated driving tasks; Wilson & MacLeod, 2003), and pupillary responses are sensitive to anxiety-related deficits also in other tasks such as learning paradigms (e.g. two-bandit arm task; Browning et al., 2015). A recent study demonstrated an evidence in high trait anxious individuals of enhanced, sustained and inflexible patterns of pupil responding during a long 10 second delay period prior to poor performance (fewer accurate eye-movements) on a pro/anti-saccade task (see Chapter 2).

In the current study, high versus low anxious individuals' electrocortical activity, pupil diameter, and antisaccade performance were compared to examine processing efficiency and effectiveness in individuals with high (versus low) symptoms of trait anxiety. High vs. low anxious individuals slow-wave cortical potentials and pupillary responses were compared during short (5 s) and long delay (10 s) periods and measured subsequent eye movement errors and latencies in delayed pro and antisaccade tasks. It was hypothesised that individuals with elevated levels of trait anxiety (trait anxious individuals) would show (1) reduced midline-frontal potentials (larger CNV) and larger pupillary responses, particularly during long delays (consistent with increased effort/poor processing efficiency), and (2) impaired task performance characterised by fewer and slower accurate eye-movements on antisaccade trials following long delays (consistent with reduced performance effectiveness and efficiency during high versus low cognitive load).

3.2 Method

3.2.1 Participants

Fifteen high trait anxious and 15 low trait anxious participants were selected from a University of Southampton participant pool based on scores on the trait version of the

State-Trait Anxiety Inventory (Spielberger et al., 1983) (see Appendix A). Consistent with previous research (Ansari et al., 2008) and Chapter 2, participants who scored ≤ 35 were categorised as low anxious (LA; *n* = 15, *mean* STAI-T = 28.80, *S.D.* = 2.93, *min* = 23, *max* = 33, *mean* age = 20.27; 10 females) and those scoring ≥ 50 as high anxious (HA; *n* = 15, *mean* STAI-T = 59.93, *S.D.* = 7.93, *min* = 50, *max* = 77; *mean* age = 20.60; 13 females). Anxiety scores were normally distributed (LA; Shapiro Wilk= .90, p=.10; HA; Shapiro Wilk= .93, p=.29)

All participants had normal or corrected-to-normal vision and were right-handed (as verified by the Edinburgh Handedness Inventory; Oldfield, 1971) (see Appendix B). Participants confirmed that they had not taken drugs, alcohol, or medication on the day preceding testing. They received either course credits or £10 for participation. All participants provided informed consent. The research protocol was approved by the University of Southampton Ethics and Research Governance committees. (Please see Appendix D Section 2 for Experiment 2 forms).

3.2.2 Data Acquisition

Electroencephalographic (EEG) data were recorded from 64 Ag/AgCl scalp electrodes mounted in an elastic electrode cap (EasyCap GmbH, Germany) and Synamps RT amplifier (Neuroscan, Inc). Electrode sites were determined using the international 10-20 system. All electrodes were referenced online to the nose and later re-referenced offline to the average of all electrodes. AFz was used as a ground electrode. Horizontal eye movements (HEOG) were recorded by placing electrodes laterally on the outer canthi of the eyes and vertical eye movements (VEOG) were recorded from electrodes placed below and above the left eye. Impedances were kept below 5 kΩ for all channels. Signals were

amplified in a DC mode at 100 Hz and sampled at 1000 Hz using Neuroscan 4.5 (Neuroscan, Inc).

Eye movements and pupillary responses were recorded using SR EyeLink 1000 desktop-mounted eye tracking system (SR Research, ON, Canada) with a sampling rate of 1 kHz. Pupillary responses were recorded using Centroid model based on pupil diameter in millimetres. The presentation was controlled by Experiment Builder v1.10.1025 software (SR Research Ltd., Ontario, Canada) on a 19-inch ViewSonic (P227f) monitor.

3.2.3 Experimental Task and Procedure

Participants were seated in front of the computer and eye-tracking system with their chin and head supported at a viewing distance of 70 cm. As seen in Figure 3.1, after successful drift correction, and fixation to central cue for 1000 ms, a central cue (letters O or X), indicating the type of the trial (prosaccade or antisaccade), was presented for 1000 ms. After either a short (5 seconds) or long (10 seconds) delay, a grey ellipse-shaped target (R=79, G=78, B=78; 3.3^{o} x 6^{o}) was displayed for 1500 ms at 11^{o} either to the left or right side of the central fixation cross. Participants were instructed to look towards the target (prosaccade) or away from the target (antisaccade). All stimuli were presented on a grey background (R = 117, G = 116, B = 116), and all trial screen displays had a mean luminosity of 22 lux. Participants were calibrated (3-point display) before completing 10 practice trials and the experimental task. The task consisted of 200 trials presented in a random order across 2 blocks of 100 trials (each comprising 50 prosaccade trials and 50 antisaccade trials). Participants were instructed to sit still and avoid head and body movements.

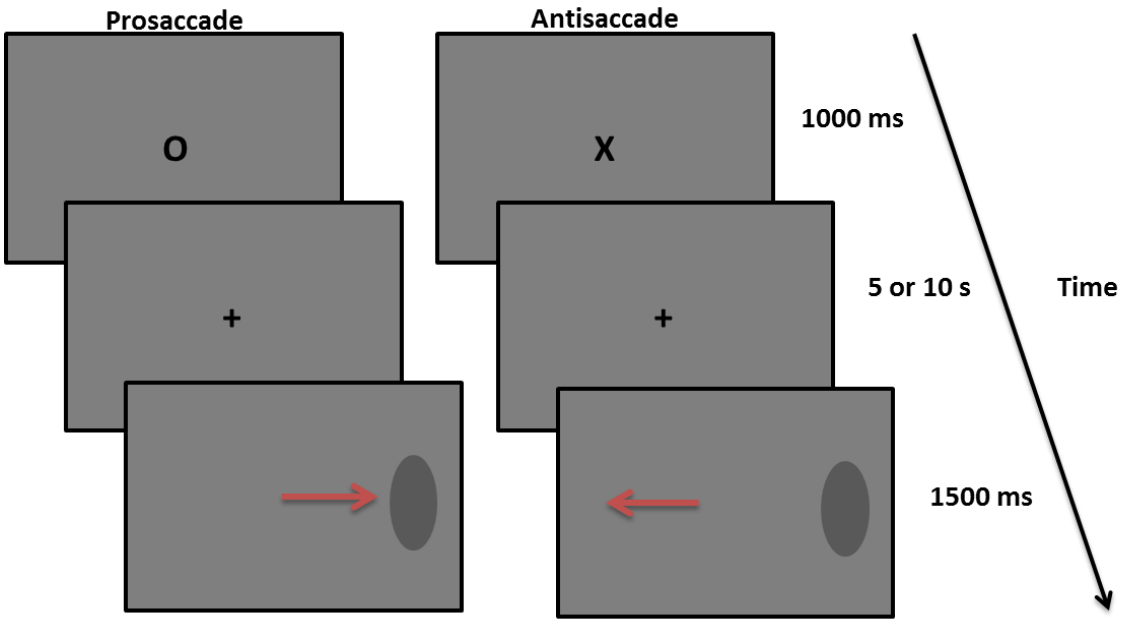


Figure 3.1 Flowchart of prosaccade and antisaccade trials in short and long delay trials. Participants were presented prosaccade (O) or antisaccade (X) cue. After 5 (low load) or 10 (high load) seconds of delay, they generated a prosaccade toward the ellipse or an antisaccade away from the ellipse.

3.2.4 Data Pre-processing

Event-Related Potentials. The continuous EEG recordings were band pass filtered offline with a high-pass cut-off of 0.1 Hz and a low-pass cut-off of 30 Hz, using a zero phase shift FIR (Finite Impulse Response) filter. Eye blinks in the continuous EEG data were identified and corrected. Muscle bursts were manually selected and removed from further analyses. The data were epoched from 100 ms pre-delay and 1000 ms post-delay, resulting in -100 to 6100 ms and -100 to 11100 ms epochs for short and long delays, respectively. All epochs were re-referenced to the average of all electrodes, and baseline corrected. Consistent with previous studies, trials with erroneous saccadic responses were excluded (Ansari & Derakshan, 2011a). Grand average waveforms were computed separately for short and long delay trials. SCP were calculated during the 5000 ms delay period (A), and during the first (B) and second (C) 5000 ms of the 10000 ms delay period. Responses during short delay (A+B/2) were compared against responses during the long

delay (C). Large positive and negative evoked potentials within 700 ms after stimulus offset (i.e. prior to SCP, see Figure 3.2 and Figure 3.3) were removed from the calculation of average SCP amplitudes (i.e. average amplitudes were calculated from 700-5000 ms). Consistent with Studer et al. (2014), supplementary analysis of mean preparatory CNV activity between -400 ms and -100 ms before target presentation was run and consistent with Ansari and Derakshan (2011b) mean activity immediately prior to target onset were examined (-50 ms before to 50 ms after target presentation, i.e. before eye movement execution). Distributions amplitudes were examined and met assumptions of normality using Shapiro-Wilk's test, p's > .05.

Pupillary Responses. Pupillary responses were pre-processed using previous standard procedures (cf. Beatty & Lucero-Wagoner, 2000; Bradley et al., 2008; Granholm et al., 2000) by using MATLAB R2013a (The Math-Work, Inc., MA, USA). Firstly, blinks and artefacts (very short increases or decreases of at least 0.375 mm within 20 ms (Partala & Surakka, 2003) were removed. Then, missing values were corrected by linear interpolation resulting (% interpolated = 10.28). Thirdly, continuous pupil data were during each delay period (5000 ms for short delay and 10000 ms for long delay). Then, baseline correction (relative to the start of epoch) was applied. Peak pupillary responses (maximum pupil diameter) and latency to peak (ms) were calculated during the 5000 ms delay period (A), and during the first (B) and second (C) 5000 ms of the 10000 ms delay period. Responses during short delay (A+B/2) were compared against responses during the long delay (C). Distributions of amplitude and latency of peak pupillary responses were examined and met assumptions of normality using Shapiro-Wilk's test, p's > .05.

Saccades. Saccade accuracies and latencies (following target onset) were extracted for the first valid saccade on each trial (i.e. latencies > 80 ms, velocities > 30°/s, and amplitudes > 3°) (Ansari & Derakshan, 2010). An erroneous saccade was defined as the first saccade landing outside the relevant interest area (i.e. the grey ellipse-shaped target area on prosaccade trials, or the mirror location on antisaccade trials). Distributions of saccadic error rates and latencies were examined and met assumptions of normality using Shapiro-Wilk's test, p's > .05.

3.3 Results [2]

3.3.1 Slow-wave Cortical Potentials: CNV

Statistical comparisons of ERP activity were conducted on data from three midline electrodes (Fz, Cz, Pz) (based on previous findings showing no laterality in delay-related slow shifts and in effort-related slow-waves; see Ansari & Derakshan, 2011a; Rämä, Carlson, Kekomi, & Hämäläinen, 1995). Mean amplitudes of the CNV were analysed with a 2 x 3 x 2 x 2 repeated measures ANOVA with Group (low-anxious, high-anxious) as the between subject factor and Area (frontal, central, parietal), Delay (short, long) and saccade type (prosaccade, antisaccade) as the within subject factors. Where assumptions of sphericity were violated, Greenhouse-Geisser corrections were applied.

A Group x Delay interaction [$F_{(1,28)} = 4.82$, $p = .03$, $\eta^2 = .18$] was characterised by greater CNV during the long delay in high anxious individuals compared to low anxious individuals $t(28) = 1.40$, $p = .04$, (see Table 3.1 and Figures 3.2, 3.3, and 3.4). There were no other effects of group, delay, area, saccade type or their interaction (Fs < 1 *ps* > .1).

[2] See Appendix F Section 2 for descriptive statistics.

Table 3.1

Means (standard deviations) of CNV amplitudes (μV) in high anxious (HA) and low anxious (LA) groups during long and short delay at Fz, Cz, and Pz.

	HA (*n*=15)			**LA (*n*=15)**		
	Fz	*Cz*	*Pz*	*Fz*	*Cz*	*Pz*
Long Delay	-.27 (2.75)	.07 (2.68)	.34 (2.48)	.55 (2.75)	1.62 (2.81)	.53 (2.43)
Short Delay	.59 (2.19)	.40 (1.89)	.16 (2.29)	.31 (1.80)	.90 (1.49)	.37 (1.89)

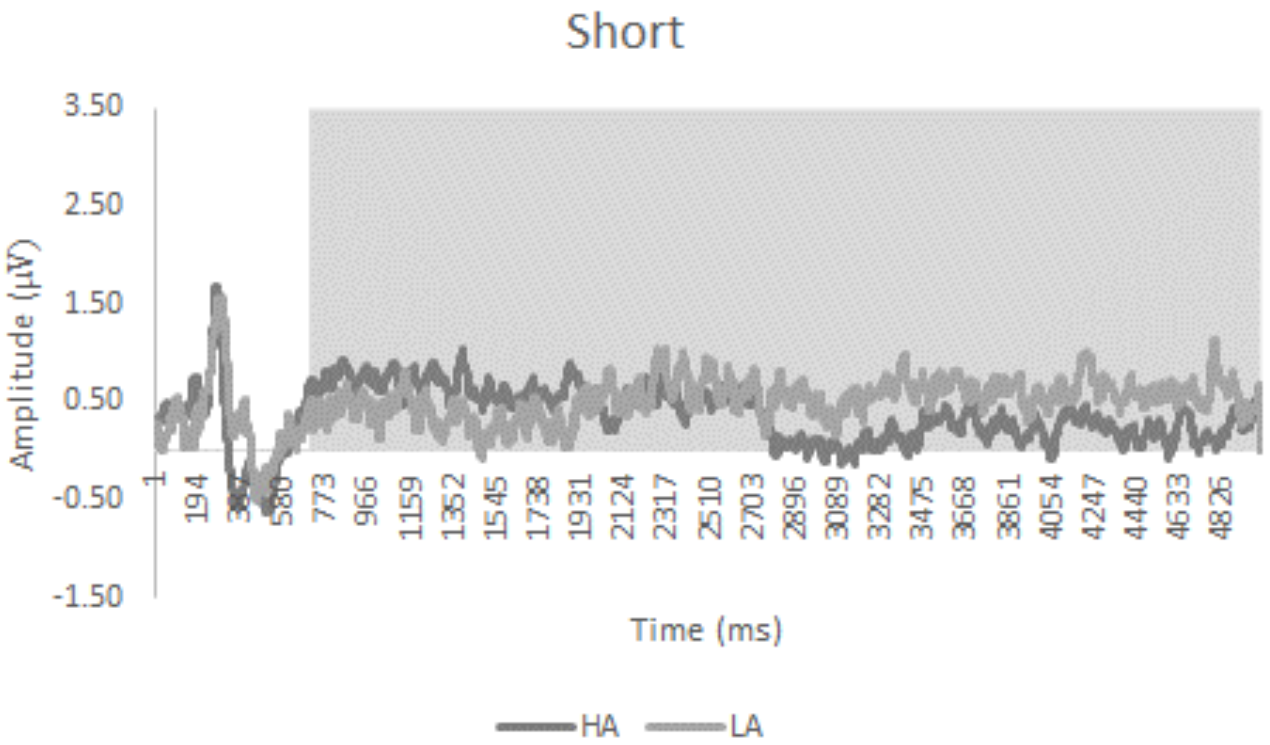


Figure 3.2 Grand average waveforms of CNV potentials during short delay in high anxious (HA) and low anxious (LA) individuals (Shaded area represents the critical period of interest). Average CNV amplitudes (between 700 and 5000 ms) of HA and LA individuals were comparable during short delay.

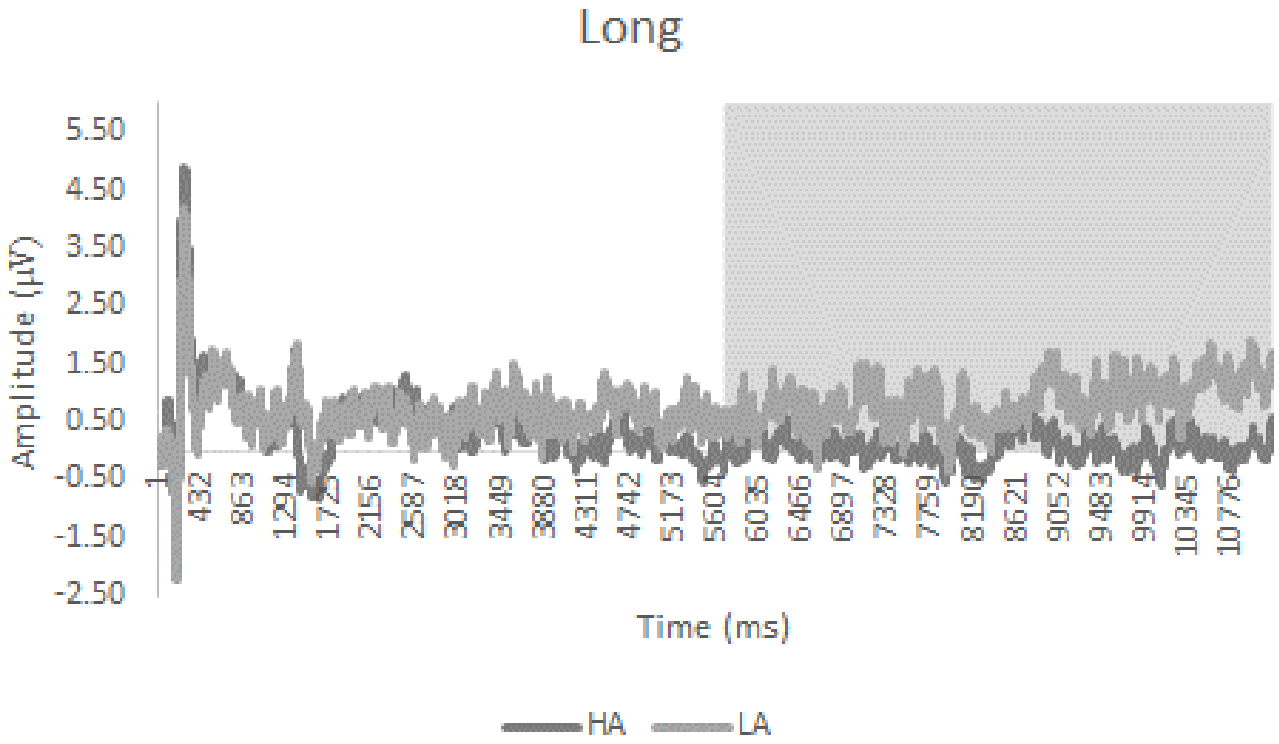


Figure 3.3 Grand average waveforms of CNV potentials during long delay in high anxious (HA) and low anxious (LA) individuals (Shaded area represents the critical period of interest). HA individuals produced greater average CNV amplitudes (between 5700 and 10000 ms) compared to LA individuals during long delay.

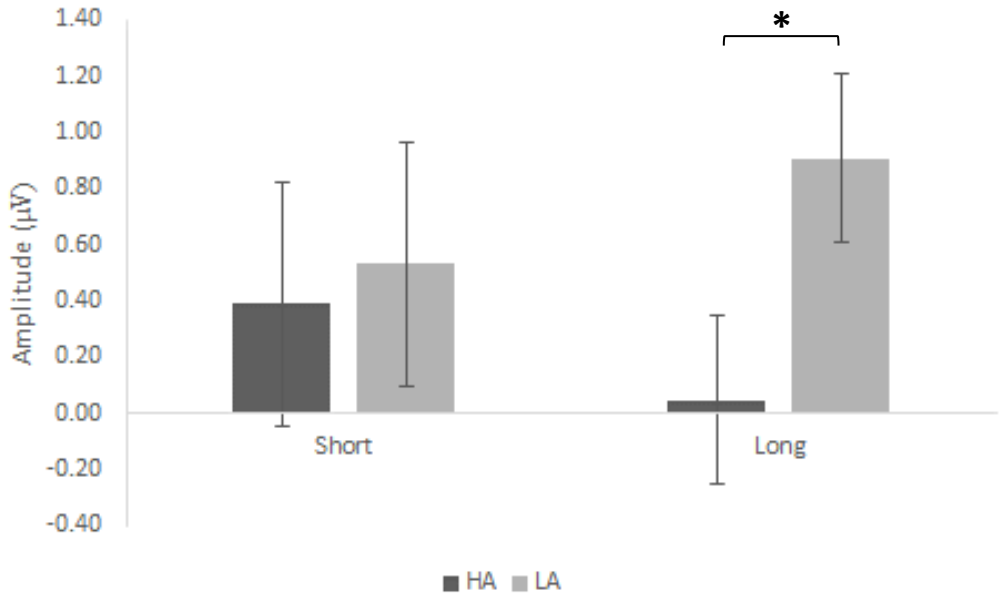


Figure 3.4 Mean CNV potentials during short and long delay in HA and LA (bars represent standard errors).

A corresponding 2 x 3 x 2 x 2 repeated measures ANOVA of mean CNV amplitudes (-400 to -100 ms before target onset) provided evidence of a Group x Delay x Area interaction [$F_{(1,58)}$ = 3.05, p = .05, η^2 = .11] characterised by greater CNV in high vs. low anxious individuals during the long delay at frontal sites $t(14)$ 2.23, p= .04 (see Figure 3.5). A corresponding analysis of cortical amplitudes -50 ms to +50 ms did not reveal effects of group, delay, area, saccade type or their interaction (Fs < 1 *ps* > .1).

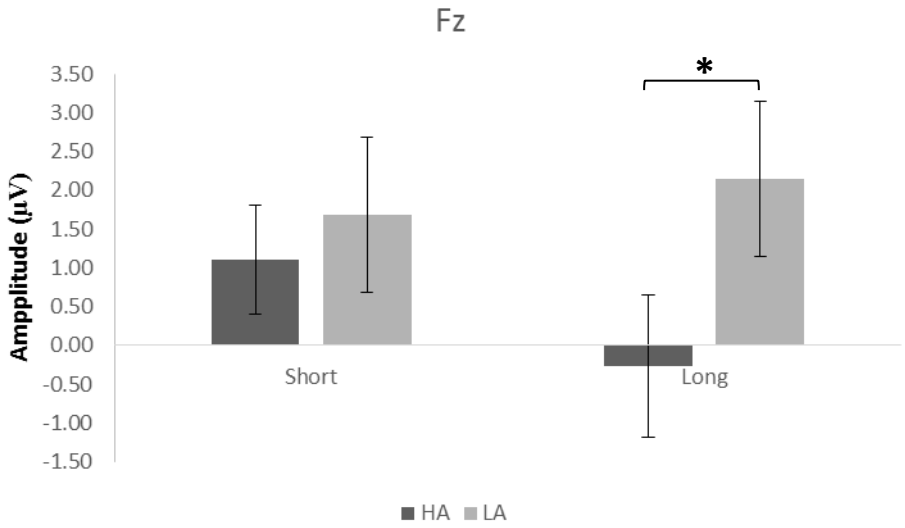


Figure 3.5 Mean CNV activity at Fz during short and long delay in high (HA) and low (LA) anxious individuals (bars represent standard errors). HA (vs LA) individuals produced greater average CNV amplitudes (between -400 and -100 ms) during long delay at Fz electrode.

3.3.2 Pupillary Responses

Amplitude and latency of peak pupil responses were entered into separate 2 x 2 repeated measures ANOVA with Group (low-anxious, high-anxious) as the between subject factor and Delay (short, long) as the within subject factor. As before, Greenhouse-Geisser corrections were applied where sphericity was violated. Follow-up supplementary time-series analyses of pupil diameter examined effects of delay and anxiety over-time across 250 consecutive 20 ms epochs as per previous research (Geva et al., 2013) (see Chapter 2). A Group x Delay interaction [$F_{(1,28)} = 4.59$, $p = .04$, $\eta^2 = .16$] was characterised by increased peak pupil amplitude in high anxious individuals during long delay compared to (1) peak responses in low anxious individuals during long delay, $t(28) = 2.15$ $p = .04$, and (2) peak responses in high anxious individuals during short delay, $t(14) = 2.48$ $p = .02$ (see Figure 3.6). Comparable analyses of peak latency and time series analysis did not reveal effects of group, delay type, or their interaction, $Fs < 1$ $ps > .1$.

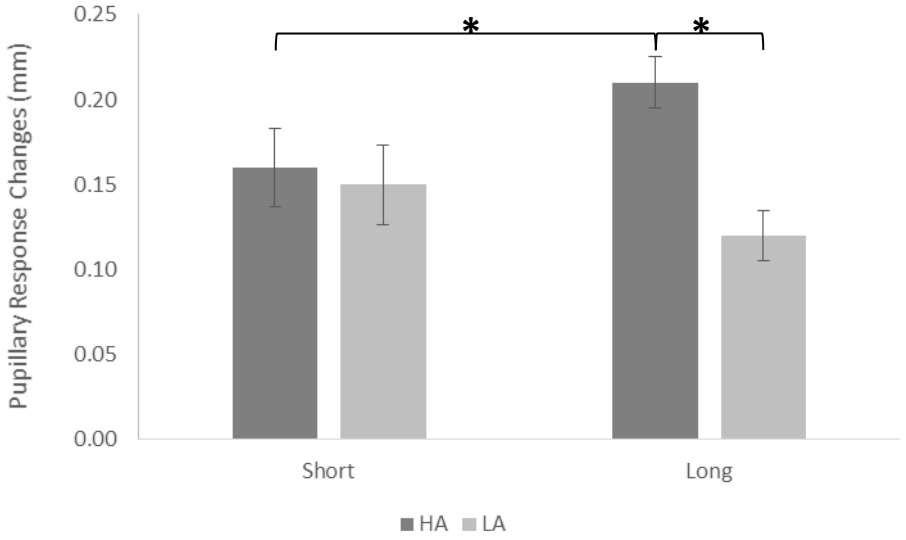


Figure 3.6 Peak pupillary responses during long and short delay trials in high anxious (HA) and low anxious (LA) groups (bars represent standard errors). HA individuals had increased pupillary responses during long delay compared to short delay. They also produced larger pupillary responses during long delay compared to LA individuals.

3.3.3 Eye-movements

Saccade errors and latencies were analysed in two separate 2 x 2 x 2 repeated measures ANOVAs with Group (low-anxious, high-anxious) as the between subject factor and Saccade Type (anti-, prosaccade) and Delay (short, long) as the within subject factors.

Participants made more errors on antisaccade (M = 46.81, $S.E.$ =2.92) vs. prosaccade trials (M = 10.86, $S.E.$ =0.91), [$F_{(1,28)}$ = 149.39, p = .001, η^2 = .84], particularly following the short delay [Saccade Type x Delay interaction, $F_{(1,28)}$ = 9.12, p < .01, η^2 = .24; Antisaccade M_{short}= 50.20, $S.E.$ = 2.60, M_{long} = 43.43, $S.E.$ = 3.60; Prosaccade M_{short} = 10.93, $S.E.$ =0.90, M_{long} = 10.80, $S.E.$ =1.30]. A significant Group x Saccade Type interaction [$F_{(1,28)}$ = 4.66, p = .04, η^2 = .14] was characterised by a greater number of eye-movement errors in high vs. low anxious individuals on antisaccade trials, $t(28)$= 2.28, p =.03 (see Table 3.2 and Figure 3.7).

Table 3.2

Means (standard deviations) of saccadic error rates (%) in high anxious (HA) and low anxious (LA) groups during long and short delay.

	HA (*n*=14)		**LA (*n*=13)**	
	Pro	*Anti*	*Pro*	*Anti*
Long Delay	11.06 (6.31)	48.86 (16.65)	10.53 (7.57)	38.00 (21.88)
Short Delay	11.33 (3.15)	58.13 (11.86)	10.53 (6.25)	42.26 (16.08)

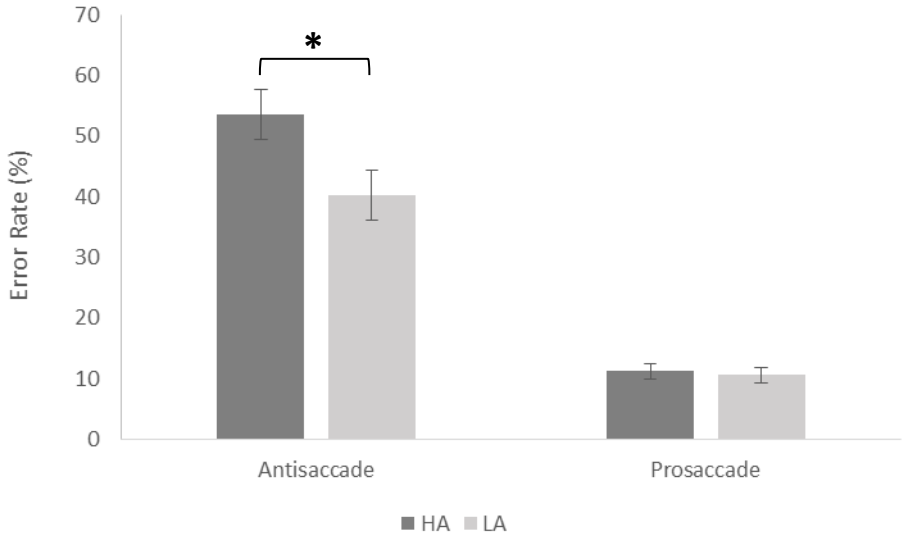


Figure 3.7 Percentage of saccade error in high-anxious (HA) and low-anxious (LA) groups on each of the antisaccade and prosaccade trials (bars represent standard errors). HA individuals made more errors compared to LA individuals only during antisaccade trials. HA and LA individual's prosaccade performance was comparable.

A corresponding analysis of eye-movement latencies revealed that participants were slower to make correct saccades on antisaccade (*M* = 366.99, *S.E.* =12.52) vs. prosaccade trials (*M* = 275.78, *S.E.* =11.05), [$F_{(1,28)}$ = 83.77, $p < .01$, $\eta^2 = .74$], and following short (*M* = 330.61, *S.E.* =13.43) compared to long delay trials (*M* = 312.16, *S.E.* =9.32), [$F_{(1,28)}$ = 4.79, $p = .03$, $\eta^2 = .14$] (see Table 3.3). Latencies were not affected by anxiety (Fs < 1 *ps* > .1).

Table 3.3

Means (standard deviations) of saccade onset latencies (ms) in high anxious (HA) and low anxious (LA) groups during long and short delay.

	HA (*n*=14)		**LA (*n*=13)**	
	Pro	*Anti*	*Pro*	*Anti*
Long Delay	244.07 (50.14)	360.81 (47.13)	285.49 (67.74)	358.25 (62.60)
Short Delay	277.69 (69.25)	357.88 (95.60)	295.87 (69.03)	390.16 (91.79)

3.3.4 Supplementary Analyses

As seen in the Figure 3.2, the trend shows greater CNV for HA (vs LA) after 2700 ms. However, previous analyses failed to show significance results. In order to detect any CNV amplitude differences between HA and LA during short delay trial, we analysed mean CNV amplitude between 700-2000 (initial CNV) ms and 2000-5000 (late CNV) ms.

Mean amplitudes of initial and late CNV during short delay trials were analysed with seperate 2 x 3 x 2 repeated measures ANOVA with Group (low-anxious, high-anxious) as the between subject factor and Area (frontal, central, parietal), and saccade type

(prosaccade, antisaccade) as the within subject factors. Where assumptions of sphericity were violated, Greenhouse-Geisser corrections were applied.

During short delay trials, mean amplitude of initial CNV [$F_{(1,28)} = 0.80$, $p = .37$, $\eta^2 = .02$] and late CNV [$F_{(1,28)} = 0.47$, $p = .49$, $\eta^2 = .01$] did not reveal significant anxiety main effect. Also, no other effects were significant (Fs < 1 *ps* > .1).

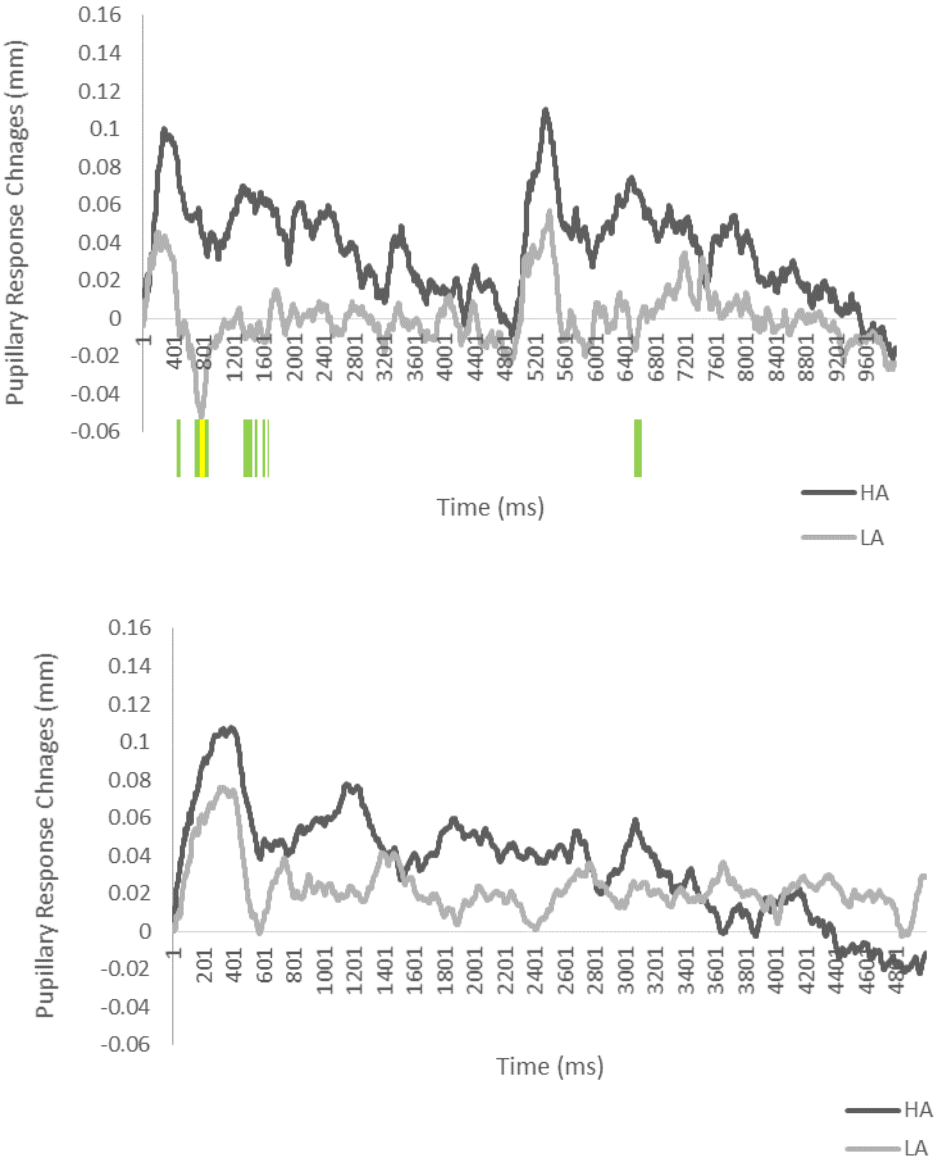


Figure 3.8 **(Top Panel)** Pupillary response time series in high-anxious (HA) and low-anxious (LA) groups during long delay trials. **(Bottom Panel)** Pupillary response time series in high-anxious (HA) and low-anxious (LA) groups during short delay trials. Both HA and LA individuals re-engaged their cognitive resources (as evidenced by the peaks after 5000 ms) after non-appearance of the target at 5 s (short delay).

3.4 Discussion

Electrophysiological, pupillometric and saccadic measures of processing efficiency and effectiveness in high and low anxious groups were examined by using delayed pro- and antisaccade tasks. High anxious compared to low anxious individuals produced greater CNV and larger pupillary responses, specifically during long delay, and subsequently made more erroneous eye movements on antisaccade trials.

Evidence of greater CNV and increased pupillary responses in high-anxious individuals, particularly during long delay trials, is consistent with models that predict increased effort/inefficiency in anxiety when task demands are high (Berggren et al., 2013). Although appearing to be present in Figure 3.2, we observed comparable CNV amplitudes of high and low anxious individuals during short delay. Our findings extend previous evidence of greater preparatory CNV in anxiety (Ansari & Derakshan, 2011a) and reveal sustained preparatory potentials over a longer time period (5-10 seconds) prior to response. These results suggest that individuals with elevated anxiety symptoms exerted increased effort during long delay trials. Our supplementary analysis of cortical potentials prior to target onset (-400 to -100 ms) suggests effects of anxiety are strongest at frontal sites, consistent with previous findings (Ansari & Derakshan, 2011a) and evidence from neuroimaging that implicates these regions in antisaccade performance accuracy (Ford, Goltz, Brown, & Everling, 2005). Though an anticipated greater CNV in anxiety was observed, a large sustained negative potential that characterises 'classic' CNV profile was not found. These findings are consistent with previous studies that have reported less positive (rather than large negative) CNVs in demanding tasks that require participants to wait for long periods after the instructional cue and before executing the response to target (Turner et al., 2015).

Pupillometry findings provide convergent evidence of increased effortful processing in anxiety. Larger peak pupillary responses were observed in high anxious individuals during long delay trials while low anxious individuals exhibited similarly small pupillary responses during short and long delays. In our previous research (see Chapter 2), high trait anxious individuals exhibited enhanced, sustained and inflexible patterns of pupil responding during affective stimulus processing and delay periods that preceded deficits in pro/antisaccade performance. Here too evidence of increased antisaccade errors in high anxious individuals was apparent, consistent with reduced performance effectiveness. However anxiety did not modulate eye-movement latency nor interact with delay, and contrary to expectations antisaccade performance was more accurate and faster following long (rather than short) delay. Although the CNV and pupillary response data were sensitive to load effect, inserting a delay between a stimulus and response might have facilitated eye movement response generation (Ansari & Derakshan, 2010, 2011a; Reuter et al., 2007. On the other hand, it is possible that the random presentation of long and short delay trials within blocks can explain this finding. The likelihood a target appeared at 5 s was 50%, whereas the likelihood of the target appearing at 10 s (after the non-appearance of the target at 5 s) was 100%. Consequently, on long delay trials participants were able to prepare accurate and quick responses with confidence (from 5 seconds onwards). In support, pupillometry data provides evidence that participants were sensitive to temporal characteristics of the trial and re-engaged resources after the non-appearance of the target at 5 s on long 10 s trials (see Figure 3.8). However, this effect was not evident in cortical potentials, i.e. changes in CNV in advance of possible target onset at 5 s and 10 s were not observed (see Figure 3.2 and Figure 3.3). Consequently, further research should consider the extent to which participants could accurately monitor elapsed time and better anticipate

target onset at 10 vs. 5 seconds to improve antisaccade performance effectiveness and efficiency.

It is important to note that, pupillary response findings are consistent with the findings from Chapter 2 only during short delay. In Chapter 2, pupillary responses of high and low anxious individuals were comparable during long delay. However, the current findings showed that long delay elicited increased pupillary responses in high anxious group. This might reflect several features of the tasks used; notably the ODR task with a visuospatial component might not be sensitive to load-related anxiety differences as ACT predicts no detrimental effects of anxiety on visuospatial working memory (Eysenck et al., 2007). On the other hand, as delayed pro-and antisaccade task is dependent purely on executive functions, load-related anxiety differences might be apparent on this task as ACT predicts effects of anxiety on executive functions.

Similar to Experiment 1 (Chapter 2), the present is not free of limitations. As suggested (see Section 2.4), future studies should match participant's gender, replicate the current results in clinical samples, and examine the effects of different delay durations.

In sum, our results provide evidence in anxious individuals of reduced performance effectiveness and efficiency across electrophysiological, pupillary and oculomotor systems and support neuropsychological models of anxiety that highlight broad deficits in processing efficiency and executive attention control as a 'hidden cost' of anxiety (Ansari & Derakshan, 2011a; Eysenck et al., 2007).

Chapter 4 further demonstrates inefficient and ineffective inhibitory control in anxiety by using inhibition-related ERP measures.

4 Effects of Anxiety and Inhibitory Load on Pupillary Responses and Prefrontal Function during Inhibitory Control

4.1 Introduction

Individuals with generalized trait anxiety experience difficulties inhibiting distraction and focussing attention, and report increased cognitive effort to complete tasks successfully and achieve their high performance goals. Anxious individuals perform less well on tasks that require inhibitory control - reaction times are slowed by distractor stimuli (see Pacheco-Unguetti et al., 2012; Wong, Mahar, Titchenere, & Freeman, 2013) and eye-movements away from distractors on the antisaccade eye-movement task are slower and less accurate (review by Ainsworth & Garner, 2013) (also see Chapter 2 and Chapter 3).

Neuropsychological models suggest that anxiety-related deficits in performance efficiency and effectiveness result from reduced activity in prefrontal structures that underlie executive control and response inhibition (Bishop, 2007; Forster, Nunez Elizalde, Castle, & Bishop, 2015). Inhibitory control is associated with greater activity in prefrontal cortical networks, including ventrolateral prefrontal cortex (VLPFC), dorsolateral prefrontal cortex (DLPFC), anterior cingulate cortex (ACC) and the inferior frontal gyrus (IFG) (Aron et al., 2004; Beste, Saft, Andrich, Gold, & Falkenstein, 2008; Bokura, Yamaguchi, & Kobayashi, 2001; Braver, Barch, Gray, Molfese, & Snyder, 2001; Falkenstein, 2006; Konishi, Nakajima, et al., 1999; Morita, Nakahara, & Hayashi, 2004a) and activity in these networks is reduced in anxiety during inhibitory processing (Arnsten, 2009; Bishop, 2009; Forster et al., 2015).

Electrocortical potentials are also sensitive to inhibitory processing and have been revealed in the Go/No-Go task. The Go/No-Go task (Donders, 1969) is an established behavioural measure of inhibitory control (see Simmonds, Pekar, & Mostofsky, 2008). Participants are instructed to respond to target stimuli during Go trials and withhold responses during No-Go trials. Evidence of good inhibitory control is characterised by few errors of omission (misses) and commission (false alarms) rates, high hit rates and fast reaction times (Falkenstein et al., 1999; Fallgatter et al., 1997; Funderud et al., 2012; Harper et al., 2014; Lavric et al., 2004). The N2 fronto-central event-related potential (ERP) is a negative component at midline frontal sites that appears 250-350 ms after the presentation of to-be-inhibited stimuli (Eimer, 1993) and is considered to reflect both pre-response inhibition mediated by the VLPFC and DLPFC, and conflict monitoring mediated by the ACC (Lavric et al., 2004). *P3* is a positive component at midline fronto-central areas that peaks between 300-500 ms after the presentation of to-be-inhibited stimuli, and it is associated with motor inhibition and evaluation of inhibition (i.e. evaluation of the preceding response and outcome of the inhibitory processes) (Bruin & Wijers, 2002a; Falkenstein et al., 1999; Righi et al., 2009). P3 to target stimuli also extends to parietal regions during response preparation and motor response (Fallgatter et al., 1997).

Initial studies suggest anxiety can modulate N2 and P3 amplitudes during response inhibition. N2 amplitudes at frontal sites are reduced in individuals with obsessive-compulsive disorder (Herrmann, Jacob, Unterecker, & Fallgatter, 2003; Kim, Kim, Yoo, & Kwon, 2007) however the effects of generalized trait anxiety are mixed. A correlational study in 18 unselected participants observed positive associations between increased trait anxiety and N2 amplitude (Righi et al., 2009). Sehlmeyer et al. (2010) also observed positive associations between trait anxiety, increased No-Go N2 amplitude, No-Go P3 amplitude and improved behavioural inhibition (reduced false alarms) across unselected

individuals reporting mild to moderate anxiety. In contrast, recent evidence suggests that higher levels of anxiety (i.e. in preselected groups of trait anxious individuals) are characterised by reduced N2, reduced P3 and hypoactivity in frontal regions (derived from source localisation) during No-Go inhibition (Yang & Li, 2014), consistent with neuropsychological models of frontal hypoactivity and distractibility in anxiety. Consequently, findings to date could reflect a curvilinear relationship between trait anxiety and inhibitory control in which moderate anxiety increases task performance and N2 inhibition, perhaps through increased compensatory effort, arousal and state anxiety in low load tasks, but where higher levels of trait anxiety reduce N2 inhibition and performance, particularly when compensatory processing is limited by greater task demands. To our knowledge no study has examined the effect of trait anxiety and task load on inhibitory control and N2/P3 amplitudes.

The demand placed on inhibitory and effortful processes could be increased by increasing the Go probability and thereby propensity to erroneously respond on No-Go trials (Van De Voorde et al., 2011). Errors of commission and N2 responses to No-Go stimuli increase further during high inhibitory load/effort (i.e. high Go, low No-Go conditions; (Bruin & Wijers, 2002a; Eimer, 1993; Low & Miller, 1999; Pfefferbaum & Ford, 1988; Polich, Ellerson, & Cohen, 1996). Consequently, prefrontal N2 could provide a useful marker of inhibitory control that is sensitive to inhibitory load and anxiety-related deficits in prefrontal inhibition as task demands and effortful processing/arousal increase.

Previous research suggests that pupil diameter increases during periods of cognitive effort and arousal (Beatty, 1982; Beatty & Lucero-Wagoner, 2000; Hess, 1975; Kahneman & Beatty, 1966; Karatekin et al., 2007) (also see Chapter 1, 2, and 3). Trait anxious individuals show increased pupillary responses during response preparation (e.g., oculomotor delayed response task; see Chapter 2), periods of high load/effort (e.g., delayed

pro- and antisaccade tasks; see Chapter 3), and sustained attention (e.g. simulated driving tasks; Wilson et al., 2006).

In the current study, the effect of anxiety and inhibitory load on No-Go performance and frontal N2 and P3 amplitudes were examined. Pupillary responses provided a concurrent measure of effort and arousal. It was hypothesised that individuals with elevated levels of trait anxiety would show increased errors, smaller (less negative) N2 and smaller (less positive) P3 frontal amplitudes (consistent with poor inhibitory control) and larger pupillary responses (effortful processing/arousal) during inhibitory control (No-Go) trials, particularly during high inhibitory load.

4.2 Method

4.2.1 Participants [3]

Fifteen high trait anxious and 15 low trait anxious participants were selected from a University of Southampton participant pool based on scores on the trait version of the State-Trait Anxiety Inventory (Spielberger et al., 1983) (see Appendix A). Consistent with previous research (Ansari et al., 2008) and Chapter 2, participants who scored ≤ 35 were categorised as low anxious (LA; n = 15, *mean* STAI-T = 28.80, *S.D.* = 2.93, *min* = 23, *max* = 33, *mean* age = 20.27; 10 females) and those scoring ≥ 50 as high anxious (HA; n = 15, *mean* STAI-T = 59.93, *S.D.* = 7.93, *min* = 50, *max* = 77; *mean* age = 20.60; 13 females). Levels of state anxiety (STAI-S) prior to the task were M=44.80, *S.D.* = 7.94 for high trait anxious and M= 26.60, *S.D.* = 5.52 for low trait anxious individuals. Anxiety

[3] Same participants performed the tasks in the Chapter 3 and Chapter 4. Task order was randomised.

scores were normally distributed (LA; Shapiro Wilk= .90, p=.10; HA; Shapiro Wilk= .93, p=.29)

All participants had normal or corrected-to-normal vision and were right-handed (as verified by the Edinburgh Handedness Inventory; Oldfield, 1971) (see Appendix B). Participants confirmed that they had not taken drugs, alcohol, or medication on the day preceding testing. They received either course credits or £10 for participation. All participants provided informed consent. The research protocol was approved by the University of Southampton Ethics and Research Governance committees. (Please see Appendix D Section 2 for Experiment 3 forms).

4.2.2 Data Acquisition

Electroencephalographic (EEG) data were recorded from 64 Ag/AgCl scalp electrodes mounted in an elastic electrode cap (EasyCap GmbH, Germany) and Synamps RT amplifier (Neuroscan, Inc). Electrode sites were determined using the international 10-20 system. All electrodes were referenced online to the nose and later re-referenced offline to the average of all electrodes. AFz was used as a ground electrode. Horizontal eye movements (HEOG) were recorded by placing electrodes laterally on the outer canthi of the eyes and vertical eye movements (VEOG) were recorded from electrodes placed below and above the left eye. Impedances were kept below 5 kΩ for all channels. Signals were amplified in a DC mode at 100 Hz and sampled at 1000 Hz using Neuroscan 4.5 (Neuroscan, Inc).

Eye movements and pupillary responses were recorded using SR EyeLink 1000 desktop-mounted eye tracking system (SR Research, ON, Canada) with a sampling rate of 1 kHz. Pupillary responses were recorded using Centroid model based on pupil diameter in millimetres. The presentation was controlled by Experiment Builder v1.10.1025 software (SR Research Ltd., Ontario, Canada) on a 19-inch ViewSonic (P227f) monitor.

4.2.3 Experimental Task and Procedure

Participants were seated in front of the computer and eye-tracking system with their chin and head supported at a viewing distance of 70 cm. After successful drift correction, a central fixation (1000 ms) and a central cue (letters O or X) was presented for 1000 ms to indicate the type of the trial (Go or No-Go) (see Figure 4.1). In Go trials participants were asked to press a response button as soon as they saw the Go cue (the letter O) but withhold their responses if they saw the No-Go cue (the letter X). All stimuli were presented on a grey background (R = 117, G = 116, B = 116), and all trial screen displays had a mean luminosity of 22 lux.

Participants were calibrated (3-point display) before completing 10 practice trials and the experimental task. The task consisted of 600 trials presented across 6 blocks of 100 trials (trial and block order were randomised). There were 3 high inhibitory load/effort blocks (20 % No-Go, 80 % Go) and 3 low inhibitory load/effort blocks (50 % No-Go, 50 % Go). Participants were instructed to maintain central fixation and minimise movements. Participants could take small breaks and were re-calibrated where appropriate.

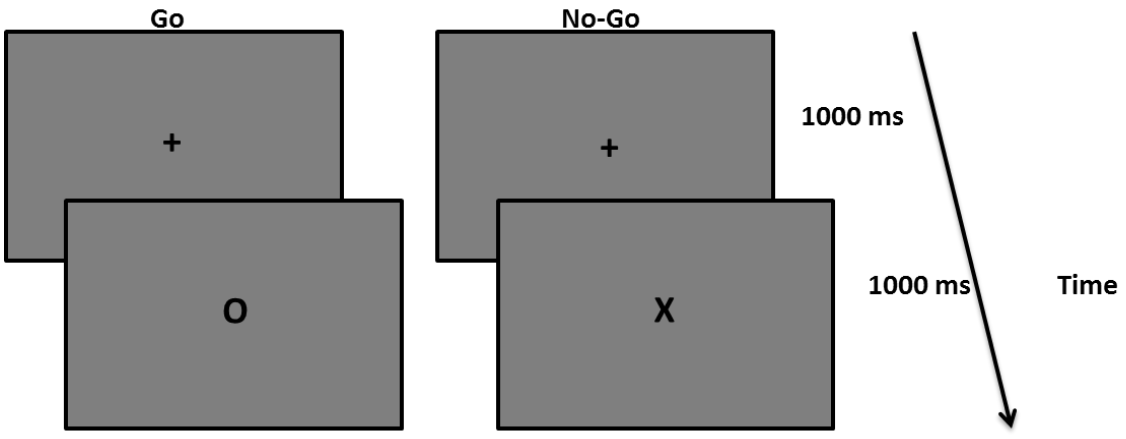


Figure 4.1 Flowchart of Go and No-Go trials. After the presentation of the fixation cross, participants were required to press a button after Go cue (O), but withhold their responses after No-Go cue (X). There were 3 high inhibitory load/effort blocks (20 % No-Go, 80 % Go) and 3 low inhibitory load/effort blocks (50 % No-Go, 50 % Go).

4.2.4 Data Pre-processing

Behavioural performance. Mean reaction times (RTs) for Hits in high load (80 % Go) and low load (50 % Go) trials and percentage of commission errors (false alarms) in high load (20 % No-Go) and low load (50 % No-Go) trials were computed. Mean RTs were not calculated for the small percentage of commission errors (1.36 %). The percentage of omission errors (misses) = 2.05 %.

Event-related potentials. The continuous EEG recordings were band pass filtered offline with a high-pass cut-off of 0.1 Hz and a low-pass cut-off of 30 Hz, using a zero phase shift FIR (Finite Impulse Response) filter. Eye blinks in the continuous EEG data were identified and corrected. Muscle bursts were manually selected and removed from further analyses. The data were epoched 100 ms pre-cue and 500 ms post-cue resulting in - 100 to 2600 ms epochs. All epochs were re-referenced to the average of all electrodes, and baseline corrected. Consistent with previous studies (Sehlmeyer et al., 2010), trials with erroneous responses (errors of commission on No-Go trials and errors of omission on Go trials) were excluded. Grand average waveforms were computed separately for 80 % Go, 20 % No-Go, 50 % Go, 50 % No-Go trials. Statistical comparisons of ERP activity were conducted on N2 (200-350 ms) and P3 (250-500 ms) components from three midline electrodes (Fz, Cz, Pz) on the basis of previous Go/No-Go studies (Bruin & Wijers, 2002a; Falkenstein et al., 1999; Righi et al., 2009; Sehlmeyer et al., 2010). Distributions of N2 and P3 amplitudes were examined and met assumptions of normality using Shapiro-Wilk's test, p's > .05.

Pupillary responses. Pupillary responses the Go/No-Go period (1000 ms) were pre-processed using previous standard procedures (cf. Beatty & Lucero-Wagoner, 2000; Bradley et al., 2008; Granholm et al., 2000) by using MATLAB R2013a (The Math-Work, Inc., MA, USA). Firstly, blinks and artefacts (very short increases or decreases of at least

0.375 mm within 20 ms (Partala & Surakka, 2003) were removed. Then, missing values were corrected by linear interpolation resulting (% interpolated = 9.89). Thirdly, continuous pupil data were during each delay period (5000 ms for short delay and 10000 ms for long delay). Then, baseline correction (relative to the start of epoch) was applied. Peak pupillary responses (maximum pupil diameter) and latency to peak (ms) were calculated during the 1000 ms Go/No-Go period. Distributions of amplitude and latency of peak pupillary responses were examined and met assumptions of normality using Shapiro-Wilk's test, p's > .05.

4.3 Results [4]

4.3.1 Go/No-Go Performance

Reaction times of hits and percentage of commission errors were entered into separate 2 x 2 mixed design ANOVA with Group (low-anxious, high-anxious) as the between subject factor and Inhibitory Load (High, Low) as the within subject factor**.** Greenhouse-Geisser corrections were applied where assumptions of sphericity were violated.

Participants made faster Go responses (GoRT) but more commission errors (CE) on No Go trials in high load compared to low load blocks [$GoRT_{High}$ = 366.81 ms *S.E.*= 9.95, $GoRT_{Low}$ = 387.58 ms *S.E.*= 7.83, mean difference = 20.78 ms $F_{(1,28)}$ = 13.76, p = .001, η^2 = .33; CE_{High} =2.33% S.E.= .27, CE_{Low} = 0.40% S.E.=.08 , mean difference = 1.93 %, $F_{(1,28)}$ = 56.71, p = .001, η^2 = .66) (see Table 4.1 and Table 4.2). There were no effects of anxiety or anxiety and inhibitory load interaction (Fs < 1 *ps* > .1).

[4] See Appendix F Section 3 for descriptive statistics.

Table 4.1

Means (standard deviations) of reaction times of hits (ms) in high anxious (HA) and low anxious (LA) groups during high and low inhibitory load/effort.

	HA (*n*=15)	**LA (*n*=15)**
High Load/Effort	371.73 (48.00)	361.89 (37.14)
Low Load/Effort	381.73 (50.52)	393.35 (58.26)

Table 4.2

Means (standard deviations) of percentage of commission errors (%) in high anxious (HA) and low anxious (LA) groups during high and low inhibitory load/effort.

	HA (*n*=15)	**LA (*n*=15)**
High Load/Effort	2.46 (1.37)	2.18 (1.61)
Low Load/Effort	.48 (.53)	.31 (.42)

4.3.2 Inhibition-related ERPs: N2 and P3

N2 and P3 amplitudes were entered into separate 2 x 3 x 2 x 2 mixed design ANOVA with Group (low-anxious, high-anxious) as the between subject factor and Area (frontal, central, parietal), Trial (Go, No-Go) and Inhibitory Load (High, Low) as the within subject factors.

N2. N2 amplitudes were larger on No-Go (*M*= -1.98 µV, *S.E.* = 0.23) compared to Go trials (*M*= -1.54 µV, *S.E.* = 0.20), $F_{(1,28)} = 8.54$, $p = .001$, $\eta^2 = .26$, and at frontal (*M*= -4.01µV, *S.E.* = 0.44) and central (*M*= -1.04 µV, *S.E.* = 0.32) sites compared to parietal site (*M*= -0.23 µV, *S.E.* = 0.28), $F_{(1,28)} = 30.80$, $p = .001$, $\eta^2 = .56$. A Trial x Inhibitory Load interaction [$F_{(1,28)} = 7.90$, $p = .01$, $\eta^2 = .24$] was characterised by larger N2 amplitudes

under high load for No-Go compared to Go trials ($t(28)$= 4.56, p=.001) (see Figure 4.2 and Figure 4.6 also see Figures 4.3, 4.4, and 4.5 for area distribution) – however, N2 amplitudes were similar across No-Go and Go trials under low load ($t(28)$= -.51, p=.60). A Trial x Area interaction [$F_{(1,28)}$ = 16.12, p = .001, η^2 = .40] was characterised by larger N2 at frontal sites for No-Go relative to Go trials ($t(28)$= 6.85, p=.001), but not at central ($t(28)$= .99, p=.32), and parietal ($t(28)$= 1.81, p=.08), sites (See Figure 4.7). These effects were subsumed under a four-way Group x Trial x Inhibitory Load x Area interaction [$F_{(1,56)}$ = 3.96, p = .02, η^2 = .14]. Follow-up ANOVAs were conducted at each site separately. At the frontal site there was evidence of a Group x Trial x Inhibitory Load interaction [$F_{(1,27)}$ = 4.57, p = .04, η^2 = .15], but no effects were observed at central or parietal sites. In low anxious individuals frontal N2 differed across Trial x Load [$F_{(1,14)}$ = 18.55, p = .001, η^2 = .58] and was characterised by larger No-Go N2 amplitudes under high (vs low) inhibitory load ($t(14)$= 2.67, p=.01). In contrast in high anxious individuals No-Go N2 amplitudes did not differ across high and low load (see Figures 4.8 and 4.9 and Table 4.3). No other effects were significant (Fs < 1 *ps* > .1).

Table 4.3

Means (standard deviations) of No-Go N2 amplitudes (μV) in high anxious (HA) and low anxious (LA) groups during high and low inhibitory load/effort at Fz, Cz, and Pz.

		HA (*n*=15)			LA (*n*=15)		
		Fz	*Cz*	*Pz*	*Fz*	*Cz*	*Pz*
No-Go	**High Load/Effort**	-4.49 (1.55)	-1.12 (1.20)	-.42 (.90)	-5.06 (1.55)	-1.24 (1.20)	.06 (.79)
	Low Load/Effort	-4.85 (1.51)	-1.03 (1.29)	-.09 (.87)	-4.53 (1.51)	-1.12 (1.29)	.07 (.73)
Go	**High Load/Effort**	-3.25 (1.05)	-1.14 (.76)	-.50 (1.03)	-2.66 (1.05)	-.16 (.76)	.30 (.42)
	Low Load/Effort	-3.38 (1.58)	-1.36 (1.14)	-1.38 (1.05)	-3.87 (1.58)	-1.21 (1.14)	.07 (.91)

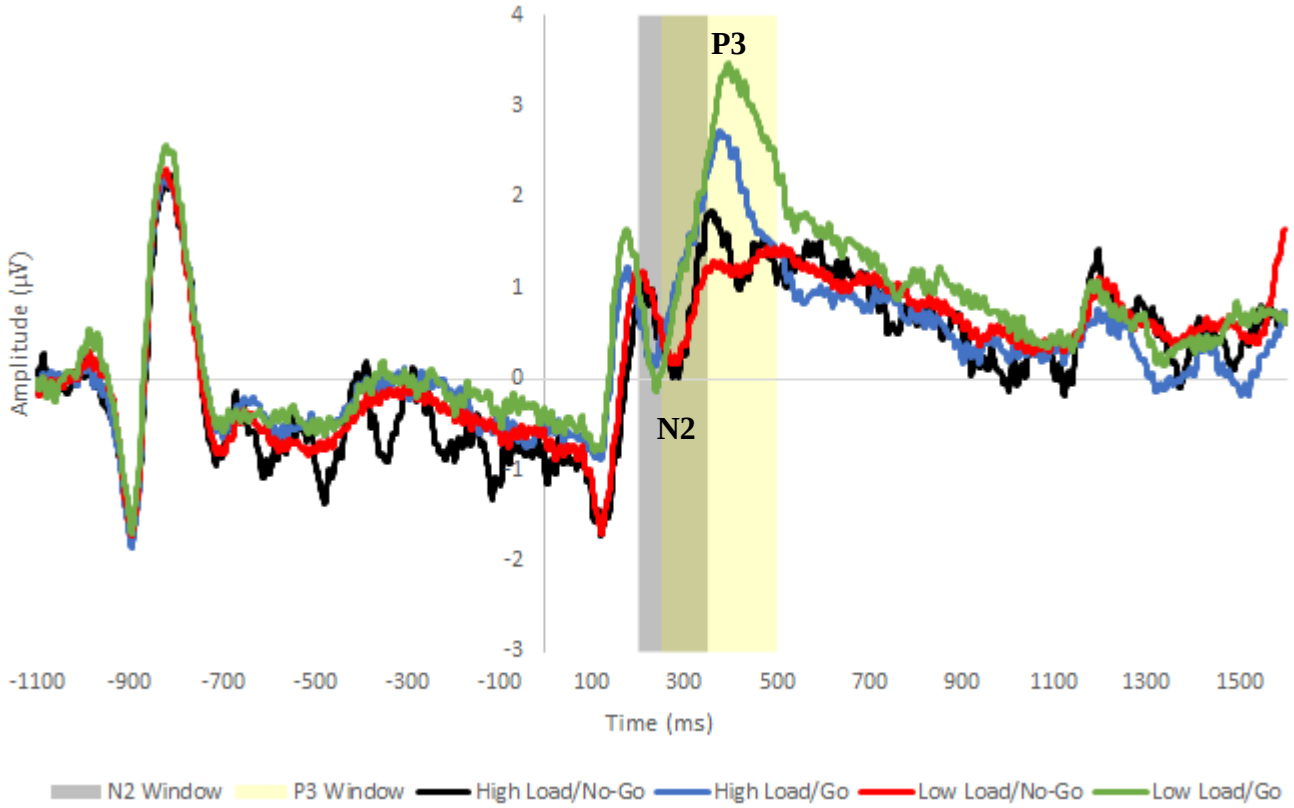


Figure 4.2 Grand average waveforms of the N2 and P3 amplitudes in No-Go and Go trials under high and low load conditions (Cue onset: 0 ms). Shaded areas represent critical periods of interest.

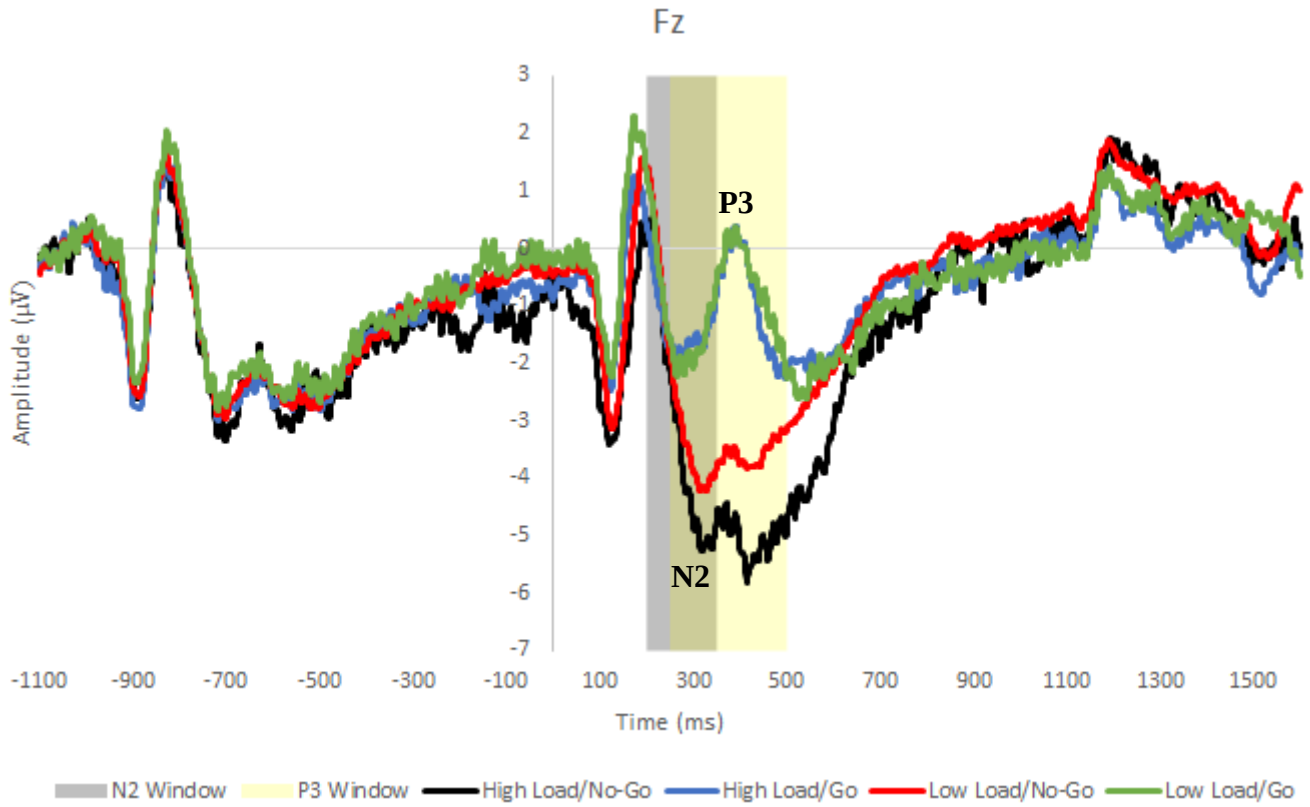


Figure 4.3 Grand average waveforms of the N2 and P3 amplitudes at Fz in No-Go and Go trials under high and low load conditions (Cue onset: 0 ms). Shaded areas represent critical periods of interest. No-Go trials elicited greater N2, especially under high load condition. Go trials elicited greater P3 and the amplitudes were comparable under high and low load conditions.

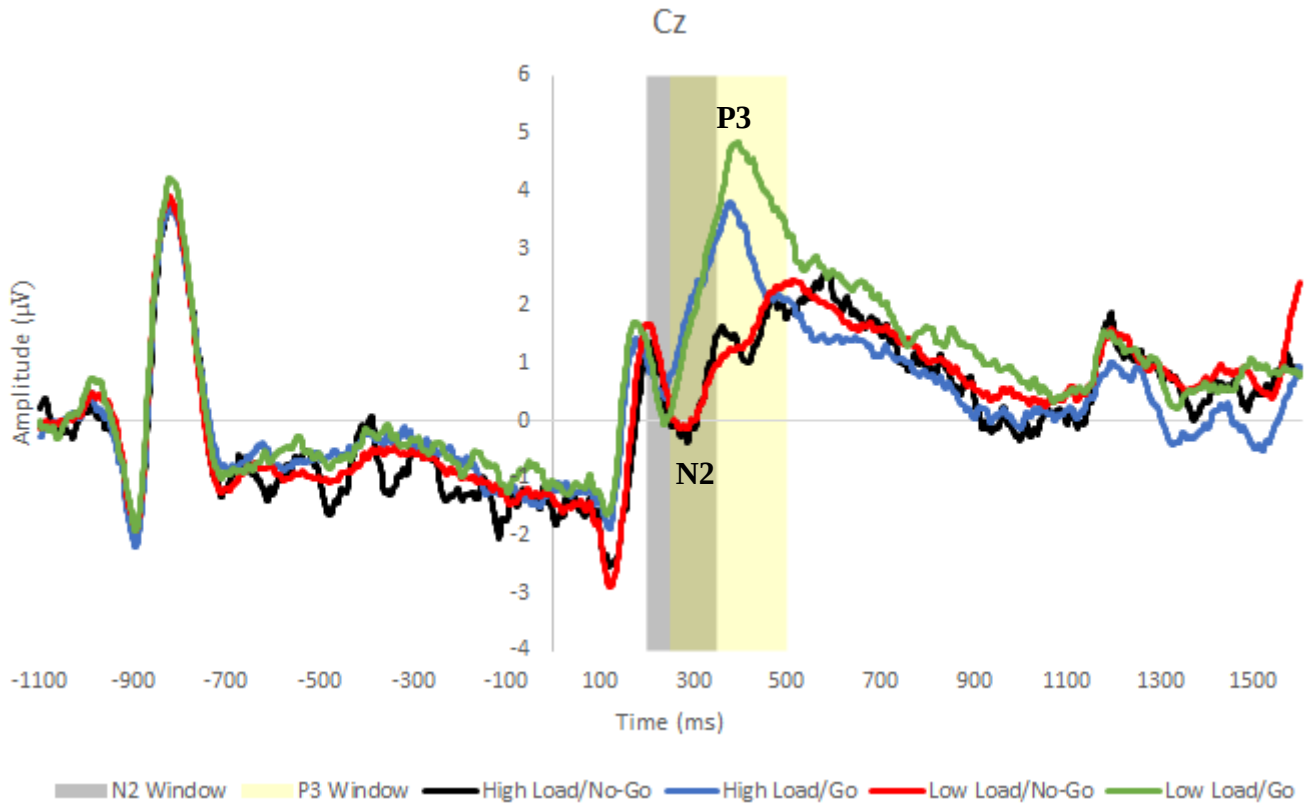


Figure 4.4 Grand average waveforms of the N2 and P3 amplitudes at Cz in No-Go and Go trials under high and low load conditions (Cue onset: 0 ms). Shaded areas represent critical periods of interest. No-Go trials elicited greater N2 and the amplitudes were comparable under high and low load conditions. Go trials elicited greater P3, especially under low load condition.

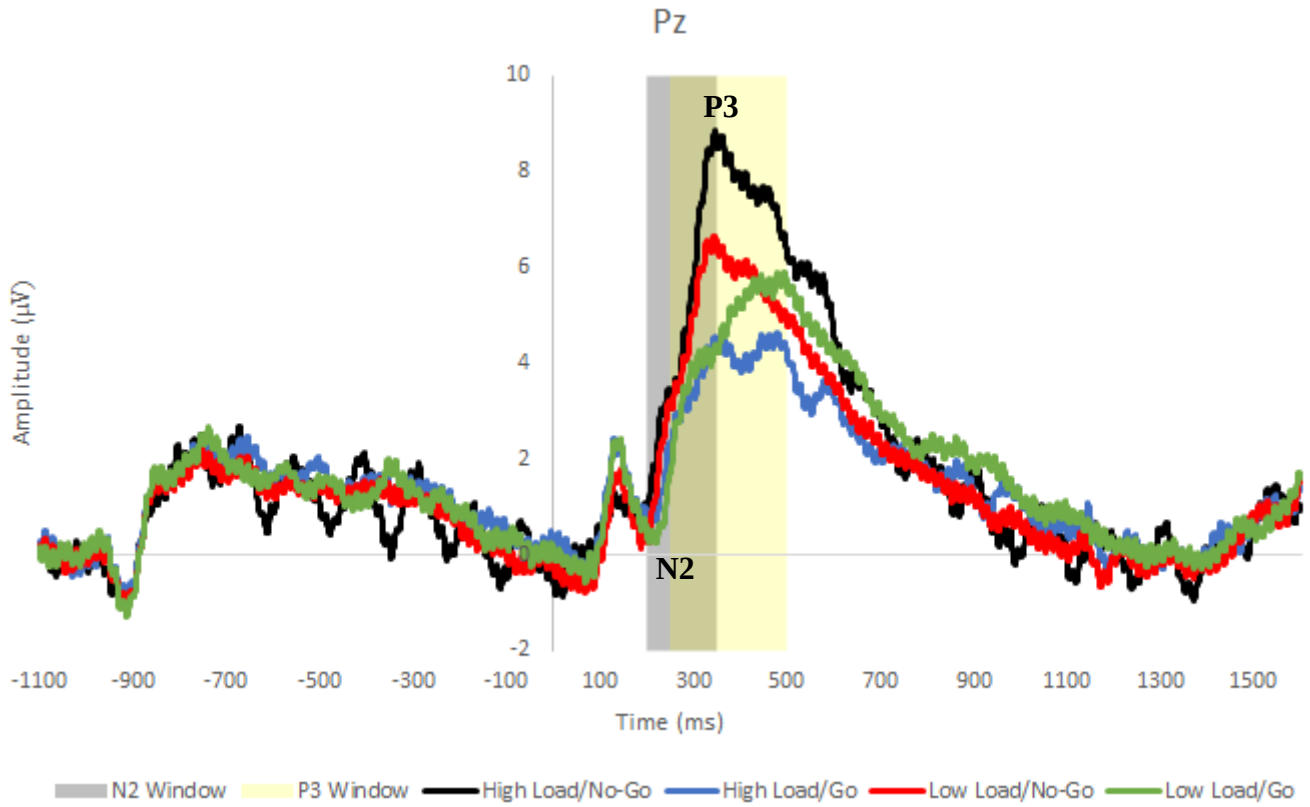


Figure 4.5 Grand average waveforms of the N2 and P3 amplitudes at Pz in No-Go and Go trials under high and low load conditions (Cue onset: 0 ms). Shaded areas represent critical periods of interest. The N2 amplitudes were comparable across all conditions. No-Go trials elicited greater P3, especially under high load condition.

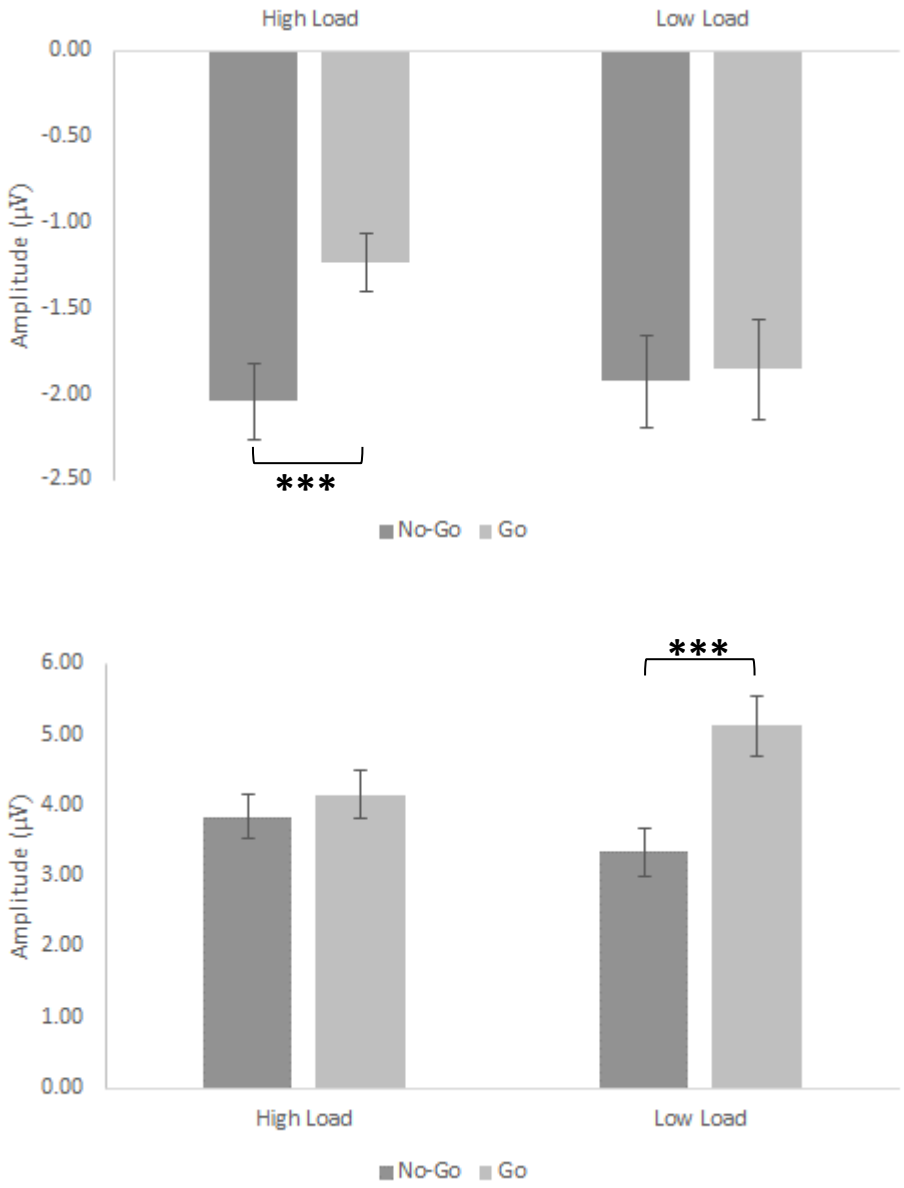


Figure 4.6 **(Top Panel)** Mean N2 amplitudes during No-Go and Go trials under high and low load conditions. Greater N2 was observed during No-Go compared to Go trials under high load. Under low load, No-Go and Go N2 amplitudes were comparable. **(Bottom Panel)** Mean P3 amplitudes during No-Go and Go trials under high and low load conditions. Greater P3 was observed during Go compared to No-Go trials under low load. Under high load, No-Go and Go N2 amplitudes were comparable. (bars represent standard errors)

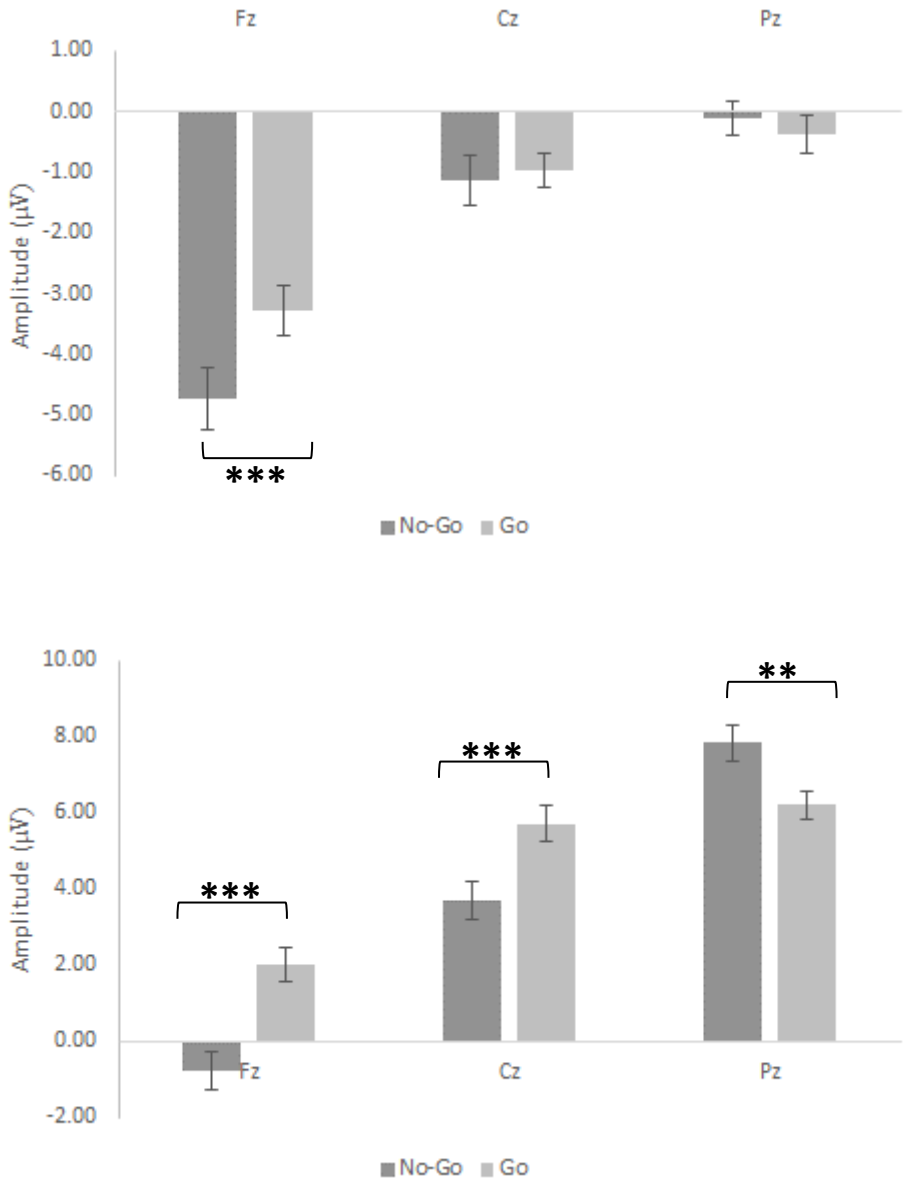


Figure 4.7 **(Top Panel)** Mean N2 amplitudes during No-Go and Go trials at Fz, Cz, and, Pz. Greater N2 was observed during No-Go compared to Go trials at Fz. At Cz and Pz, No-Go and Go N2 amplitudes were comparable. **(Bottom Panel)** Mean P3 amplitudes during No-Go and Go trials at Fz, Cz, and, Pz Greater P3 was observed during Go compared to No-Go trials at Fz and Cz. At Pz, P3 amplitudes were larger in No-Go than Go trials (bars represent standard errors).

Figure 4.8 Grand average waveforms of frontal N2 amplitudes in No-Go trials under high and low load conditions in high-anxious (HA) group. N2 amplitudes under high and low load conditions were comparable in HA.

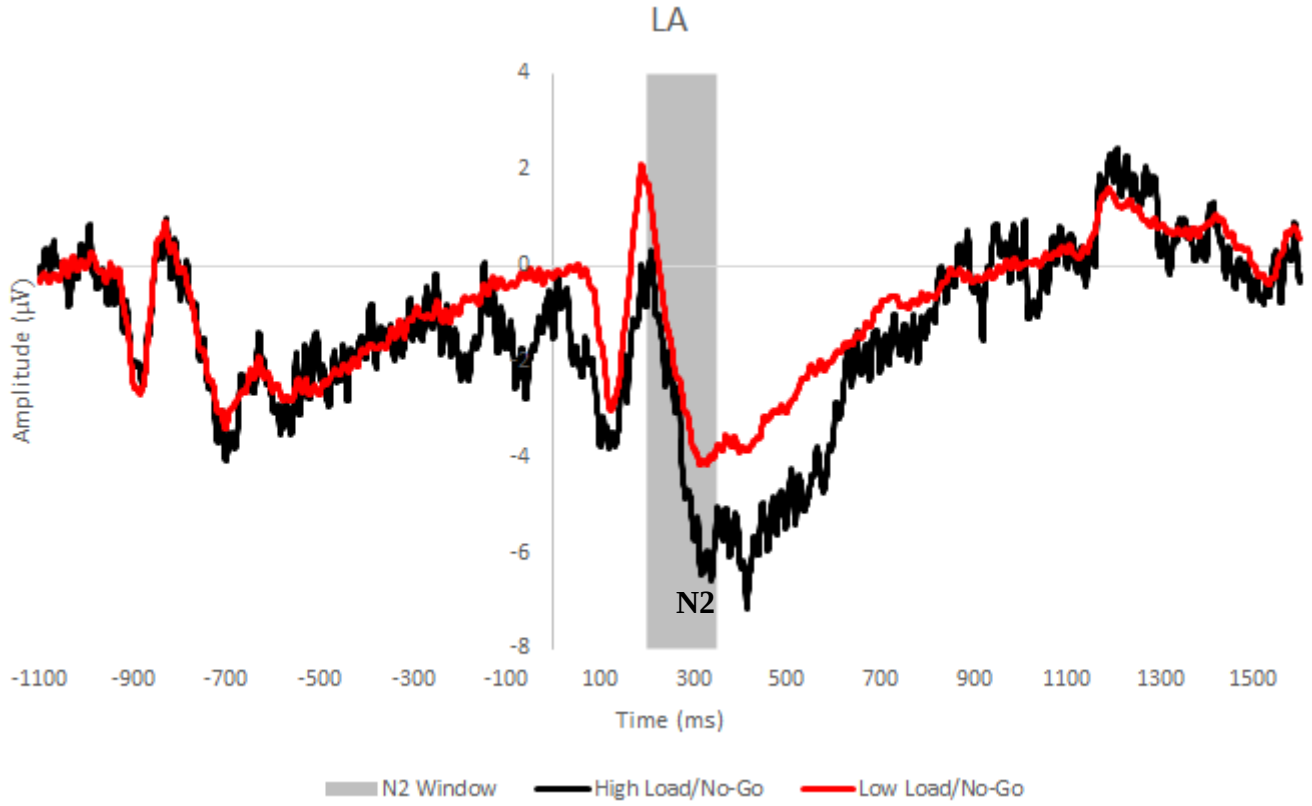


Figure 4.9 Grand average waveforms of frontal N2 amplitudes in No-Go trials under high and low load conditions in low-anxious (LA) group. Greater N2 was observed under high (vs low) load in LA.

P3. A significant Trial x Inhibitory Load interaction [$F_{(1,28)}$ = 16.79, p = .001, η^2 = .42] was characterised by greater positivity under low load in Go compared to No-Go trials ($t(28)$= -4.97, p=.001), but not under high load, ($t(28)$= -1.75, p=.09) (see Figure 4.2 and Figure 4.6 also see Figures 4.3, 4.4, and 4.5 for area distribution). A Trial x Area interaction [$F_{(1,28)}$ = 29.45, p = .001, η^2 = .56] was characterised by larger Go vs. No-Go P3 at (i) frontal ($t(28)$= -5.80, p=.001) and central ($t(28)$= -5.38, p=.001) sites but (ii) larger No-Go vs. Go P3 at parietal site ($t(28)$= 5.11, p=.009) (see Figure 4.7 and Table 4.4). No other effects were observed (Fs < 1 *ps* > .1).

Table 4.4

Means (standard deviations) of No-Go P3 amplitudes (μV) in high anxious (HA) and low anxious (LA) groups during high and low inhibitory load/effort at Fz, Cz, and Pz.

		HA (*n*=15)			LA (*n*=15)		
		Fz	*Cz*	*Pz*	*Fz*	*Cz*	*Pz*
No-Go	**High Load/Effort**	-0.88 (1.34)	4.35 (1.46)	8.96 (1.67)	-0.45 (1.39)	3.32 (1.52)	7.68 (1.73)
	Low Load/Effort	-1.26 (1.64)	3.77 (1.49)	8.25 (1.27)	-0.49 (1.70)	3.27 (1.55)	6.53 (1.32)
Go	**High Load/Effort**	2.05 (1.40)	4.87 (1.34)	5.71 (.86)	1.49 (1.45)	5.31 (1.40)	5.47 (.89)
	Low Load/Effort	2.69 (1.36)	6.19 (1.53)	7.61 (1.37)	1.79 (1.42)	6.45 (1.59)	6.03 (1.43)

4.3.3 Pupillary Responses during Go/No-Go Period

Amplitude and latency of peak pupil dilation (i.e. maximum pupil diameter) and peak pupil constriction (i.e. minimum pupil diameter) were entered into separate 2 x 2 x 2 repeated measures of ANOVA with Group (low-anxious, high-anxious) as the between subject factor and Trial (Go, No-Go) and Inhibitory Load (High, Low) as the within subject factor. Follow-up supplementary time-series analyses of pupil diameter examined effects of delay and anxiety over-time across 50 consecutive 20 ms epochs as per previous research (Geva et al., 2013) and Chapter 2 and 3.

Peak dilation responses were larger during high load blocks (M = 0.05 mm, $S.E.$ = 0.006) compared to low load (M = 0.03 mm, $S.E.$ = 0.005) blocks, $F_{(1,28)} = 8.22$, $p = .001$, $\eta^2 = .22$. A Trial x Inhibitory Load interaction [$F_{(1,28)} = 7.14$, $p = .01$, $\eta^2 = .20$] was characterised by increased peak pupillary responses to No-Go stimuli during high load compared to No-Go low load trials ($t(29) = 3.55$, $p = .001$) (see Figure 4.10 and Table 4.5). Supplementary time series analyses suggest that differences in pupil dilation between high and low load conditions in No-Go trials were most pronounced from 200-400 ms after No-Go cue onset (see Figure 4.11). Time-series analyses also provide evidence that high anxious individuals exhibited an increase in pupil diameter from 240-340 ms compared to low anxious individuals (irrespective of trial and load, see Figure 4.12). Comparable analyses of peak dilation latency did not reveal significant effects of group, trial, inhibitory load nor their interaction, Fs < 1 *ps* > .1.

Table 4.5

Means (standard deviations) of peak pupillary responses (mm) in high anxious (HA) and low anxious (LA) groups during high and low inhibitory load/effort.

	HA (*n*=15)		**LA (*n*=15)**	
	Go	*No-Go*	*Go*	*No-Go*
High Load/Effort	.04 (.03)	.05 (.03)	.04 (.02)	.06 (.05)
Low Load/Effort	.05 (.03)	.03 (.03)	.03 (.02)	.03 (.02)

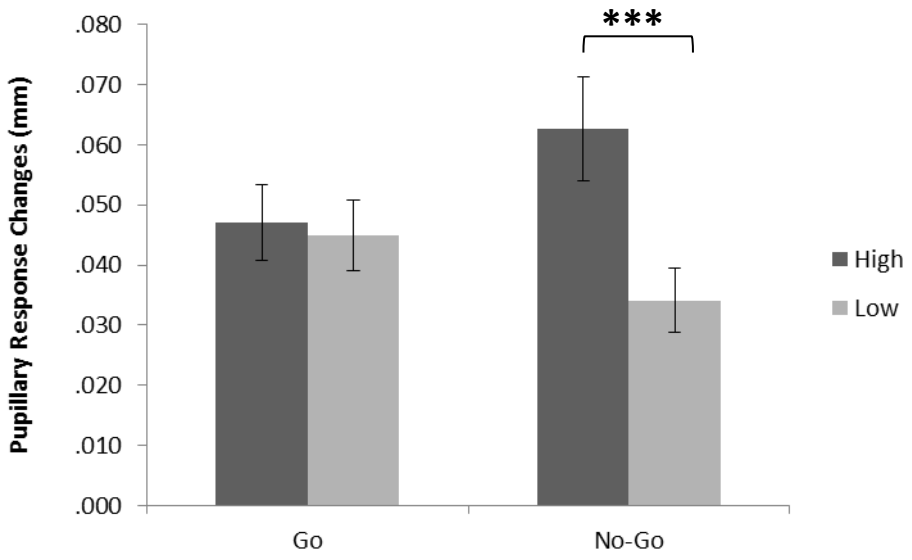


Figure 4.10 Peak pupillary responses during high and low inhibitory effort blocks in Go and No-Go trials (bars represent standard errors). No-Go trials elicited larger pupillary responses under high load compared to low load.

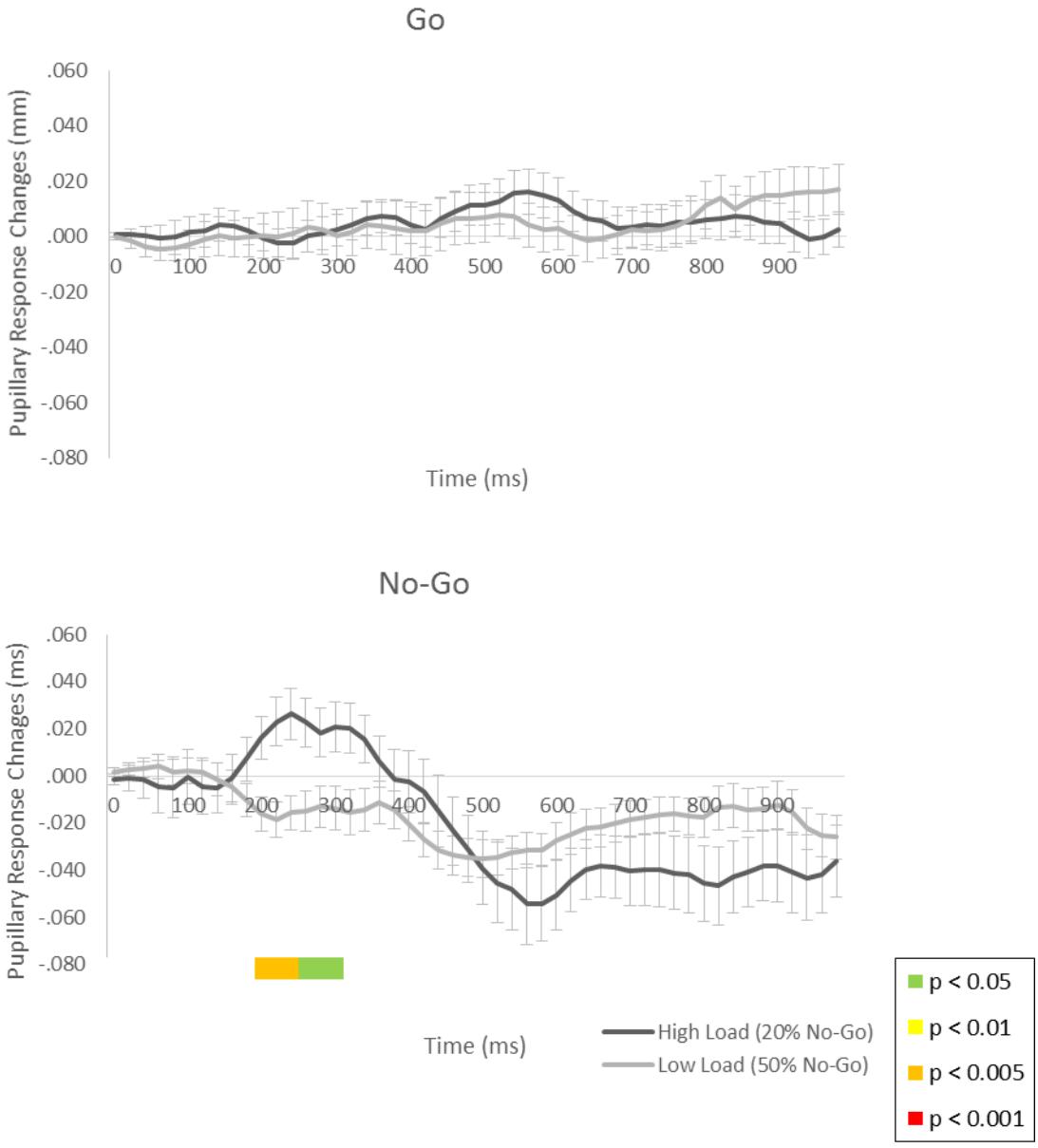


Figure 4.11 **(Top Panel)** Pupillary response time series during Go trials under high and low load. **(Bottom Panel)** Pupillary response time series during No-Go trials under high and low load. High load elicited increased pupillary responses compared to low load during No-Go trials, especially betwwn 200-400 ms. However, high and low load were comparable during Go trials.

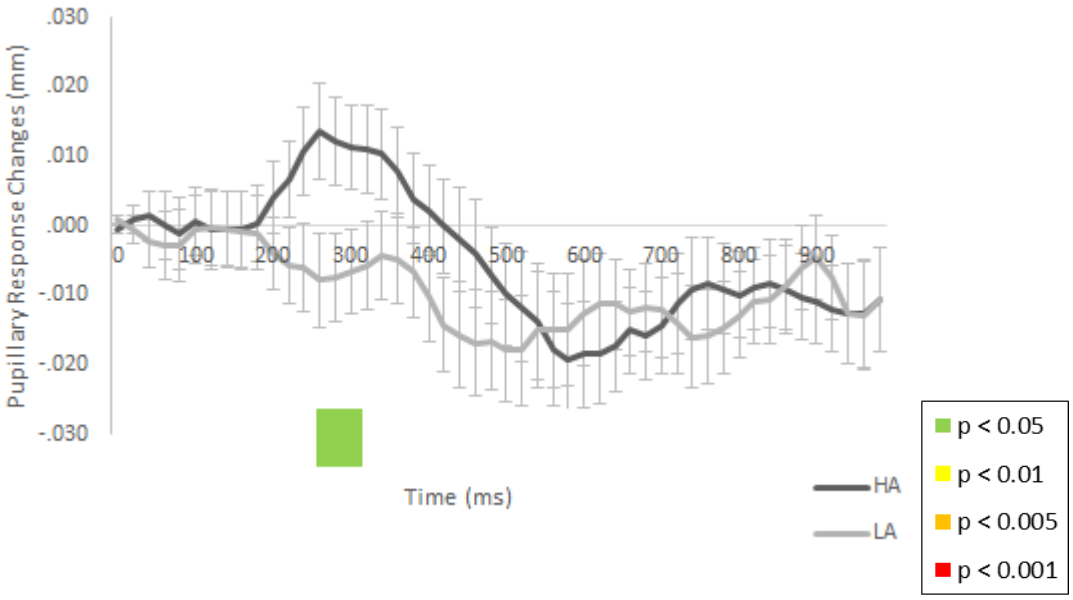


Figure 4.12 Pupillary response time series in high-anxious (HA) and low-anxious (LA) groups (bars represent standard errors). Pupillary responses of HA individuals are bigger compared to LA individuals, especially between 240-340 ms.

4.4 Discussion

Behavioural, electrophysiological and pupillometric correlates of inhibitory control in high and low anxious groups under high and low inhibitory load/effort were examined by using a Go/No-Go task. Across groups, participants produced faster but less accurate behavioural responses in high load blocks and larger pupillary responses in high load blocks, especially during inhibitory control (No-Go trials). High (vs low) anxious individuals produced larger pupillary responses. Low (vs high) anxious individuals produced greater N2 amplitude in high load blocks at the frontal area during inhibitory control (No-Go trials).

Consistent with previous studies in unselected samples (Bruin & Wijers, 2002a; Low & Miller, 1999), the behavioural data showed a reduction in reaction time and an increase in error rate during high load blocks. An effect of anxiety on reaction times (on Go trials)

nor error rates (on No-Go trials) were not observed – consistent with previous null behavioural results (Righi et al., 2009; Sehlmeyer et al., 2010; Yang & Li, 2014), but contrary to deficits on processing efficiency (and effectiveness) predicted by ACT. The Go/No-Go task (with Go/No-Go ratios of 80:20 and 50:50) might not place sufficiently high cognitive demands on the executive functions to produce behavioural differences in individuals with elevated levels of anxiety.

In accordance with previous research, N2 (but not P3) component amplitudes were moderated by trait anxiety (Herrmann et al., 2003; Kim et al., 2007; Righi et al., 2009; Sehlmeyer et al., 2010), suggesting that N2 indices of (pre-) response inhibition (i.e. response monitoring and error detection) might be more sensitive to anxiety-related deficits in response inhibition than P3 indices of motor inhibition/ evaluation of inhibition (i.e., evaluation of the preceding response and outcome of the inhibitory processes). Consistent with our predictions, a trend of smaller No-Go N2 in high load and greater No-Go N2 in low load blocks at frontal areas were observed in high anxious group. This finding corroborates studies that reported smaller No-Go N2 amplitudes at frontal areas in patients with obsessive-compulsive disorder (Herrmann et al., 2003; Kim et al., 2007). Yet others found greater frontal No-Go N2 amplitudes in anxious individuals (Righi et al., 2009; Sehlmeyer et al., 2010). Smaller No-Go N2 amplitudes at frontal sites might reflect the dysfunction of the inhibitory control (Eysenck & Derakshan, 2011; Eysenck et al., 2007) and reduced recruitment of frontal cortex (Bishop, 2009) in high anxious individuals, especially during cognitively demanding high load blocks. Also, low anxious individuals exhibited enhanced frontal No-Go N2 amplitude in high compared to low load blocks. This might reflect low anxious individuals' capacity to reduce inhibitory control/effort in low load trials – consistent with flexible resource allocation in low anxious individuals (as evidenced by load-dependent pupillary responses in low anxious individuals (Browning et al., 2015), also see Chapter 2).

Consistent with previous research (Benikos, Johnstone, & Roodenrys, 2013; Gajewski & Falkenstein, 2013), P3 amplitude differences between Go and No-Go trials were apparent only under low load conditions (i.e. easy tasks). Both our findings and previous research confirm that P3 is inversely related to load. However, unlike previous research (Harper et al., 2014), we found greater P3 amplitudes in Go compared to No-Go trials. As P3 amplitude is also related to cortical updating (Donchin & Coles, 2010), participants might have increased cortical updating during Go trials (i.e. motor response) in order to prevent erroneous responses, consistent with negligible misses and increased hit rate. Also, contrary to previous findings, greater P3 at fronto-central areas for No-Go trials and at parietal areas for Go trials were not observed. Rather, we found greater Go P3 at fronto-central areas and No-Go P3 at parietal area. This finding is consistent with previous research that used oddball paradigm (similar to Go/No-Go task, in this task participants respond to targets but they do not respond to infrequent distractor), showing greater No-Go P3 at parietal areas (Falkenstein et al., 1999; Katayama & Polich, 1998).

Evidence of large pupillary responses in high (vs low) anxious group extends evidence of increased pupillary responses on other inhibitory tasks (e.g. antisaccade performance) (see Chapter 2 and Chapter 3). In the current study anxiety-group differences were most pronounced between 240-340 ms after the onset of the cue (both Go and No-Go) and were slower to return to baseline, consistent with our previous findings showing sustained pupillary responses in high anxious individuals (see Chapter 2). These findings are consistent with (1) models that suggest anxious individuals invest greater effort to achieve performance goals (Beatty, 1982; Beatty & Lucero-Wagoner, 2000; Kahneman & Beatty, 1966; Karatekin et al., 2007) and (2) findings from Chapter 2 and Chapter 3 . However, contrary to our predictions and previous findings from Chapter 3, larger pupillary responses in high (vs low) anxious individuals during high load blocks nor

specifically on inhibitory control (No-Go) trials were not observed. Rather, across participants there was evidence of larger pupillary responses during high load blocks in inhibitory control (No-Go) trials that was pronounced between 200-400 ms after the onset of the cue and was slower to return to baseline. Consistent with the findings from Chapter 2 showing sustained but inflexible pupillary responses in anxiety, this result might reflect that high anxious individuals increased cognitive effort regardless of task demand and type.

The present study comes with certain limitations as in Experiments 1 and 2 (i.e. Chapters 2 and 3). Future studies should include equal numbers of males and females and also replicate findings in clinical samples. As a major limitation, high percentage of correct responses in the Go/No-Go task indicates that it was an easy task. Although we observed the effect of cognitive load on behavioural, pupillary and electrophysiological levels, anxiety-related effects of behavioural measures were missing. Future studies might consider using tasks with increased demands. Additionally, we selected N2 and P3 windows based on previous ERP studies. However, it would be beneficial to select different time windows after visual inspection and reanalyse N2 and P3 amplitudes.

Taken together, our findings provide evidence of impaired inhibitory control and increased use compensatory strategies (i.e., cognitive effort) in anxiety (Eysenck et al., 2007), may be attributable to dysfunctional prefrontal recruitment during inhibitory control (Bishop, 2009) and response preparation (see Chapter 3). Results further suggest that anxiety is characterised by the dysfunction in the early stages (that involves response/conflict monitoring and error detection), but not in the late stages (that involves evaluation of inhibition and performance) of inhibitory control.

5 General Discussion

5.1 Review of the Aims and Summary of the Results

Current models of anxiety postulate that high (vs. low) anxious individuals have impaired inhibitory control (Eysenck et al., 2007) and reduced dorsolateral prefrontal control of attention (Bishop, 2009). However, previous research has shown that these individuals exert greater cognitive effort and allocate more cognitive resources in order to compensate for task performance and maintain performance effectiveness and efficiency (Eysenck & Derakshan, 2011; Eysenck et al., 2007). These effects are known to be exacerbated in the presence of threat-related stimuli and high cognitive load (Eysenck & Derakshan, 2011; Eysenck et al., 2007).

Empirical research in this area is extensive but limited to behavioural and eye-movement measures (i.e., RT, accuracy, saccade onset latency, saccade accuracy) (e.g., Ansari & Derakshan, 2010; Bar-Haim et al., 2007; Derakshan et al., 2009; Mogg et al., 2007; Mogg, Millar, & Bradley, 2000). Recent empirical studies have begun to utilise ERP (e.g., Ansari & Derakshan, 2011a; Ansari & Derakshan, 2011b; Bar-Haim, Lamy, & Glickman, 2005; Fox, Derakshan, & Shoker, 2008; Righi et al., 2009; Sehlmeyer et al., 2010) and pupillary response (e.g., Browning et al., 2015; Kret et al., 2013; Price et al., 2013) techniques in order to examine online attentional processing in individuals with high trait anxiety. However, further exploration of high trait individuals ERPs and pupillary responses during inhibitory control in the absence and presence of threat and increased load is needed.

This body of research presented 3 experimental chapters that examined the effect of subclinical trait anxiety on inhibitory control by investigating:

(1) the role of stimulus valence and cognitive load/effort;

(2) the role of high vs low load/effort;

(3) the role of high vs low inhibitory load/effort.

Experiment 1 investigated the effect of threat-related stimuli (i.e., emotional faces) and cognitive load (high: 10 s delay, low: 5s delay) on pupillary responses and eye-movements by using an oculomotor delayed response task. Experiment 2 explored the effect of high (10 s delay) and low (5 s delay) cognitive effort/load on eye-movements, pupillary responses and slow-wave cortical potentials by using delayed prosaccade and antisaccade tasks. Experiment 3 examined the effect of inhibitory load/effort on pupillary responses and event-related potentials (N2 and P3) during inhibitory control (see Table 5.1. for aims and key findings). Overall, findings show that although high trait anxious individuals exerted greater cognitive effort and allocated compensatory resources (as evidenced by increased pupillary responses and reduced slow-wave cortical potentials), they have impaired inhibitory control (as evidenced by erroneous antisaccade eye movements and less negative N2) especially under high load/effort conditions during inhibitory control.

Results of this thesis are consistent with existing neurocognitive and attentional control theories of anxiety. The following discussion will consider theoretical and clinical implications in the context of the predominant theories of neurocognitive and attentional control theories of anxiety. Finally, the discussion will consider the limitations and directions for further research.

Table 5.1

Key Findings

Experiment (Chapter)	Key Findings			
	Behavioural	***Oculomotor***	***Pupillary***	***Neurophysiological***
Experiment 1 (Chapter 2)		▪ Increased eye movement errors in HA under high load	▪ Increased peak pupillary responses in HA ▪ Increased peak pupillary responses in response to angry faces ▪ Increased peak pupillary responses in HA regardless of load	
Experiment 2 (Chapter 3)		▪ Increased eye movement errors in HA in antisaccade trials	▪ Increased peak pupillary responses in HA under high load	▪ Greater CNV in HA under high load ▪ Greater CNV in HA at Fz under high load
Experiment 3 (Chapter 4)	▪ Faster but erroneous responses under high load		▪ Increased peak pupillary responses under high load, especially during No-Go trials ▪ Increased peak pupillary responses in HA	▪ Greater N2 in No-Go trials under high load ▪ Greater P3 in Go trials under low load ▪ Greater N2 in No-Go trials at Fz ▪ Greater P3 in Go trials at Fz and in No-Go trials at Pz ▪ Greater N2 in No-Go trials under high load in LA, smaller N2 in No-Go trials under high load

5.2 Theoretical Implications

5.2.1 Selective Attention to Threat in Anxiety

Theoretical models of anxiety suggest that individuals with elevated or clinical levels of anxiety are biased in favour of threat-related stimuli (Bar-Haim et al., 2007; Beck & Clark, 1997; Mathews et al., 1997; Mogg & Bradley, 1998; Williams et al., 1988). This effect is apparent across different experimental tasks and conditions. Previous pupillary and oculomotor research in this area showed that threat-related stimuli elicited increased pupil diameters (Kret et al., 2013; Price et al., 2013), saccadic errors (Garner et al., 2011) and saccadic latencies (Derakshan et al., 2009; Reinholdt-Dunne et al., 2012) in high anxious individuals.

Contrary to our predictions and previous experimental evidence, pupillary and oculomotor findings (from Experiment 1) showed no threat-related stimuli bias in high anxious individuals. Rather, consistent with early appraisal and attention to face stimuli in anxiety (Cisler & Koster, 2010), high (vs. low) anxious individuals showed increased and sustained pupillary responses for face stimuli regardless of emotion. Also, angry faces elicited larger pupillary responses compared to happy faces in all participants. This finding is consistent with previous pupillometry studies showing increased pupil diameters for highly-arousing emotional stimuli (see Bradley et al., 2008 for visual; Partala & Surakka, 2003 for auditory stimuli).

In summary, results from Experiment 1 failed to show selective attention to threat-related stimuli in high anxious individuals across different methodologies. It is possible that repetitive presentation of threat-related faces (Van Dam et al., 2012), delay period (Berggren et al., 2013), and face processing in order to adjust the illumination may have

reduced affective salience of the faces in order to create performance and psychophysiological differences.

5.2.2 Response Inefficiency and Cognitive Effort in Anxiety

According to attentional control theory (Eysenck & Derakshan, 2011; Eysenck et al., 2007), individuals with elevated levels of anxiety use compensatory strategies such as increased effort and enhanced use of cognitive resources in order to increase performance effectiveness. In the current thesis, pro- and antisaccade tasks and Go/No-Go tasks were used in order to examine behavioural, oculomotor, pupillary, and electrocortical indices of processing inefficiency and cognitive effort in high anxious individuals under high and low cognitive load. In order to study inefficiency and cognitive effort, eye-movement latencies (in pro- and antisaccade tasks), pupillary responses (in pro- and antisaccade and Go/No-Go task), and slow-wave cortical potentials (in pro- and antisaccade tasks) were measured.

Behavioural and oculomotor findings showed comparable response inefficiency in high and low anxious individuals. That is, we did not observe the effects of effort/load on behavioural (reaction times; in Experiment 3) and oculomotor (saccade onset latency; Experiment 1 and Experiment 2) levels in individuals with elevated anxiety. These findings may be attributable to delay period (in Experiment 1 and Experiment 2) and Go/No-Go probability (in Experiment 3). However, it has been previously shown that there are differences in efficiency and effectiveness in the absence of behavioural effects (e.g., Righi et al., 2009; Roche, Garavan, Foxe, & O'Mara, 2005). Indeed the current thesis identifies a clear pattern of pupillary and electrophysiological function across anxiety and load manipulations.

Pupillary response findings showed that high (vs. low) anxious individuals had larger pupillary responses (in Experiment 2 and Experiment 3), especially under high cognitive load conditions (in Experiment 2). However, results from Experiment 1 demonstrated that

both high and low cognitive load elicited larger pupillary responses in high anxious individuals. In Experiment 2, longer delay period is argued to facilitate response preparation by increasing executive processing without any demands on visuospatial working memory (Ansari & Derakshan, 2010, 2011a; Reuter et al., 2007). However, the emotional oculomotor delayed response task used in Experiment 1 includes the generation of memory guided saccades and activates both visuospatial memory and executive function networks (Curtis & D'Esposito, 2003; Luna & Velanova, 2011). So, when the task includes both visuospatial and executive functions, load-related pupillary response changes might not be apparent in individuals with elevated trait anxiety (as seen by similarly larger pupillary responses in high anxious individuals during both long and short delay). However, when the task demand is dependent on executive functioning, load-related pupillary response changes in high anxiety might be observed (as seen by larger pupillary responses in high anxious individuals during long delay). This explanation is consistent with attentional control theory that predicts detrimental effects of anxiety on the executive functions but not on the visuospatial working memory (Eysenck et al., 2007). In summary, as previous research showed that increased pupillary responses are associated with increased effort and resource recruitment (Beatty & Lucero-Wagoner, 2000; Hess, 1975; Kahneman & Beatty, 1966; Karatekin et al., 2007) (also see Chapter 2), it could be concluded that high anxious individuals (compared to low anxious individuals) exerted more effort and used more cognitive resources in task that measure attentional control, especially under high cognitive load.

Consistent with our pupillary response findings and previous research (Ansari & Derakshan, 2011a), reduced slow-wave cortical potentials and greater (more negative) contingent negative variation at frontal areas were observed in high anxious individuals only under high cognitive load. These results imply that high (vs. low) anxious individuals

exhibited greater cognitive effort indicating increased allocation of cognitive resources and prefrontal recruitment during more demanding high load task. This result is consistent with attentional control theories prediction showing that anxious individuals use compensatory strategies such as increased cognitive effort (Eysenck et al., 2007).

In summary, findings suggest that although not evident at behavioural and oculomotor levels, high anxious individuals exert increased cognitive effort and use additional cognitive resources (as evidenced by pupillary and electrophysiological responses) for an effective performance.

5.2.3 Response Inefficiency during Inhibitory Control

Attentional control theory further posits that high anxious individuals are more inefficient in inhibitory control tasks (Eysenck & Derakshan, 2011; Eysenck et al., 2007). In the current thesis, peak N2 and P3 amplitudes were measured in a Go/No-Go task under high and low load conditions in order to examine the inefficient inhibitory control in high anxious individuals.

This thesis showed reduced recruitment of frontal areas during inhibitory control. Attentional control theory suggests hypo-activity in goal-directed control processes (i.e., reduced activity in the dorsolateral prefrontal cortex), especially under high cognitive load. Consistent with this, peak N2 amplitude is greater in low (vs high) anxious at frontal areas during more demanding inhibitory control task. That is, high anxious individuals are more ineffective (compared to low anxious individuals) during response inhibition under high load condition. This finding support (1) attentional control theories prediction that cognitive demand should deteriorate performance in individuals with elevated levels of anxiety and (2) previous research showing that cognitive load disrupts anxious individuals performance (Berggren et al., 2013). Also, this finding is partially consistent with Bishop (2009)'s account that trait anxiety is characterised by reduced recruitment of prefrontal

mechanisms under low perceptual load. However, it is important to note that, attentional control theory posits that anxiety affects inhibitory control at a cognitive level (not on a perceptual level), and in the present thesis, impaired inhibitory control was observed in high anxious individuals only under high cognitive load.

On the other hand, consistent with previous studies (Herrmann et al., 2003; Kim et al., 2007; Righi et al., 2009; Sehlmeyer et al., 2010), anxiety did not modulate P3 amplitude. However, there are some contradictory findings too (Yang & Li, 2014). As N2 and P3 amplitudes reflect different stages of inhibitory control, it is possible that (pre-) response inhibition (i.e. response monitoring and error detection) might be more vulnerable to anxiety than motor inhibition and evaluation of inhibition stage. That is, N2 might be a better biomarker of response inhibition than P3 in anxiety.

To sum up, high anxious individuals showed reduced prefrontal activity during inhibitory control tasks under high load. This finding indicate that high anxiety is associated with hypo-activity and inefficiency in top-down control processes (especially during inhibitory control) when the task demand is high.

5.2.4 Performance Ineffectiveness during Inhibitory Control

Current attentional control and neurocognitive models of anxiety emphasize the importance of impaired inhibitory control and dysfunctional recruitment of frontal cortex during inhibitory control (Bishop, 2009; Eysenck & Derakshan, 2011; Eysenck et al., 2007). In this thesis, pro- and antisaccade tasks and Go/No-Go tasks were used to (1) examine the impaired inhibitory control in high anxious individuals, and (2) monitor electrocortical functions during impaired inhibitory control in high anxious individuals. In order to study response ineffectiveness during inhibitory control in anxiety, eye-movement errors (in pro- and antisaccade tasks) were measured.

According to attentional control theory (Eysenck et al., 2007), anxiety is believed to increase the influence of bottom-up (stimulus-driven) processing over the top-down (goal-directed) processing. In inhibitory control tasks (such as antisaccade and No-Go) top-down attentional control is needed in order to (1) inhibit reflexive responses, and (2) withhold or generate task-relevant responses. The current eye-movement findings of this thesis demonstrated that antisaccades elicited increased eye-movement errors in high (vs. low) anxious individuals. However, error rates of high and low anxious individuals during prosaccades were not different. This finding is consistent with previous research (see Ainsworth & Garner, 2013, for a review) and suggests that high anxious individuals show impaired performance effectiveness when inhibiting reflective saccades.

Taken together, eye movement findings from Experiment 1 and Experiment 2 suggest that anxiety is associated with performance ineffectiveness during inhibitory control and extend attentional control theory and research by highlighting that this ineffectiveness is apparent under high cognitive load.

5.3 Clinical Implications

Recent studies have emphasized the need for working memory (Hadwin & Richards, 2016; Sari, Koster, Pourtois, & Derakshan, 2015) and executive control (Cohen et al., 2016) training for intervention and prevention of elevated anxiety and anxiety disorders. These models aim to reduce anxiety by using various experimental tasks (such as adaptive dual n-back and flanker tasks). After working memory training participants consistently showed reduced attention to threat, increased attentional (especially inhibitory) control, and even lower levels of anxiety (Hadwin & Richards, 2016; Sari et al., 2015). Also, executive control training (Cohen et al., 2016) resulted in dampened emotional reactivity (by reducing the amygdala activity) and but better behavioural performance (by increasing the connectivity between the amygdala and the frontal cortex).

The findings of the current thesis fit well with the rationale underlying working memory and executive control training interventions. High anxious individuals require training in order to increase performance effectiveness and response efficiency, as well as to reduce the levels of trait anxiety. Specifically, the current findings raise the possibility that these training models should also aim to examine training distinct components of attentional control (such as the inhibitory control) in order to find the exact processes that need targeting for training.

5.4 Limitations and Directions for Further Research

It is important to note that the current work has some limitations. Firstly, participants were selected from a participant pool according to their self-reported trait anxiety scores. Although previous studies have shown similar effect sizes in clinical and subclinical groups for threat-related attentional bias (Bar-Haim et al., 2007) and attentional control (Najmi, Amir, Frosio, & Ayers, 2015; Vytal, Cornwell, Arkin, & Grillon, 2012), current findings require replication in clinical groups.

Secondly, the same participants completed the delayed pro- and antisaccade tasks (Experiment 2) and the Go/No-Go tasks (Experiment 3) in a random order. Although it is a common practice to use the same cohort for multiple studies, current results warrants replication by using different participants for each study.

Thirdly, the present research relied on varying delay durations in the Experiment 1 (Chapter 2) and Experiment 2 (Chapter 3) and task contingencies the Experiment 3 (Chapter 4). The present research adopted oculomotor delayed response tasks and delayed pro- and antisaccade tasks that require inhibition or/and generation of eye movements after a delay period (5 s or 10 s). Previous studies have varied the delay duration up to 24 s in oculomotor delayed response tasks (Curtis & D'Esposito, 2003) and from 600 ms to 1500

ms in delayed pro- and antisaccade tasks (Ansari & Derakshan, 2010, 2011a; Reuter et al., 2007). Similar to previous oculomotor delayed response research, in the current thesis, slightly longer delays (5 s and 10 s) were used in order to monitor processing inefficiency during response preparation and performance effectiveness during response generation in high anxious individuals. In order to fully understand the time-course of preparatory processes and inhibitory control, further research should consider varying delay durations. In addition, it is important to note that varying task contingencies (i.e. No-Go probabilities) in the Go/No-Go task has been widely used (e.g., Van De Voorde et al., 2011). However, evidence of inefficiency and ineffectiveness of high anxious individuals under high load across oculomotor, pupillary, and neurophysiological responses warrants replication by using other types of load (see Chapter 1 Section 1.1.1.2 for various load manipulations).

Finally, in regards to the ERP analyses, large number of trials of the same experimental condition are averaged in order to have reliable ERP signals. By averaging, important single-participant and single-trial information can be neglected. Future research may supplement ERP analyses with single-participant analyses in order to understand clinical/subclinical and control group characteristics. This would give more information for researchers and clinicians that is essential for case studies in neuropsychology, especially when examining a specific cognitive or sensory impairment. However, it is important to note that single-participant analyses may not fulfil assumptions of normality and may include artefacts (Oruc et al., 2011; Picton et al., 2000). In addition, although ERPs provide excellent temporal resolution, their spatial resolution is not that accurate. Future research may combine ERP measures with MRI, fMRI, and PET measures in order to have high temporal and spatial resolution.

These limitations notwithstanding, the current research could provide intriguing avenues for further research. As this thesis is only focused on inhibition component of the executive system (Miyake et al., 2000), it would be beneficial to address attentional control

in general, thus, future research should examine shifting and updating components of the executive system in anxious individuals by using different methodologies.

5.5 Conclusion

The work summarised in this thesis investigated impaired efficiency and effectiveness in high anxious individuals during inhibitory control under low and high cognitive load. These findings demonstrated a clear pattern of inefficiency and ineffectiveness in anxious individuals through oculomotor, pupillary, and electrophysiological measures, especially under high cognitive load. These results suggest that, although high anxious individuals exert more effort and use more cognitive resources, they are still ineffective during inhibitory control. From a theoretical point of view, the findings of the thesis (1) are consistent with existing attentional control (Eysenck et al., 2007) and neurocognitive (Bishop, 2009) frameworks of anxiety, (2) extend these frameworks by contributing to the field by showing pupillary and electrophysiological evidence. From a clinical point of view, the findings of the current thesis can also inform clinical interventions in order to (1) reduce anxiety by improving attentional control, and (2) protect against the development of clinical anxiety (Sari et al., 2015).

APPENDICES

Appendix A : State-Trait Anxiety Inventory (Spielberger et al., 1983)

A number of statements which people have used to describe themselves are given below. Read each statement and then circle the appropriate number to the right of the statement to indicate how you ***generally feel***. There are no right or wrong answers. Do not spend too much time on any one statement but give the answer which seems to describe how you generally feel.

	Almost never	**Sometimes**	**Often**	**Almost always**
1. I feel pleasant	1	2	3	4
2. I feel nervous and restless	1	2	3	4
3. I feel satisfied with myself	1	2	3	4
4. I wish I could be as happy as others seem to be	1	2	3	4
5. I feel like a failure	1	2	3	4
6. I feel rested	1	2	3	4
7. I am “calm, cool, and collected”	1	2	3	4
8. I feel that difficulties are piling up so that I cannot overcome them	1	2	3	4
9. I worry too much over something that really doesn’t matter	1	2	3	4
10. I am happy	1	2	3	4
11. I have disturbing thoughts	1	2	3	4
12. I lack self-confidence	1	2	3	4
13. I feel secure	1	2	3	4
14. I make decisions easily	1	2	3	4
15. I feel inadequate	1	2	3	4
16. I am content	1	2	3	4
17. Some unimportant thought runs through my mind and bothers me	1	2	3	4
18. I take disappointments so keenly that I can’t put them out of my mind	1	2	3	4
19. I am a steady person	1	2	3	4
20. I get in a state of tension or turmoil as I think over my recent concerns and interests	1	2	3	4

Appendix B : Edinburgh Handedness Inventory (Oldfield, 1971)

Please indicate your preferences in the use of hands in the following activities by putting + in the appropriate column. Where the preference is so strong that you would never try to use the other hand unless absolutely forced to, put ++. If in any case you are really indifferent put + in both columns.

Some of the activities require both hands. In these cases the part of the task, or object, for which hand preference is wanted is indicated in brackets.

Please try to answer all the questions, and only leave a blank if you have no experience at all of the object or task.

		LEFT	RIGHT
1	Writing		
2	Drawing		
3	Throwing		
4	Scissors		
5	Toothbrush		
6	Knife (without fork)		
7	Spoon		
8	Broom (upper hand)		
9	Striking Match (match)		
10	Opening box (lid)		
i	Which foot do you prefer to kick with?		
ii	Which eye do you use when using only one?		

Appendix C : Other Questionnaires

COGNITIVE FAILURES QUESTIONNAIRE (Broadbent et. al., 1982)

The following questions are about minor mistakes which everyone makes from time to time, but some of which happen more often than others. We want to know how often these things have happened to you in the past 6 months. Please circle the appropriate number.

		Very often	Quite often	Occasion - ally	Very rarely	Never
1.	Do you read something and find you haven't been thinking about it and must read it again?	4	3	2	1	0
2.	Do you find you forget why you went from one part of the house to the other?	4	3	2	1	0
3.	Do you fail to notice signposts on the road?	4	3	2	1	0
4.	Do you find you confuse right and left when giving directions?	4	3	2	1	0
5.	Do you bump into people?	4	3	2	1	0
6.	Do you find you forget whether you've turned off a light or a fire or locked the door?	4	3	2	1	0
7.	Do you fail to listen to people's names when you are meeting them?	4	3	2	1	0
8.	Do you say something and realize afterwards that it might be taken as insulting?	4	3	2	1	0
9.	Do you fail to hear people speaking to you when you are doing something else?	4	3	2	1	0
10.	Do you lose your temper and regret it?	4	3	2	1	0
11.	Do you leave important letters unanswered for days?	4	3	2	1	0
12.	Do you find you forget which way to turn on a road you know well but rarely use?	4	3	2	1	0
13.	Do you fail to see what you want in a supermarket (although it's there)?	4	3	2	1	0
14.	Do you find yourself suddenly wondering whether you've used a word correctly?	4	3	2	1	0

		Very often	Quite often	Occasion - ally	Very rarely	Never
15.	Do you have trouble making up your mind?	4	3	2	1	0
16.	Do you find you forget appointments?	4	3	2	1	0
17.	Do you forget where you put something like a newspaper or a book?	4	3	2	1	0
18.	Do you find you accidentally throw away the thing you want and keep what you meant to throw away – as in the example of throwing away the matchbox and putting the used match in your pocket?	4	3	2	1	0
19.	Do you daydream when you ought to be listening to something?	4	3	2	1	0
20.	Do you find you forget people's names?	4	3	2	1	0
21.	Do you start doing one thing at home and get distracted into doing something else (unintentionally)?	4	3	2	1	0
22.	Do you find you can't quite remember something although it's "on the tip of your tongue"?	4	3	2	1	0
23.	Do you find you forget what you came to the shops to buy?	4	3	2	1	0
24.	Do you drop things?	4	3	2	1	0
25.	Do you find you can't think of anything to say?	4	3	2	1	0

GENERALISED ANXIETY DISORDER SCALE -7 (Spitzer et. al., 2006)

Over the last **2 weeks** how often have you been bothered by the following problems? Rate each word by drawing a vertical line on the scale below to indicate the extent you have felt that way.

FEELING NERVOUS, ANXIOUS OR ON EDGE

Not at all sure Several days Over half the days Nearly every day

……..

NOT BEING ABLE TO STOP OR CONTROL WORRYING

Not at all sure Several days Over half the days Nearly every day

……..

WORRYING TOO MUCH ABOUT DIFFERENT THINGS

Not at all sure Several days Over half the days Nearly every day

……..

TROUBLE RELAXING

Not at all sure Several days Over half the days Nearly every day

……..

BEING SO RESTLESS THAT IT IS HARD TO SIT STILL

Not at all sure Several days Over half the days Nearly every day

……..

BECOMING EASILY ANNOYED OR IRRITABLE

Not at all sure Several days Over half the days Nearly every day

……..

FEELING AFRAID AS IF SOMETHING AWFUL MIGHT HAPPEN

Not at all sure Several days Over half the days Nearly every day

……..

SOCIAL PHOBIA INVENTORY (Connor et. al., 2000)

Please check how much the following problems have bothered you during the past week.

Please circle only one box for each problem, and be sure to answer all items.

	Not at all	A little bit	Somewhat	Very much	Extremely
1. I am afraid of people in authority.	0	1	2	3	4
2. I am bothered by blushing in front of people.	0	1	2	3	4
3. Parties and social events scare me.	0	1	2	3	4
4. I avoid talking to people I don't know.	0	1	2	3	4
5. Being criticized scares me a lot.	0	1	2	3	4
6. Fear of embarrassment causes me to avoid doing things or speaking to people.	0	1	2	3	4
7. Sweating in front of people causes me distress.	0	1	2	3	4
8. I avoid going to parties.	0	1	2	3	4
9. I avoid activities in which I am the centre of attention.	0	1	2	3	4
10. Talking to strangers scares me.	0	1	2	3	4
11. I avoid having to give speeches.	0	1	2	3	4
12. I would do anything to avoid being criticized.	0	1	2	3	4
13. Heart palpitations bother me when I am around people.	0	1	2	3	4
14. I am afraid of doing things when people might be watching.	0	1	2	3	4
15. Being embarrassed or looking stupid are my worst fears.	0	1	2	3	4
16. I avoid speaking to anyone in authority.	0	1	2	3	4
17. Trembling or shaking in front of others is distressing to me.	0	1	2	3	4

HOSPITAL ANXIETY AND DEPRESSION SCALE (Zigmond & Snaith, 1983)

Read each item and circle the reply which comes closest to how you have been feeling in the past week. Don't take too long over your replies: your immediate reaction to each item will probably be more accurate than a long thought out response.

I feel tense or 'wound up':	
Most of the time	
A lot of the time	
Time to time, occasionally	
Not at all	

I feel as if I am slowed down:
Nearly all of the time
Very often
Sometimes
Not at all

I still enjoy the things I used to enjoy:
Definitely as much
Not quite so much
Only a little
Not at all

I get a sort of frightened feeling like 'butterflies in the stomach':	
Not at all	
Occasionally	
Quite often	
Very often	

I get a sort of frightened feeling like something awful is about to happen:	
Very definitely and quite badly	
Yes, but not too badly	
A little, but it doesn't worry me	
Not at all	

I have lost interest in my appearance:
Definitely
I don't take as much care as I should
I may not take quite as much care
I take just as much care as ever

I can laugh and see the funny side of things:
As much as I always could
Not quite so much now
Definitely not so much now
Not at all

I feel restless as if I have to be on the move:	
Very much indeed	
Quite a lot	
Not very much	
Not at all	

Worrying thoughts go through my mind:	
A great deal of the time	
A lot of the time	
From time to time but not too often	
Only occasionally	

I look forward with enjoyment to things:
A much as I ever did
Rather less than I used to
Definitely less than I used to
Hardly at all

I feel cheerful:
Not at all
Not often
Sometimes
Most of the time

I get sudden feelings of panic:	
Very often indeed	
Quite often	
Not very often	
Not at all	

I can sit at ease and feel relaxed:	
Definitely	
Usually	
Not often	
Not at all	

I can enjoy a good book or radio or TV programme:
Often
Sometimes
Not often
Very seldom

ATTENTIONAL CONTROL SCALE (Derryberry & Reed, 2002)

A number of statements are given below. Read each statement and then circle the appropriate number to the right of the statement to indicate how you generally feel. There are no right or wrong answers.

	Almost never	**Sometimes**	**Often**	**Always**
1. It's very hard for me to concentrate on a difficult task when there are noises around.	1	2	3	4
2. When I need to concentrate and solve a problem, I have trouble focusing my attention.	1	2	3	4
3. When I am working hard on something, I still get distracted by events around me.	1	2	3	4
4. My concentration is good even if there is music in the room around me.	1	2	3	4
5. When concentrating, I can focus my attention so that I become unaware of what's going on in the room around me.	1	2	3	4
6. When I am reading or studying, I am easily distracted if there are people talking in the same room.	1	2	3	4
7. When trying to focus my attention on something, I have difficulty blocking out distracting thoughts.	1	2	3	4
8. I have a hard time concentrating when I'm excited about something.	1	2	3	4
9. When concentrating I ignore feelings of hunger or thirst.	1	2	3	4
10. I can quickly switch from one task to another.	1	2	3	4
11. It takes me a while to get really involved in a new task.	1	2	3	4
12. It is difficult for me to coordinate my attention between the listening and writing required when taking notes during lectures.	1	2	3	4

	Almost never	Sometimes	Often	Always
13. I can become interested in a new topic very quickly when I need to.	1	2	3	4
14. It is easy for me to read or write while I'm also talking on the phone.	1	2	3	4
15. I have trouble carrying on two conversations at once.	1	2	3	4
16. I have a hard time coming up with new ideas quickly.	1	2	3	4
17. After being interrupted or distracted, I can easily shift my attention back to what I was doing before.	1	2	3	4
18. When a distracting thought comes to mind, it is easy for me to shift my attention away from it.	1	2	3	4
19. It is easy for me to alternate between two different tasks.	1	2	3	4
20. It is hard for me to break from one way of thinking about something and look at it from another point of view.	1	2	3	4

Appendix D : Experiment Forms

D.1 Materials used in Experiment 1

Participant Information Sheet (Version 1.1, 02 / 01 / 2014)

Study Title: The role of emotions and cognitive load on pupillary responses and memory-guided saccades in low and high anxious individuals

Researcher: Piril Hepsomali **Ethics number**: 9195

Please read this information carefully before deciding to take part in this research. If you are happy to participate you will be asked to sign a consent form.

What is the research about?
The aim of the study is to explore how emotion and cognitive load affect visuo-spatial working memory and attention allocation of anxious and non-anxious individuals in terms of saccade accuracies, latencies and pupillary responses. Generally speaking, it is aimed to examine the effects of anxiety on working memory guided eye movements and pupillary responses.

Why have I been chosen?
You have been invited to take part because you responded to our advertisement either online or via email.

What will happen to me if I take part?
The study will consist of one experimental session, involving eye tracking and pupillary response measurement. You will be asked to place your head onto a chin rest and respond to stimuli presented on a display monitor. You will be presented a face stimulus and you will be asked to encode the location of that stimulus. After some delay, you will be are asked to generate saccades towards or away from that stimulus.

Are there any benefits in my taking part?
You may either receive 6 research credits or monetary reward of £6 for your contribution.

Are there any risks involved?
Since eye and pupil tracking are non-invasive measures, you may only feel a minimal, non-hazardous discomfort (eye-strain).

Will my participation be confidential?
You will be given a unique identifiying number for the experiment, which will be disconnected from your name/student ID numbers. All data will therefore be stored in an anonymised format.

What happens if I change my mind?
You may withdraw your consent at any time. You will not be penalised for this.

What happens if something goes wrong?
In the unlikely case of concern or complaint, please contact the Chair of the Ethics Committee, School of Psychology, University of Southampton, Southampton, SO17 1BJ. Phone: 023 8059 4663.

Where can I get more information?
You may contact the lead researcher (Piril Hepsomali) at any time:
Email: **P.Hepsomali@soton.ac.uk**

CONSENT FORM (Version 1.2, 14 / 01 / 2014)

Study title: The role of emotions and cognitive load on pupillary responses and memory-guided saccades in low and high anxious individuals

Researcher name: Piril Hepsomali
Study reference: PH6
Ethics reference: 9195

Please initial the box(es) if you agree with the statement(s):

I have read and understood the information sheet (**Version 1.1, 02 / 01 / 2014**) and have had the opportunity to ask questions about the study.	☐
I agree to take part in this research project and agree for my data to be used for the purpose of this study	☐
I understand my participation is voluntary and I may withdraw at any time without my legal rights being affected	☐
I am happy to be contacted regarding other unspecified research projects. I therefore consent to the University retaining my personal details on a database, kept separately from the research data detailed above. The 'validity' of my consent is conditional upon the University complying with the Data Protection Act and I understand that I can request my details be removed from this database at any time.	☐

Data Protection
I understand that information collected about me during my participation in this study will be stored on a password protected computer and that this information will only be used for the purpose of this study. All files containing any personal data will be made anonymous.

Name of participant (print name)……

Signature of participant……..

Date……

Study Reference: 9195

Debriefing Statement

The role of emotions and cognitive load on pupillary responses and memory-guided saccades in low and high anxious individuals (Version 1)

The aim of the study is to explore how emotion and cognitive load affect visuo-spatial working memory and attention allocation of anxious and non-anxious individuals in terms of saccade accuracies, latencies and pupillary responses. Generally speaking, it is aimed to examine the effects of anxiety on the central executive and the visuo-spatial slave system of working memory as well as the autonomic nervous system. It is expected that anxious individuals perform slow and erroneous on anti-saccade trials, but this performance are expected to be worsened when the cue is threat-related and when there is high cognitive load. Also, on high load conditions, pupillary responses of anxious participants are expected to be bigger in terms of diameters and this effect is expected to be elevated when the cue is threat-related.

If you find some of the questions sensitive and seek support or advice, we can direct you to appropriate support sources, for example, your GP or the First Support Team at the University of Southampton Student Services.

This experiment did not use deception. You are entitled to a copy of this summary, along with a copy of the research findings when they become available if you so wish.

If you have any further questions, please contact me;

Piril Hepsomali

School of Psychology

P.Hepsomali@soton.ac.uk

Thank you for your participation in this research.

Signature _____ Date _____

Name _____

If you have questions about your rights as a participant in this research, or if you feel that you have been placed at risk, you may contact the Chair of the Ethics Committee, Department of Psychology, University of Southampton, Southampton, SO17 1BJ.

Phone: 023 8059 4663.

D.2 Materials used in Experiment 2 and Experiment 3

Participant Information Sheet (Version 1, 13 / 03 / 2015)

Study Title: Neural, pupillary, and oculomotor correlates of inhibition function in anxiety

Researcher: Piril Hepsomali **Ethics number**: 14316

Please read this information carefully before deciding to take part in this research If you are happy to participate you will be asked to sign a consent form.

What is the research about?
The aim of the study is to explore how inhibition function of the central executive of working memory are affected by anxiety in terms of event related potentials, pupillary and oculomotor responses in both high and low load conditions.

Why have I been chosen?
You have been invited to take part because you responded to our invitation via email.

What will happen to me if I take part?
The study will consist of two different experiments and during both experiments your brain waves, pupillary and saccadic responses will be collected via electroencephalograph and eye tracker, respectively.

You will be asked to complete some questionnaires before and after the session. Then, you will be asked to place your head and chin onto a head and chin rest and experimenter will adjust the height of the chin rest. After, you will be asked to follow dots on the computer screen in order to complete calibration. If calibration is not successful, unfortunately you won't be able to take part in the experiment. If calibration is successful then experimenter will start capping you.

Experimenter will place an EEG cap with 64 electrodes on your scalp, 4 electrodes around your eyes and 1 reference electrode on your nose. Also, experimenter will put a gel into each electrode in order to make a good contact between the cap and your scalp.

After calibration and capping, you will be presented experiments on a display monitor. In the first experiment, according to the type of cue, you are expected to look towards to or away from a stimulus. In the second experiment, you will be asked to respond to some stimuli but withhold your response to other stimuli.

Are there any benefits in my taking part?
You are going to receive 10 credits or £10 for your participation.

Are there any risks involved?
Since electroencephalography and eye-tracking are non-invasive measures, you may only feel a minimal, non-hazardous discomfort.

Will my participation be confidential?
You will be given a unique identifiying number for the experiment, which will be disconnected from your name/student ID numbers. All data will therefore be stored in an anonymised format.

What happens if I change my mind?
You may withdraw your consent at any time. You will not be penalised for this.

What happens if something goes wrong?
In the unlikely case of concern or complaint, please contact the Chair of the Ethics Committee, School of Psychology, University of Southampton, Southampton, SO17 1BJ. Phone: 023 8059 4663.

Where can I get more information?
You may contact the lead researcher (Piril Hepsomali) at any time:
Email: **P.Hepsomali@soton.ac.uk**

CONSENT FORM (Version 1, 13 / 03 / 2015)

Study title: Neural, pupillary, and oculomotor correlates of inhibition function in anxiety

Researcher name: Piril Hepsomali
Ethics reference: 14316

Please initial the box(es) if you agree with the statement(s):

I have read and understood the information sheet (**Version 1, 13 / 03 / 2015**) and have had the opportunity to ask questions about the study.	☐
I agree to take part in this research project and agree for my data to be used for the purpose of this study	☐
I understand my participation is voluntary and I may withdraw at any time without my legal rights being affected	☐
I am happy to be contacted regarding other unspecified research projects. I therefore consent to the University retaining my personal details on a database, kept separately from the research data detailed above. The 'validity' of my consent is conditional upon the University complying with the Data Protection Act and I understand that I can request my details be removed from this database at any time.	☐

Data Protection
I understand that information collected about me during my participation in this study will be stored on a password protected computer and that this information will only be used for the purpose of this study. All files containing any personal data will be made anonymous.

Name of participant (print name)……

Signature of participant……

Date……

Ethics Reference: 14316

Debriefing Statement

Neural, pupillary, and oculomotor correlates of inhibition function in anxiety (Version 1)

The aim of the study is to explore how inhibition function affects brain waves, pupillometric and saccadic responses of individuals with elevated anxiety symptoms. Generally speaking, it is aimed to examine the effects of anxiety on central and autonomic nervous systems. It is expected that inhibition function elicit increased pupillary responses as inhibition is affected by anxiety. Also, regardless of task load, anxious individuals are expected to show increased pupillary responses suggesting that those individuals exert the same amount of effort regardless of task difficulty in order to compensate for task performance. As a neural marker of effort, contingent negative variation and frontal negativity are expected to be observed in highly anxious individuals as well as general, task-related potentials like N2 at frontal and central areas.

If you find some of the questions sensitive and seek support or advice, we can direct you to appropriate support sources, for example, your GP or the First Support Team at the University of Southampton Student Services.

This experiment did not use deception. You are entitled to a copy of this summary, along with a copy of the research findings when they become available if you so wish.

If you have any further questions, please contact me;

Piril Hepsomali

School of Psychology

P.Hepsomali@soton.ac.uk

Thank you for your participation in this research.

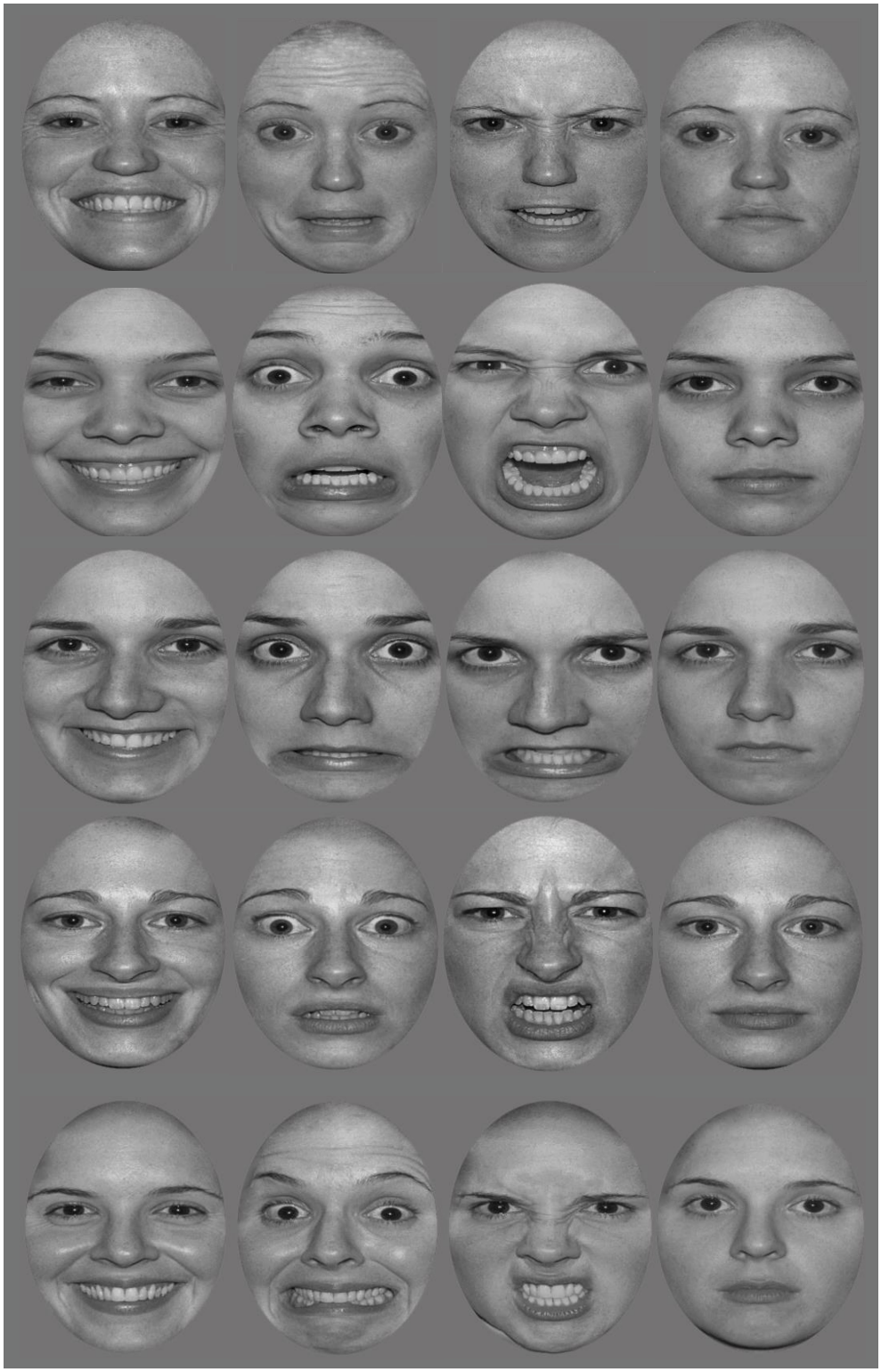
Signature _____ Date _____

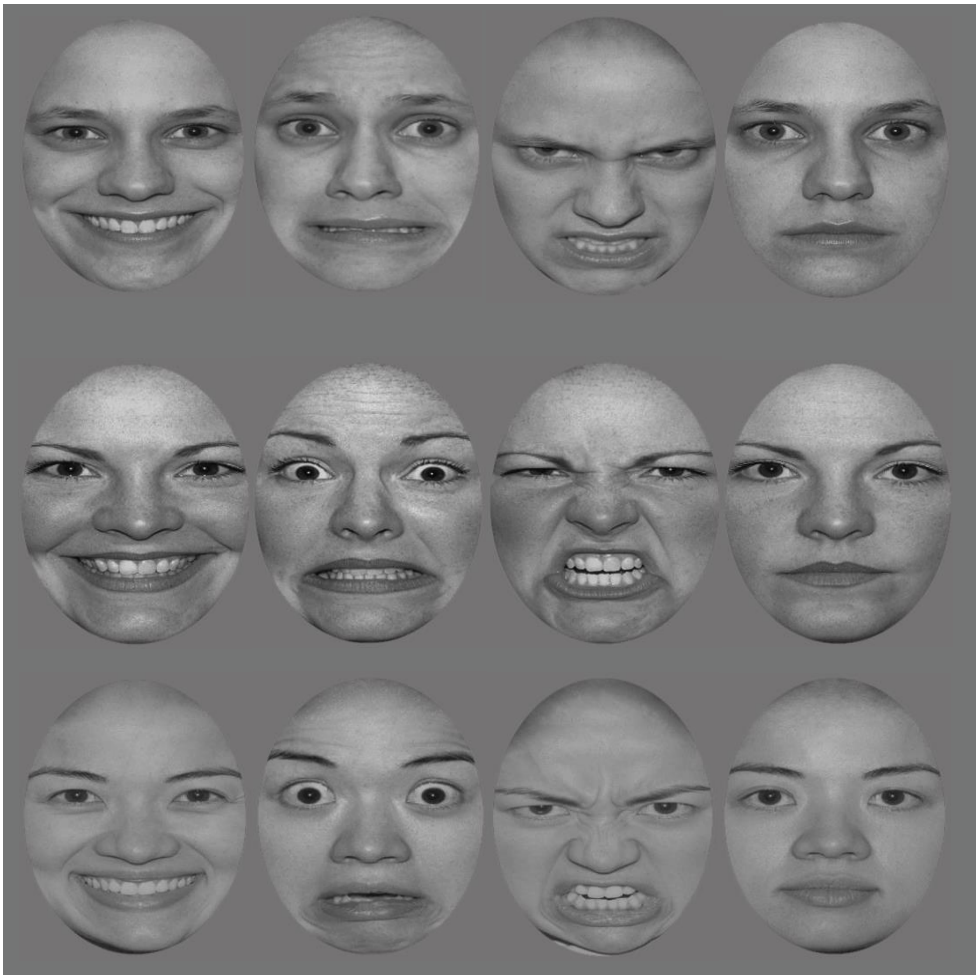
Name _____

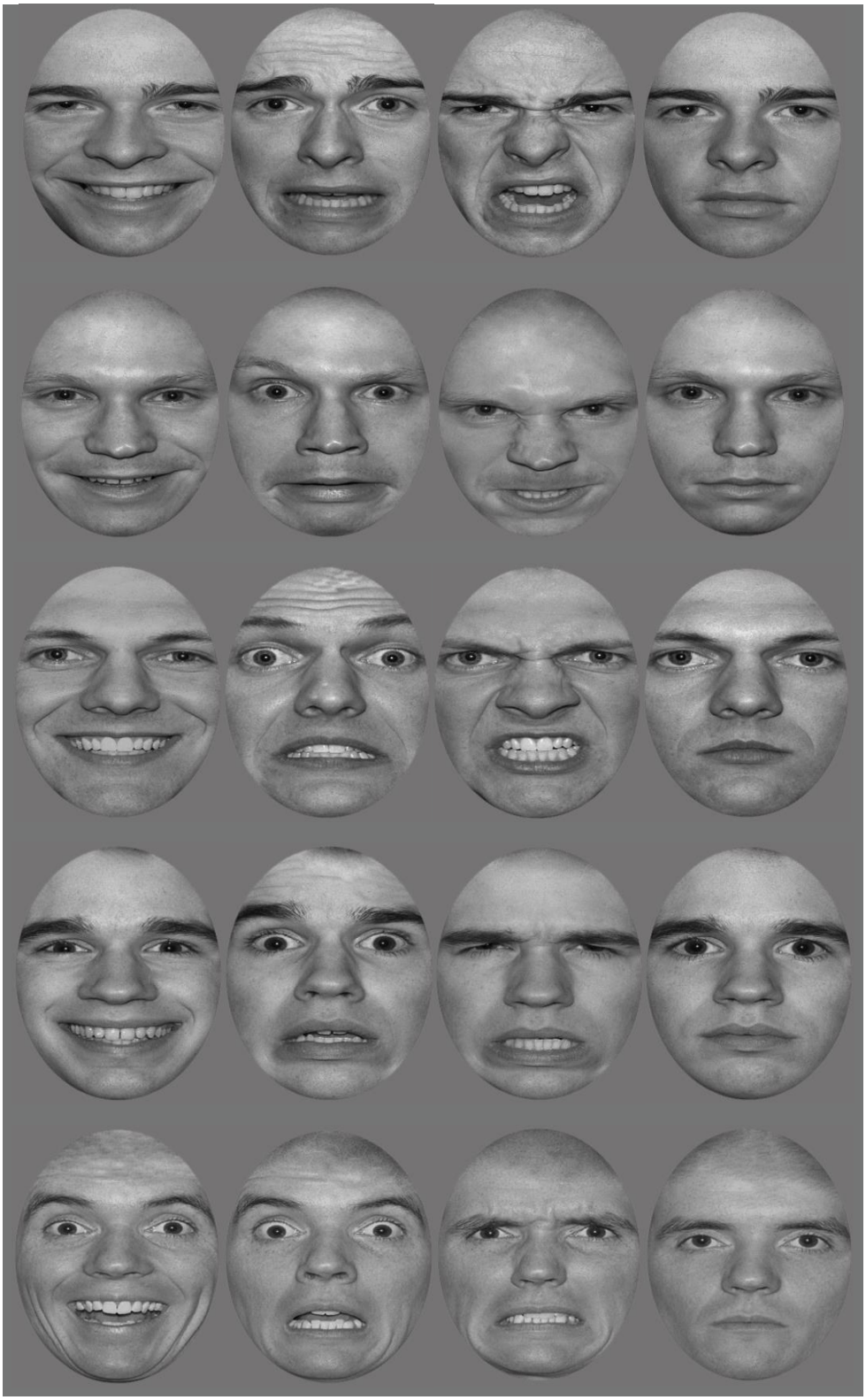
If you have questions about your rights as a participant in this research, or if you feel that you have been placed at risk, you may contact the Chair of the Ethics Committee, Department of Psychology, University of Southampton, Southampton, SO17 1BJ.

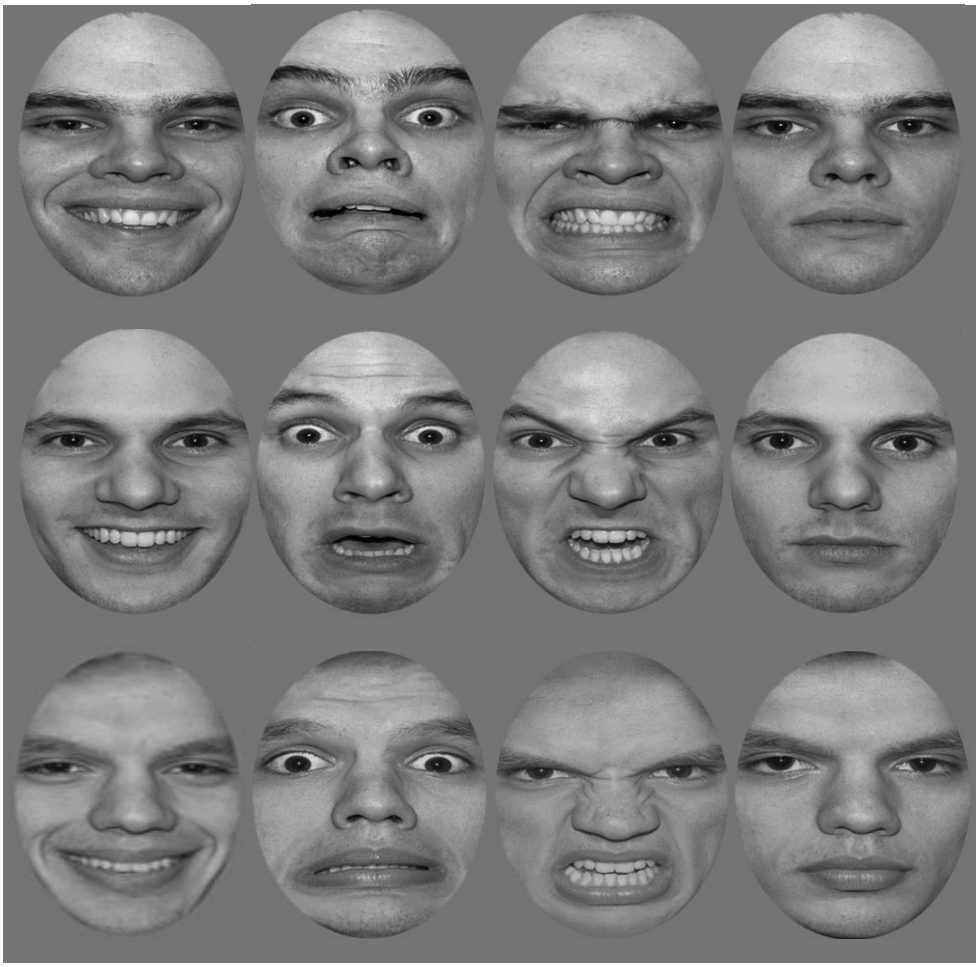
Phone: 023 8059 4663.

Appendix E : Selected Nim-Stim Faces









Appendix F : Descriptive Statistics

F.1 Experiment 1

F.1.1 Pupillary Responses

Table F.1.1.1.

Means (standard deviations) of peak pupillary responses (mm) in high anxious (HA) and low anxious (LA) groups for each emotion.

	HA (*n*=14)	**LA (*n*=13)**
Angry	.17 (.13)	.16 (.09)
Fearful	.18 (.14)	.10 (.06)
Happy	.13 (.10)	.06 (.04)
Neutral	.17 (.12)	.12 (.05)

Table F.1.1.2.

Means (standard deviations) of peak pupillary responses (mm) in high anxious (HA) and low anxious (LA) groups during long and short delay.

	HA (*n*=14)	**LA (*n*=13)**
Long Delay	.17 (.07)	.17 (.07)
Short Delay	.16 (.07)	.10 (.07)

Table F.1.1.3.

Means (standard deviations) of latency to peak (ms) in high anxious (HA) and low anxious (LA) groups for each emotion.

	HA (*n*=14)	**LA (*n*=13)**
Angry	195.76 (127.04)	229.20 (123.00)
Fearful	242.46 (117.34)	155.50 (111.95)
Happy	261.76 (111.81)	128.20 (98.00)
Neutral	257.69 (154.50)	175.60 (98.38)

Table F.1.1.4.

Means (standard deviations) of latency to peak (ms) in high anxious (HA) and low anxious (LA) groups during long and short delay.

	HA (*n*=14)	**LA (*n*=13)**
Long Delay	3377.64 (1416.04)	3058.15 (1331.26)
Short Delay	3232.71 (1483.44)	2336.00 (1552.07)

F.1.2 Eye Movements

Table F.1.2.1

Means (standard deviations) of saccadic error rates (%) in high anxious (HA) and low anxious (LA) groups during long and short delay for pro- and antisaccade tasks for each emotion.

		HA (*n*=14)		**LA (*n*=13)**	
		Pro	*Anti*	*Pro*	*Anti*
Angry	**Long Delay**	18.39 (14.60)	23.66 (13.46)	15.90 (10.09)	14.05 (13.04)
	Short Delay	19.19 (11.87)	18.30 (11.35)	15.80 (9.04)	16.92 (9.36)
Fearful	**Long Delay**	22.32 (14.02)	20.98 (14.83)	11.73 (10.20)	15.16 (5.94)
	Short Delay	19.19 (12.37)	17.41 (13.90)	14.06 (11.44)	17.70 (13.46)
Happy	**Long Delay**	19.64 (11.97)	33.03 (20.57)	7.92 (6.54)	21.87 (15.41)
	Short Delay	20.98 (17.78)	21.87 (14.02)	13.26 (13.63)	17.18 (18.06)
Neutral	**Long Delay**	22.76 (13.78)	19.19 (16.34)	11.33 (7.80)	13.68 (12.96)
	Short Delay	16.96 (8.64)	19.64 (13.61)	11.12 (8.46)	20.31 (13.77)

Table F.1.2.2

Means (standard deviations) of saccadic latencies (ms) in high anxious (HA) and low anxious (LA) groups during long and short delay for pro- and antisaccade tasks for each emotion.

		HA (*n*=14)		**LA (*n*=13)**	
		Pro	*Anti*	*Pro*	*Anti*
Angry	**Long Delay**	227.70 (62.98)	230.10 (60.77)	212.59 (76.21)	209.56 (54.34)
	Short Delay	234.67 (52.07)	285.83 (77.07)	222.38 (45.20)	233.15 (63.35)
Fearful	**Long Delay**	218.86 (54.68)	256.19 (73.71)	233.44 (95.91)	230.05 (74.18)
	Short Delay	273.46 (92.11)	256.17 (62.75)	248.11 (68.25)	252.29 (51.60)
Happy	**Long Delay**	247.68 (56.80)	254.86 (71.21)	196.84 (57.84)	232.56 (70.65)
	Short Delay	244.86 (45.86)	268.92 (59.74)	224.33 (67.71)	238.34 (51.58)
Neutral	**Long Delay**	237.35 (65.27)	249.07 (60.01)	224.98 (85.58)	217.33 (89.47)
	Short Delay	247.04 (39.85)	284.72 (82.80)	244.38 (67.71)	247.68 (96.13)

F.2 Experiment 2

F.2.1 Slow-wave Cortical Potentials

Table F.2.1.1.

Means (standard deviations) of SCP amplitudes (μV) in high anxious (HA) and low anxious (LA) groups during long and short delay at Fz, Cz, and Pz.

	HA (*n*=15)			**LA (*n*=15)**		
	Fz	*Cz*	*Pz*	*Fz*	*Cz*	*Pz*
Long Delay	-.27 (2.75)	.07 (2.68)	.34 (2.48)	.55 (2.75)	1.62 (2.81)	.53 (2.43)
Short Delay	.59 (2.19)	.40 (1.89)	.16 (2.29)	.31 (1.80)	.90 (1.49)	.37 (1.89)

Table F.2.1.2.

Means (standard deviations) of CNV amplitudes (μV) in high anxious (HA) and low anxious (LA) groups during long and short delay at Fz, Cz, and Pz.

	HA (*n*=15)			**LA (*n*=15)**		
	Fz	*Cz*	*Pz*	*Fz*	*Cz*	*Pz*
Long Delay	-.26 (3.93)	1.34 (2.01)	1.35 (3.16)	1.94 (3.03)	.15 (1.35)	1.35 (3.92)
Short Delay	1.10 (2.75)	1.42 (2.57)	2.34 (5.63)	1.54 (2.66)	.21 (.89)	1.61 (2.91)

F.2.2 Pupillary Responses

Table F.2.2.1.

Means (standard deviations) of peak pupillary responses (mm) in high anxious (HA) and low anxious (LA) groups during long and short delay.

	HA (*n*=14)	**LA (*n*=13)**
Long Delay	.21 (.08)	.12 (.08)
Short Delay	.16 (.04)	.15 (.06)

Table F.2.2.2.

Means (standard deviations) of latency to peak (ms) in high anxious (HA) and low anxious (LA) groups during long and short delay.

	HA (*n*=14)	**LA (*n*=13)**
Long Delay	974.50 (934.21)	1222.42 (1381.12)
Short Delay	1258.71 (1397.97)	1699.64 (1760.32)

F.2.3 Eye Movements

Table F.2.3.1.

Means (standard deviations) of saccadic error rates (%) in high anxious (HA) and low anxious (LA) groups during long and short delay.

	HA (*n*=14)		**LA (*n*=13)**	
	Pro	*Anti*	*Pro*	*Anti*
Long Delay	11.06 (6.31)	48.86 (16.65)	10.53 (7.57)	38.00 (21.88)
Short Delay	11.33 (3.15)	58.13 (11.86)	10.53 (6.25)	42.26 (16.08)

Table F.2.3.2.

Means (standard deviations) of saccade onset latencies (ms) in high anxious (HA) and low anxious (LA) groups during long and short delay.

	HA (*n*=14)		**LA (*n*=13)**	
	Pro	*Anti*	*Pro*	*Anti*
Long Delay	244.07 (50.14)	360.81 (47.13)	285.49 (67.74)	358.25 (62.60)
Short Delay	277.69 (69.25)	357.88 (95.60)	295.87 (69.03)	390.16 (91.79)

F.3 Experiment 3

F.3.1 Behavioural Responses

Table F.3.1.1.

Means (standard deviations) of reaction times of hits (ms) in high anxious (HA) and low anxious (LA) groups during high and low inhibitory load/effort.

	HA (*n*=15)	**LA (*n*=15)**
High Load/Effort	371.73 (48.00)	361.89 (37.14)
Low Load/Effort	381.73 (50.52)	393.35 (58.26)

Table F.3.1.2.

Means (standard deviations) of percentage of commission errors (%) in high anxious (HA) and low anxious (LA) groups during high and low inhibitory load/effort.

	HA (*n*=15)	**LA (*n*=15)**
High Load/Effort	2.46 (1.37)	2.18 (1.61)
Low Load/Effort	.48 (.53)	.31 (.42)

Table F.3.1.3.

Means (standard deviations) of percentage of omission errors (%) in high anxious (HA) and low anxious (LA) groups during high and low inhibitory load/effort.

	HA (*n*=15)	**LA (*n*=15)**
High Load/Effort	4.64 (16.97)	.74 (.87)
Low Load/Effort	2.53 (8.73)	.30 (.89)

F.3.2 Electrophysiological Responses

Table F.3.2.1.

Means (standard deviations) of No-Go and Go N2 amplitudes (μV) in high anxious (HA) and low anxious (LA) groups during high and low inhibitory load/effort at Fz, Cz, and Pz.

		HA (*n*=15)			**LA (*n*=15)**		
		Fz	*Cz*	*Pz*	*Fz*	*Cz*	*Pz*
No-Go	**High Load/Effort**	-4.49 (1.55)	-1.12 (1.20)	-.42 (.90)	-5.06 (1.55)	-1.24 (1.20)	.06 (.79)
	Low Load/Effort	-4.85 (1.51)	-1.03 (1.29)	-.09 (.87)	-4.53 (1.51)	-1.12 (1.29)	.07 (.73)
Go	**High Load/Effort**	-3.25 (1.05)	-1.14 (.76)	-.50 (1.03)	-2.66 (1.05)	-.16 (.76)	.30 (.42)
	Low Load/Effort	-3.38 (1.58)	-1.36 (1.14)	-1.38 (1.05)	-3.87 (1.58)	-1.21 (1.14)	.07 (.91)

Table F.3.2.2.

Means (standard deviations) of No-Go and Go P3 amplitudes (μV) in high anxious (HA) and low anxious (LA) groups during high and low inhibitory load/effort at Fz, Cz, and Pz.

		HA (*n*=15)			**LA (*n*=15)**		
		Fz	*Cz*	*Pz*	*Fz*	*Cz*	*Pz*
No-Go	**High Load/Effort**	-0.88 (1.34)	4.35 (1.46)	8.96 (1.67)	-0.45 (1.39)	3.32 (1.52)	7.68 (1.73)
	Low Load/Effort	-1.26 (1.64)	3.77 (1.49)	8.25 (1.27)	-0.49 (1.70)	3.27 (1.55)	6.53 (1.32)
Go	**High Load/Effort**	2.05 (1.40)	4.87 (1.34)	5.71 (.86)	1.49 (1.45)	5.31 (1.40)	5.47 (.89)
	Low Load/Effort	2.69 (1.36)	6.19 (1.53)	7.61 (1.37)	1.79 (1.42)	6.45 (1.59)	6.03 (1.43)

F.3.3 Pupillary Responses

Table F.3.3.1.

Means (standard deviations) of peak pupillary responses (mm) in high anxious (HA) and low anxious (LA) groups during high and low inhibitory load/effort in Go and No-Go tasks.

	HA (*n*=15)		**LA (*n*=15)**	
	Go	*No-Go*	*Go*	*No-Go*
High Load/Effort	.04 (.03)	.05 (.03)	.04 (.02)	.06 (.05)
Low Load/Effort	.05 (.03)	.03 (.03)	.03 (.02)	.03 (.02)

Table F.3.3.2.

Means (standard deviations) of latency to peak (ms) in high anxious (HA) and low anxious (LA) groups during high and low inhibitory load/effort in Go and No-Go tasks.

	HA (*n*=15)		**LA (*n*=15)**	
	Go	*No-Go*	*Go*	*No-Go*
High Load/Effort	592.53 (274.45)	231.33 (71.12)	504.53 (335.18)	176.07 (127.49)
Low Load/Effort	505.67 (381.14)	342.67 (314.59)	593.20 (308.34)	378.27 (359.26)

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