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Executive Control and Emotional Processing in ADHD and Anxiety. Evidence from Eye-Tracking Experiments

by

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Abstract

Attention-deficit/hyperactivity disorder (ADHD) and anxiety co-occur at above chance levels in both clinical and sub-clinical cases. However, little is known about the underlying neuropsychological basis of this overlap. In this thesis, we addressed this question by exploring a pattern of dysfunctional cognitive control linked to these conditions. Our hypothesis was that ADHD would be associated with core deficits in cognitive control in both non-emotional and emotional contexts. In addition, we anticipated cognitive control deficits in anxiety to manifest in situations involving processing of emotional stimuli and particularly in threat contexts. Furthermore, we predicted that the combination of these cognitive control challenges would be exacerbated in the case of co-occurring ADHD and anxiety.

We investigated these hypotheses using eye-movement measurements in a Go/No-Go paradigm to examine inhibitory control (i.e., suppression of reflexive saccades) and sustained attention (i.e., saccadic execution) in emotional and non-emotional contexts. We also designed an eye-movement version of the Spatial Cueing paradigm to examine attentional orienting in the presence of emotional cue distractors using representations of another person's eye-gaze. The current thesis contains four empirical chapters discussing the relationship between ADHD and anxiety symptom dimensions (and their interaction) on task performance. We examined the Go/No-Go task using symptoms of ADHD and anxiety in typically developing (TD) children/adolescents (n= 27) and healthy adults (n=27) (Chapter 3), and symptoms of ADHD and Generalised Anxiety Disorder (GAD) in a larger sample of children and adolescents (n=68), that included both TD children/adolescents and clinical cases of ADHD and anxiety (Chapter 4). We then examined the Spatial Cueing task in the same samples across Chapters 5 and 6.

High levels of ADHD were associated with impaired inhibitory control and disrupted processing, in the context of threat (such as angry faces) (Chapter 3) with reduced sustained attention regardless of the emotional valence of the stimuli used (Chapter 4). Individuals with ADHD did not effectively use social cues (i.e., poorer attentional orienting), especially in the presence of negative emotional expressions (such as angry and fearful faces) relative to other emotional expressions (Chapters 5 and 6).

Anxiety symptoms were associated with faster processing of negative facial expressions (Chapter 3) and improved attentional orienting following social cues of negative emotional expressions, relative to other facial expressions (Chapter 5). Anxiety was also associated with better attentional orienting following social cues of angry faces relative to fearful faces (Chapter 6).

In terms of the interactions between anxiety and ADHD, elevated anxiety symptoms were associated with attenuation of disrupted attentional processes found in ADHD including faster processing of negative emotional expressions relative to positive ones (Chapter 3 and 4), improved sustained attention (Chapter 4) and better attentional orienting processes (Chapters 5 and 6).

Overall, our results showed that ADHD was associated with deficits in cognitive control, particularly in emotionally charged contexts. However, anxiety was associated with improved attentional processes in response to negative emotional stimuli. Contrary to our predictions, we found that co-occurring ADHD and anxiety were associated with improved attentional control and emotional processing. Overall, the synergistic effects between ADHD and anxiety provide evidence towards a potentially distinct cognitive phenotype.

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Declaration of Authorship

I, Athina Manoli, declare that the thesis entitled:

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and the work presented in it is my own and has been generated by me as the result of my own original research.

I confirm that:

- This work was done wholly or mainly while in candidature for a research degree at this University;
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- Where I have consulted the published work of others, this is always clearly attributed;
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Abbreviations

ACC	Anterior Cingulate Cortex
ADHD	Attention-Deficit/Hyperactivity Disorder
ASD	Autism Spectrum Disorder
CD	Conduct Disorder
CE	Commission Errors
CoDG	Cone of Direct Gaze
Conner's CBRS	Conner's Comprehensive Rating Scale
CSS	Current Symptom Scale
DISC	Diagnostic Interview Scale
DLPC	Dorsolateral Prefrontal Cortex
DSM	Diagnostic and Statistical Manual
EC	Executive Control
EF	Executive Function
ERP	Event-Related Potential
FEFs	Frontal Eye fields
GLMMs	Generalised Linear Mixed Models
IC	Inhibitory Control
LMMs	Linear Mixed Models
MINI	Mini International Neuropsychiatric Interview
mPFC	Medial Prefrontal Cortex
ODD	Oppositional Defiant Disorder
OE	Omission Error
PD	Panic Disorder
PFC	Prefrontal Cortex
RT	Reaction Time
SAD	Separation Anxiety Disorder
SC	Superior Colliculus
SMA	Supplementary Motor Area
SoAD	Social Anxiety Disorder
SP	Specific Phobia
STAI	Spielberg's Trait Anxiety Inventory
TD	Typically Developing
WISC	Wechsler's Interview Scale -Children

Chapter 1 Introduction

1.1 Literature Review

1.1.1 Attention

Attention is a mental process that refers to the allocation of information processing resources either internally (in our mind/memory) or externally in our physical environment. Based on functional and anatomical levels, attention has been divided in three interrelated networks: alerting, orienting and executive network (Posner & Petersen, 1990; Raz & Buhle, 2006). Although some studies suggest that the three attentional networks have distinct functional and neural substrates (Fan, McCandliss, Sommer, Raz, & Posner, 2002; Mackie, Van Dam, & Fan, 2013), more recent studies have shown that attentional networks interact to co-ordinate cognitive control and behaviour (Fan et al., 2009; Xuan et al., 2016).

Alerting is defined as the ability to achieve and maintain an alert state in preparation to respond to incoming stimuli and involves activity in the locus coeruleus (LC), thalamus, frontal and parietal areas (Xuan et al., 2016). Alerting is divided in the phasic and the tonic modes of alertness. Phasic alertness refers to response readiness following a warning cue that precedes target presentation, whereas tonic alertness refers to sustained vigilance and arousal in the absence of any warning signal (Périn, Godefroy, Fall, & de Marco, 2010).

The orienting attentional network enables selection of information from multiple sensory stimuli and involves activation in the pulvinar, superior colliculus (SC), superior parietal and superior temporal lobes, and frontal eye fields (FEF) (Corbetta & Shulman, 2002; Fan, McCandliss, Fossella, Flombaum, & Posner, 2005; Thompson, Biscoe, & Sato, 2005). Orienting of attention can either be achieved exogenously (reflexively) due to the appearance of a target stimulus in the visual field or endogenously (voluntarily) when the allocation of information is directed by internal processes and is based on an individual's goals (Jonides, 1981). Orienting has traditionally been examined with Posner's visual cueing task (Posner, 1980), in which a target appears at a cued location (valid trials) or at an uncued location (invalid trials). A facilitation effect in the orienting function can be observed with faster response times and better accuracy during the valid trials than during

the invalid trials. This facilitation effect during the valid trials is commonly referred to as the *validity* or *cueing effect*.

The executive attention network is founded in cortical and sub-cortical loops (Takeuchi et al., 2013) and involves mainly activation in the lateral prefrontal cortex (PFC) and anterior cingulate cortex (ACC) (Matsumoto & Tanaka, 2004) and includes mechanisms of monitoring and conflict resolution in processes such as decision-making, planning, error detection and overcoming habitual actions (Botvinick, Braver, Barch, Carter, & Cohen, 2001). The executive attention network also allows individuals to control their feelings, thoughts and behavioural responses (Rueda, Posner, & Rothbart, 2005). The voluntary control processes that involve suppression of inappropriate attentional responses, thoughts, feelings and behaviours over more appropriate ones are often referred as self-regulation in child development and self-control in adults (Petersen & Posner, 2012). Self-regulation and self-control are linked to interference control and inhibitory control (suppression of prepotent, automatic responses), including the ability to control behaviour and emotions in order to avoid impulsiveness (i.e., via behavioural and oculomotor inhibition) (Adele Diamond, 2013). Generally, these processes have been empirically examined in a variety of experimental paradigms including the stop-signal task (Logan, 1994), Go/No-Go task (e.g. Cragg & Nation, 2008; Righi, Mecacci, & Viggiano, 2009), Stroop task (Stroop, 1935), flanker task (Eriksen & Eriksen, 1974) and the anti-saccade task (Hallett, 1978). These tasks involve the inhibition of a prepotent, automatic response, linked to interference control (*e.g.* Stroop task, flanker task) or inhibition of action (*e.g*. Go/No-Go task, stop signal task, anti- saccade task). The former refers to the ability of selectively focused attention on target- stimuli while supressing attention to distractor-stimuli (Stroop task), while the latter refers to either the cancellation of an already initiated response (stop-signal task) or the inhibition of automatic responses or tendencies to response to stimuli (Go/No-Go task).

Dysfunction and atypical development in brain regions associated with attentional control tasks have been well-documented in psychiatric and neurodevelopmental disorders including anxiety (Bishop, 2007) and ADHD (Casey et al., 2007; Tamm, Menon, & Reiss, 2006). Empirical evidence has shown that both anxiety and ADHD are characterised by inhibitory control deficits including difficulty suppressing prepotent responses (Oosterlaan & Sergeant, 1998; Pacheco-Unguetti, Acosta, Lupiáñez, Román, & Derakshan, 2012) and

reflexive saccades (Castellanos et al., 2000; Derakshan, Ansari, Hansard, Shoker, & Eysenck, 2009), or that result from impaired suppression of working memory information (*e.g*. worrisome thoughts in high anxious individuals) (Eysenck, Derakshan, Santos, & Calvo, 2007) and difficulties managing stimulus competition (Berggren & Derakshan, 2013).

In summary, attention is multifaceted construct responsible for the allocation of mental resources and prioritization of available information. There are different functional, distinct but interrelated attentional networks that underlie attention and that interact via complex cortical and subcortical relationships to achieve cognitive control (Fan et al., 2009). Research in development and psychopathology has increasingly focused on understanding the role of cognitive factors and attentional processes as potential mechanisms underpinning the onset and maintenance of internalising and externalising disorders (Casey & Riddle, 2012). Exploring the attentional mechanisms underlying psychiatric disorders will help in elucidating etiological factors linked to their onset, as well as in the development of new therapeutic treatments.

1.1.2 The Development of Attentional Control

Typical development of cognitive control is evident early in infancy (Johnson, 1995) and continues to develop until late adolescence (Luna, Garver, Urban, Lazar, & Sweeney, 2004). Its protracted emergence reflects myelination and synaptic pruning, processes that interact and support brain circuits responsible for the development of cognitive control (Casey & Riddle, 2012; Luna, 2009). Synaptic pruning reduces unnecessary neuronal connections to enhance efficient information processing and computational capacity across different brain circuitries that support higher–order cognitive control (Huttenlocher, 1990). Myelination increases the speed of neuronal transmission across long-distant brain regions responsible for top-down cognitive control (Giedd et al., 1999).

Executive functions (EFs) are evident from 7-to-12 month old (Diamond & Goldman-Rakic, 1989) and continue to develop through childhood and adolescence until individuals reach adult level of performance. Studies that have examined the development of cognitive processes using eye-movement tasks, found that processing speed and voluntary response inhibition continues to mature through adolescence (around the age of 15), where they reach adult-like control (Luna, Garver, Urban, Lazar, & Sweeney, 2004). Evidence from an anti-saccade task showed that children as young as 8 years old are able

to make inhibitory responses with the rate of correct inhibitory responses increasing with age (Luna et al., 2004; Velanova, Wheeler, & Luna, 2009). The anti-saccade task is an oculomotor test that requires participants to inhibit reflexive saccades to the appearance of a peripheral target, and instead make voluntary saccades away from that target (Hallett, 1978). Functional neuroimaging evidence in an anti-saccade task showed that similar prefrontal and motor control areas were engaged across age groups (children, adolescents and adults), with children having greater activation in these regions, suggesting increased effort to perform task goals (Velanova, Wheeler, & Luna, 2008). Furthermore, brain activity across the areas responsible for oculomotor control (including FEF, SMA/ preSMA, PPC and striatum) was greater for correct, compared to error anti-saccade trials, and was similar across age groups, supporting early development of core oculomotor control regions responsible for correct performance. However, sustained brain activity (as measured within trials in the same task), and error monitoring showed a more protracted development between adolescence and young adulthood (Velanova et al., 2009).

In summary cognitive control and, specifically, the ability to make inhibitory responses start to develop early in childhood, whereas the ability to monitor incorrect performance and adjust inhibitory control continuously throughout a task emerges later and continues to mature into adulthood.

1.1.3 Attentional Control and Emotional Processing

A large body of research has examined how attentional control can be modulated during the processing of emotionally charged stimuli, as well as how the experience of internal emotional states can affect cognitive control. Generally, the relationship between cognition and emotion has long been debated as either a push-pull system; in which executive control brain regions (such as dorsal –medial PFC, dorsolateral PFC) show hypoactivation in the presence of emotional stimuli while affective-related areas (such as amygdala and ventrolateral PFC) show hyperactivation (Dolcos & McCarthy, 2006). Alternatively, an interactive mechanism (also known as 'dual competition framework'; Pessoa, 2009) has been suggested, in which executive control brain regions are engaged during both cognitive and emotional processing (Pessoa, 2008).

For example, studies have shown a double dissociation between prefrontal cortices and limbic structures (such as amygdala) during attentional processes in the presence of

negative emotional stimuli (Drevets & Raichle, 1998). This double dissociation has been characterised by increased prefrontal activation and decreased amygdala activation during attentional demanding tasks and decreased prefrontal activity and increased amygdala activation has been positively related to the inhibition of high intensity negative affect in healthy individuals (Drevets & Raichle, 1998; Phan et al., 2005). However, later meta-analyses have shown that emotion and motivation can either enhance or impair behavioural performance depending on their interaction with EFs (Pessoa, 2009). Specifically, evidence from human and animal studies showed that both the ACC and mPFC contribute to emotional processing with dorsal ACC/mPFC regions involved in emotional appraisal and expression, whereas, the ventral ACC/mPFC regions are more involved in regulation of emotional interference (see review by Etkin, Egner, & Kalisch, 2011). Rather than differentiate cognitive function through dorsal –PFC and emotional function through ventral-PFC, these findings support the interactive system between cognitive control and emotion regulation processes that guide our behaviour.

It has been suggested that the presence of emotion during executive control tasks can either enhance or impair performance depending on the emotional intensity and the task relevance of the stimuli used (Pessoa, 2015). For example, it has been found that stimuli with low-emotional intensity such as happy and fearful faces, improved response inhibition in the stop-signal task by decreasing stop signal reaction time, whereas high-intensity stimuli (faces previously paired with a mild electrical shock) impaired response inhibition by increasing stop signal reaction time (Pessoa, Padmala, Kenzer, & Bauer, 2011). These results indicate that response inhibition is impaired due to the increased emotional potency of the task- relevant stimuli used, which require more processing resources to be recruited for successful inhibition. Conversely, it has been argued that when the emotional strength of the stimuli is small combined with task-irrelevant stimuli then the effect on cognitive and behavioural performance can also be small and vice versa (Pessoa, 2015). For example, greater interference was previously observed in trials involving anticipation of potential shock (i.e. threat trials) compared to neutral trials during a conflict-response task, suggesting that attentional allocation to task-irrelevant, high-arousing stimuli, created greater interference on task performance, compared to the trials that emotional interference was absent (Choi, Padmala, & Pessoa, 2012).

The interaction between emotion and cognition has also important implications in pathological conditions especially those associated with heighten emotional dysregulation including anxiety (Suveg & Zeman, 2004), depression (Fales et al., 2008), schizophrenia (Strauss et al., 2015), bipolar disorder (Green, Cahill, & Malhi, 2007), aggressive behaviours (Helmsen, Koglin, & Petermann, 2012) and ADHD (Graziano & Garcia, 2016). For example, anxiety has been associated with selective attentional bias towards threat–related stimuli (e.g., angry and fearful faces) and reduced inhibitory control in the presence of threat-related stimuli (review by Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van IJzendoorn, 2007). Childhood anxiety disorders have been associated with difficulties regulating negative emotional states such as worry, anger and sadness, and thus emphasising the challenges with emotion regulation strategies employed by anxious individuals (Suveg & Zeman, 2004). Interestingly, previous evidence showed that emotion dysregulation as measured through emotional expression of sadness and anger, awareness of personal feelings and emotions, as well as emotional management (e.g. rumination) predicted subsequent development of anxiety symptoms (McLaughlin, Hatzenbuehler, Mennin, & Nolen-Hoeksema, 2011).

In addition, emotion dysregulation has also been recognised in externalising disorders, such ADHD, that has been associated with challenges related to encoding of emotional expressions (Pelc, Kornreich, Foisy, & Dan, 2006) and processing social information (Semrud-Clikeman, 2010) and disrupted executive control in tasks that include emotionally-charged stimuli (Kochel, Leutgeb, & Schienle, 2013; Köchel, Leutgeb, & Schienle, 2012).

Overall, research on emotional processing and its influence on cognitive control is important to extend our understanding of the emotional and cognitive mechanisms underpinning psychopathology and especially conditions characterised by emotion dysregulation. Particular consideration also needs to be given to the impact of specific emotional stimuli (i.e. positive or negative) during different task manipulations (i.e. task-relevance or irrelevance of stimuli to task goals).

1.1.4 Developmental Psychopathology: Clinical and Cognitive profile of ADHD, Anxiety and co-morbid ADHD/Anxiety

1.1.4.1 **ADHD**. Attention deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder affecting around 5-7% of children and adolescents and 2.5-5 % of adults worldwide (American Psychiatric Association, 2013; Willcutt, 2012). Individuals with ADHD are characterized by symptoms of inattention and/or overactivity and impulsivity (APA, 2013). According to the Diagnostic and Statistical Manual for Mental Disorders (DSM-5; APA, 2013), the symptoms of ADHD are divided into three main presentations: predominantly inattentive presentation, predominantly hyperactive/impulsive presentation and combined presentation. Epidemiological research has shown that ADHD is more commonly diagnosed in boys than girls (Gershon, 2002), with an approximate ratio of around 2:1 (Willcutt, 2012).

Diagnostic evaluation for ADHD includes examination of symptom presentation and information of psychosocial impairment in family and school setting for young people, and family and workplace for adults (Banaschewski et al., 2017). However, recent propositions have pointed towards the use of dimensional measures for psychiatric disorders (Kraemer, Noda, & O'Hara, 2004) including ADHD, that is a complex and heterogeneous disorder (Heidbreder, 2015; Sonuga-Barke, 2016). Indeed, taxonomic studies find no evidence of taxa for ADHD in terms of a discontinuity in underlying neuro-biological and neuro-cognitive risk with increasing severity of symptoms (Haslam, Holland, & Kuppens, 2012; McLennan, 2016).

ADHD has been characterised as a heterogeneous disorder because of its clinical symptomatology, its neuropsychological functioning and the high comorbidity rates with other disorders (Castellanos, Sonuga-Barke, Milham, & Tannock, 2006; Wåhlstedt, Thorell, & Bohlin, 2009). It has also been associated with impairments in school performance and education; academic underachievement (Garner et al., 2013; Loe & Feldman, 2007) as well as with poor social (Nijmeijer et al., 2008) and family functioning (Johnston & Mash, 2001).

Both children and adults diagnosed with ADHD have high co-morbidity rates with both internalising (e.g., anxiety and depression) and externalising disorders (e.g., oppositional defiant disorder (ODD) and conduct disorder (CD)) (Biederman, 2005). For example, several studies have shown that up to 25% of children and up to 47% of adults

with ADHD also meet the diagnostic criteria for an anxiety disorder (Biederman, 2005; Jarrett & Ollendick, 2008; Kessler et al., 2006). Other highly comorbid disorders among adults with ADHD include depressive disorder, substance use disorder and personality disorders (Kessler et al., 2006; Sobanski, 2006). In addition, up to 30-40% of children and adolescents with ADHD meet the criteria for CD and ODD (Maughan, Rowe, Messer, Goodman, & Meltzer, 2004; Newcorn et al., 2001). The overlapping symptomatology and the high comorbidity rates with other disorders cause challenges to diagnosis and treatment (Katzman, Bilkey, Chokka, Fallu, & Klassen, 2017).

Considering the neurocognitive heterogeneity in ADHD, empirical studies have shown impairments with sustained attention (Marchetta, Hurks, De Sonneville, Krabbendam, & Jolles, 2007) and reaction time performance; with slower and more variable responding for children with ADHD than typically developing peers (Andreou et al., 2007). Further evidence has shown that ADHD is associated with impairments in EF such as inhibitory control (Bitsakou, Psychogiou, Thompson, & Sonuga-Barke, 2008), verbal and spatial working memory components (Martinussen, Hayden, Hogg-Johnson, & Tannock, 2005), planning (Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005) and shifting functions (Halleland, Haavik, & Lundervold, 2012). A growing body of literature has also reported dysfunction in reward (Haenlein & Caul, 1987) and motivational processes (Volkow et al., 2011), as well as impaired delayed gratification where individuals with ADHD show preference for small immediate rewards over larger delayed rewards (Marx, Hacker, Yu, Cortese, & Sonuga-Barke, 2018; Sonuga-Barke, 2003). The complexity and heterogeneity of the disorder suggests that not all individuals are characterised by a common single cognitive deficit, but instead some individuals show persistent deficits in specific cognitive domains while some others do not (Nigg, Willcutt, Doyle, & Sonuga-Barke, 2005; Salum et al., 2014; Sonuga-Barke, 2002, 2005).

1.1.4.2 **Executive control in ADHD**. Research has shown that EF deficits constitute an important aspect of the underlying neuropsychological mechanisms of ADHD (Willcutt et al., 2005), with response inhibition being considered as a central deficit (Barkley, 1997). For example, Barkley (1997) proposed a unifying theory of ADHD in which he suggested that response inhibition is the primary deficit in ADHD that potentially leads to other secondary deficits including self-regulation of affect and motivation and difficulties processing information in verbal and non-verbal working memory. Related studies have

examined response inhibition as a primary deficit in ADHD and support has mainly come from the stop-signal task (Logan, Cowan, & Davis, 1984) and the Go/No-Go task (Rubia, Smith, & Taylor, 2007). For both tasks, participants are required to respond to the Go cues, typically with a motor response (e.g. button press) and withhold a response in the presence of the No-Go cues (i.e., auditory or visual). In the stop signal task the stop signal is presented after the presentation of the Go cue and therefore a cancellation of an initiated response is required, whereas in the Go/No-Go task, response inhibition requires withholding of a prepared, but not necessarily initiated response. An inhibitory deficit is reflected in longer stop signal reaction times (SSRTs; the time elapsed from the presentation of the No-Go cue until the participants cancel their initiated response) as well as from the high error rates during stop signal trials in the stop signal task and the increased number of commission errors (response during the presence of a No-Go signal) in the Go/No-Go (Oosterlaan, Logan, & Sergeant, 1998; Quay, 1997; Schachar, Mota, Logan, Tannock, & Klim, 2000).

Accumulating evidence both from the stop-signal task and the Go/No-Go task have shown that children and adults with ADHD are characterised by an increased number of commission errors (Rubia, Smith, & Taylor, 2007), slower and variable mean reaction times during the Go cues (Epstein et al., 2011; Klein, Wendling, Huettner, Ruder, & Peper, 2006) as well as higher errors of omission (absence of responses on Go trials) (Bluschke, Roessner, & Beste, 2016), when compared to healthy controls. Errors of commission have been traditionally associated with symptoms of impulsivity and reduced inhibitory control in the ADHD population, whereas the errors of omission along with the slow and variable response times have been attributed to symptoms of inattention and difficulty to sustain attention to meet task goals (Bezdjian, Baker, Lozano, & Raine, 2009). Furthermore, a number of significant moderators including, younger age, more dimensional diagnostic approaches (instead of discrete categorical diagnostic assessment criteria), dynamic stop-signal paradigms (i.e., when the timing of stop signal presentation dynamically changes – increases or decreases- based on the individual's response), increased number of experimental trials and visuospatial (rather than phonological) Go stimuli on the stop signal task have shown to contribute to the large effect sizes for mean reaction time differences between children with and without ADHD (Alderson, Rapport, & Kofler, 2007).

In addition, cognitive deficits in ADHD have been found to be persistent under several task manipulations. For example, Durston et al. (2003) manipulated the task difficulty in the Go/No-Go task to examine behavioural interference susceptibility between children with and without ADHD. The task difficulty was increased by increasing the number of Go trials preceding the No-Go trials. Typically developing children showed increased susceptibility to interference with increased difficulty, whereas children with ADHD showed increased susceptibility to interference regardless of the task difficulty (with either one or more than one Go trials preceding the No-Go trial). These behavioural results have been accompanied by decreased fronto-striatal activation for children with ADHD compared to those without ADHD. Similarly, in a separate study (Epstein et al., 2011), event rate and reward manipulations were applied in a battery of neuropsychological tests including the Go/No-Go and the stop- signal tasks. The event rate involved three different timings of target presentation (1.5s, 3.5s and 5.5s) within each task and the reward manipulations involved earning points for either the first or the second half of each task. Children with ADHD showed increased reaction time variability regardless of the event rate and reward manipulations that were targeted to modify arousal state.

Evidence from neuroimaging studies on attentional control in ADHD have shown decreased activity and volumes in anterior cingulate and parietal cortices, as well as prefrontal cortex, basal ganglia, and the cerebellum (Castellanos et al., 1996, 2001; Durston et al., 2003; Tamm et al., 2006). Electrophysiological studies focusing on response inhibition and conflict monitoring via the No-Go P3 and N2 amplitudes, respectively have shown reduced No-Go P3 amplitudes that were associated with increased rate of false alarms on stop-signal task and thus poor response inhibition (Smith, Johnstone, & Barry, 2008) and reduced No-Go N2 amplitudes; reflecting reduced conflict monitoring (monitoring of inhibition outcome) (Falkenstein, Hoormann, & Hohnsbein, 1999; Liotti, Pliszka, Higgins, Perez, & Semrud-Clikeman, 2010; Pliszka, Liotti, & Woldorff, 2000). Furthermore, impairments with response inhibition in ADHD are usually preceded by reduced parietal Cue-P3 amplitude; that reflects attentional allocation and the subsequent reduced central contingent negative variation (CNV); an index of response preparation (Banaschewski et al., 2003, 2004; Valko et al., 2009). These attentional and inhibitory control deficits have been found in both children and adolescents (Banaschewski et al., 2004; Doehnert, Brandeis, Imhof, Drechsler, & Steinhausen, 2010) as well as in adults with ADHD (McLoughlin et al., 2009).

Overall, ADHD has been associated with impairments in different domains of cognitive control. Impaired response inhibition does not, however, represent a single deficit in ADHD. Theoretical models and empirical evidence have supported cognitive heterogeneity in ADHD and have promoted a double dissociation between the so called 'cool' EF deficits (that encompass 'pure', top-down EF deficits such as inhibitory control, set shifting and working memory) (Zelazo & Müller, 2002) versus 'hot', bottom- up, motivational EF deficits (associated also with impaired signalling of delayed rewards) (Castellanos et al., 2006; Nigg et al., 2005; Sonuga-Barke, 2005). Indeed, neuroimaging findings on ADHD, have shown both an association between EF deficits with prefrontal-striatal circuits (Dickstein, Bannon, Castellanos, & Milham, 2006) and dysregulation of affect and motivation with frontolimbic circuits (Matthews, Nigg, & Fair, 2014; Nigg & Casey, 2005).

1.1.4.3 **Emotion regulation in ADHD.** Emotion dysregulation is a core feature in individuals with ADHD (Shaw, Stringaris, Nigg, & Leibenluft, 2014) that can negatively affect different aspects in daily functioning (Anastopoulos et al., 2011). Challenges with emotion regulation, defined as emotional reaction to the social norms; emotional lability (i.e. unexpected mood shifts) and attentional allocation to emotional stimuli have been reported to characterise between 25–45% of children and 30–70% of adults with ADHD (Shaw et al., 2014). There is evidence showing that individuals with ADHD are particularly sensitive to frustration (Paraskevi Bitsakou, Antrop, Wiersema, & Sonuga-Barke, 2006), show disruption in attentional performance in the presence of emotional stimuli (e.g. Villemonteix et al., 2017) and have problems recognising emotional expression in faces (Pelc et al., 2006). Studies have shown that children with ADHD show difficulties recognising facial emotional expressions such as anger, sadness, disgust and surprise (Pelc et al., 2006; Yuill & Lyon, 2007) with particular difficulties in decoding threat-related emotions (Williams et al., 2008).

Difficulties with cognitive control and executive dysfunction in ADHD are thought to underpin emotion dysregulation (Graziano & Garcia, 2016; Van Cauwenberge, Sonuga-Barke, Hoppenbrouwers, Van Leeuwen, & Wiersema, 2015). For example, Kochel, Leutgeb, and Schienle (2013) examined inhibitory control using an emotional Go/No-Go task in children with ADHD and healthy controls, and found increased commission errors in the presence of angry and sad faces compared to happy and neutral faces. In this study,

participants had to inhibit a button response in the presence of a No-Go facial expression (happy, angry or sad) at a time. Children with ADHD also exhibited longer RTs in the presence of angry faces and quicker RTs in the presence of happy faces. Recognition of facial affect was also examined in this study and results showed that children with ADHD had more difficulties recognising angry and sad faces than happy and neutral ones. In addition, event- related potentials (ERPs) indicated reduced P3 amplitude during inhibition of angry cues, which further suggested inhibitory control difficulties specific to angry faces. In support, electrophysiological data were previously examined in an adult male sample with ADHD on a similar task (Köchel et al., 2012), and results showed reduced right parietal late positivity during response inhibition of negative facial emotions (angry, sad and fearful faces) compared to happy and neutral faces.

Further evidence come from studies on attentional orienting in response to socially relevant cue, such as eye-gazes. For example, children and adolescents with ADHD showed difficulty to perceive and respond to eye-gaze cues, suggesting challenges with social interaction and communication (e.g. Marotta et al., 2014). Related studies have shown that difficulties with emotion regulation (i.e. an inability to resist in emotional distractors during an executive control task) have an independent contribution to the differences found between children with ADHD and typically developing controls (e.g. Sjöwall, Roth, Lindqvist, & Thorell, 2013). However, another study that examined emotional interference between the two groups using an emotional n-back task, found no differences between the two groups specific to emotion regulation (Van Cauwenberge et al., 2015).

Overall, evidence on emotion regulation suggests that individuals with ADHD show difficulties recognising and processing emotional stimuli and for some studies, these difficulties were independent of executive function deficits. However, other studies have shown that emotion dysregulation can exacerbate cognitive control difficulties. The discrepancy in the findings may be attributed to different task manipulations, task measurements and the choice of emotionally relevant stimuli (i.e. social stimuli such as faces or emotional words).

1.1.4.4 **Anxiety.** The DSM-5 outlines several anxiety disorders that are most likely to develop during childhood (e.g. separation anxiety disorder, selective mutism and specific phobia), adolescence (e.g. social anxiety disorder) or adulthood (e.g. panic disorder, generalized anxiety disorder, agoraphobia) (APA, 2013). Anxiety disorders are among the most common clinical disorders for children and adolescents, with prevalence rates between 2% to 24% (Merikangas et al., 2010) and a median age of onset around 11 years and. The lifetime prevalence estimates for anxiety disorders varies between 14.5% - 33.7% across different epidemiological studies (Bandelow & Michaelis, 2015) .

Individuals with anxiety disorders are characterised by excessive worry, fear and share common cognitive features (i.e., worrisome thoughts), physiological arousal and behavioural avoidance (APA, 2013). In contrast to ADHD, research consistently shows that females are more commonly diagnosed with anxiety disorders compared to males with an approximate 2:1 ratio (Kessler et al., 1994; McLean, Asnaani, Litz, & Hofmann, 2011). Similar to ADHD, anxiety disorders are also associated with difficulties in psychosocial functioning (Ginsburg, Greca, & Silverman, 1998; Strahan, 2003) and poor engagement with school; lowered attendance and academic underachievement (Mazzone et al., 2007; Van Ameringen, Mancini, & Farvolden, 2003; Waite & Creswell, 2014).

Apart from pathological anxiety disorders, dimensional measures of trait and state anxiety might characterise typical populations. State anxiety refers to situational interpretation of threat and trait anxiety has been considered as a personality construct related a general and chronic anticipation of threat (Pacheco-Unguetti, Acosta, Callejas, & Lupiáñez, 2010; Spielberger, 2013). Studies have shown distinctive neurocognitive mechanisms underlying the trait and state anxiety dimensions. For example, empirical evidence on the efficiency across the three different attentional networks (alerting, orienting and executive control) using the Attention Network Test (ANT; (Callejas, Lupiáñez, & Tudela (2004), showed that in the absence of emotional stimuli, trait anxiety interfered more with executive control network, indicating that it is closely related to top-down mechanisms, whereas state-anxiety interfered more with alerting and orienting network, suggesting a closer relationship with stimulus-driven processes (Pacheco-Unguetti et al., 2010).

There is also extensive empirical research on trait anxiety and cognitive performance, as trait anxiety disrupts the balance between goal-directed and stimulus-

driven attentional processes (Eysenck & Calvo, 1992; ACT: Eysenck et al., 2007). It has been proposed that the imbalance between these two systems enhances difficulties with inhibition of irrelevant information and shifting attention between different tasks, as well challenges updating information form working memory. Furthermore, evidence related with attentional control in anxiety have focused on selective attention towards threat–related information (reviews by Bar-Haim et al., 2007; Bishop, 2007); mechanisms associated with the onset and maintenance of anxiety. Research evidence show that the attentional biases associated with trait anxiety do not differ from those observed in clinical anxiety (Bar-Haim et al., 2007; Dudeney, Sharpe, & Hunt, 2015), therefore the mechanisms related to emotional processing and attentional biases in trait anxiety are also important in understanding effects related to clinical anxiety.

1.1.4.5 **Executive control in anxiety.** Theories have been developed to explain the effects of anxiety on cognitive performance and associated mechanisms. Earlier, processing efficiency theory (Eysenck & Calvo, 1992), proposed that anxiety impairs the efficiency of the central executive component of Baddeley's working memory model (Baddeley, 1986) that controls functions such as attentional focus, inhibitory response and shifting of attention. The theory also emphasises the distinction between performance effectiveness (i.e. quality of performance) and processing efficiency (i.e. the relationship between effectiveness and the resources/effort allocated to achieve task goals). According to this theory, processing efficiency is impaired by anxiety more than performance effectiveness, as anxious individuals might increase their effort to meet their task goals. Based on these assumptions, later, attentional control theory (ACT) (Eysenck et al., 2007) emphasises that impairments in efficiency, particularly in tasks involving inhibition and shifting functions. Both inhibition and shifting contribute to the control of the central executive and involve increased attentional control in order to supress distracting and irrelevant stimuli, as well as to shift attention between tasks and focus on relevant stimuli. ACT also suggests that anxiety impairs top-down attentional control and increases allocation of attention to threat-related stimuli (bottom-up attentional system). Therefore, a conflict between top-down/goal-directed and bottom-up/stimulus-driven systems is evident. This imbalance between the two systems is argued to lead to impairments in efficiency of inhibition and shifting function to become greater in the presence of threat-related stimuli.

Increasing evidence also come from eye-movement paradigms showing slower saccade latencies during inhibition of eye- movements in anti-saccade paradigms (Derakshan, Ansari, Hansard, Shoker, & Eysenck, 2009), as well as increased pupil dilations on tasks involved high cognitive demands, thus reflecting increased effort (Hepsomali, Hadwin, Liversedge, & Garner, 2017). Electrophysiological evidence from anti-saccade paradigms showed decreased fronto-central and central negative activity for high anxious individuals in the period preceded the onset of the target, that participants were required to inhibit during correct anti-saccade trials, thus highlighting further challenges with response preparation (Ansari & Derakshan, 2011). Furthermore, evidence from functional neuroimaging studies showed reduced activation in the dorsolateral PFC for high anxious individuals, during trials involving increased cognitive conflict (i.e., presence of an incongruent letter distractor) and low perceptual load ((i.e., identifying a target letter among six identical letters), whereas the opposite was found for low anxious individuals, under the same condition. These findings further highlight the association between anxiety and reduced recruitment of prefrontal attentional resources during task completion (Bishop, 2009). However, other neuroimaging studies showed increased prefrontal activation during cognitively demanding tasks in anxious individuals (i.e. Basten, Stelzel, & Fiebach, 2011). In this study, Basten et al., (2011) examined interference control in a colour Stroop task and found stronger dorsolateral PFC activation but reduced functional connectivity among several regions involved in attentional control including dorsal ACC, the dorsolateral PFC, during incongruent trials. The authors suggested that the results represent reduced neural processing efficiency for anxious individuals and recruitment of extra attentional resources to compensate for interference control.

In has been suggested that efficiency (i.e. the amount of effort or resources used) of cognitive processing in anxious individuals can be modulated by the motivational and emotional levels engaged during attentional control (Berggren & Derakshan, 2013). More precisely, tasks that involve, for example, decreased motivational levels may lead to poor recruitment of attentional control resources and thus poor performance for individuals high in anxiety, whereas tasks that involve increased motivational and emotional demands can lead to better performance because individuals can recruit more attentional recourses to meet task goals (Eysenck & Derakshan, 2011). Similarly, apart from the role of motivation, cognitive load and general task demands also appear to modulate cognitive efficiency in anxiety (Berggren & Derakshan, 2013). In other words, cognitive demanding

tasks and clear task goals can engage additional recruitment of compensatory strategies so that anxious individuals can maintain task goals and perform in a similar way as that of low anxious individuals.

1.1.4.6 **Attentional control and emotional processing in anxiety.** Further theoretical frameworks have been developed to explain the association between anxiety and attentional biases towards emotional stimuli and social threat (e.g. Beck & Clark, 1997; Eysenck, Derakshan, Santos, & Calvo, 2007; Mathews & Mackintosh, 1998; Mogg & Bradley, 1998). Empirical studies on attentional biases to threat–related stimuli in anxious individuals have confirmed a number of effects, including facilitated attentional orienting towards threatening stimuli, especially angry and fearful faces, compared to happy or neutral faces (Fox, 2002; Koster, Verschuere, Crombez, & Van Damme, 2005), difficulty disengaging attention from threating stimuli (review by Dudeney, Sharpe, & Hunt, 2015; Koster, Crombez, Verschuere, & De Houwer, 2004; Richards, Benson, & Hadwin, 2012) as well as attentional avoidance (i.e., from negative scenes; Koster, Crombez, Verschuere, Van Damme, & Wiersema, 2006; Mogg, Bradley, Miles, & Dixon, 2004).

It has been suggested that the different attentional biases found across studies can be explained in terms of the type of information processing required (i.e. whether automatic or strategic) in relation to the cognitive mechanisms of attentional control and strategies of emotion regulation (i.e., emotional experience and expression). In their review, Cisler and Koster (2010), for example, suggested that automatic facilitation towards threatening information is mediated by neural amygdala activation, whereas processes involved attentional control and strategic information processes guided by prefrontal circuitries could explain avoidance and disengagement hypotheses. However, the variation in methodological manipulations including the wide range of paradigms used and cognitive processes involved, cognitive load manipulations, and the nature and levels of anxiety being measured, have meant that the utility of models, to precisely capture attentional biases in anxiety, difficult.

Studies using spatial cueing paradigms and attentional orienting from threating stimuli (e.g. Fox, Russo, Bowles, & Dutton, 2001; Mogg, Holmes, Garner, & Bradley, 2008) supported the hypothesis of delayed attentional disengagement from threatening stimuli. In this paradigm, anxious individuals demonstrated slower RTs when they oriented attention away from invalid (i.e. where cues draw attention to the opposite direction of the

target) threatening cues (i.e. angry faces versus happy and neutral faces) (e.g. Fox et al., 2001; Fox et al., 2002). In addition to disengagement difficulties, some studies showed attentional facilitation towards highly threatening images compared to moderate threatening ones, for anxious individuals at brief presentation durations (i.e. 100ms), whereas at longer durations (i.e. 500ms) this was not found (e.g. Koster et al., 2006). Further evidence showed that following this quick and enhanced attentional facilitation towards negative stimuli, high anxious individuals show subsequent attentional avoidance (i.e. directing attention away) from those stimuli (Koster, Crombez, Verschuere, Van Damme, & Wiersema, 2006; Sagliano, Trojano, Amoriello, Migliozzi, & D'Olimpio, 2014), thus supporting the vigilance- avoidance hypothesis (Mogg et al., 2004; Mogg & Bradley, 1998). Attentional facilitation has also been demonstrated in attentional-probe paradigms (e.g. Seefeldt, Krämer, Tuschen-Caffier, & Heinrichs, 2014) and visual search tasks (e.g. Becker, 2009; Waszczuk, Brown, Eley, & Lester, 2015). In the case of dot-probe tasks, high anxious individuals show faster attentional orienting in the location previously presented with threatening (i.e. angry faces) image than at the location previously occupied by a neutral face (Klumpp & Amir, 2009; MacLeod, Mathews, & Tata, 1986). Similarly, in the case of visual search, high anxious individuals show faster initial fixations to negative targets compared to neutral ones (e.g. Rinck, Reinecke, Ellwart, Heuer, & Becker, 2005).

Recent theoretical accounts propose that differences in the expression of attentional biases in anxiety may vary as a function of the severity of different stressors. In turn, this variation influencing the balance between goal-driven/top-down and stimulus-driven/bottom-up processes, so that top-down processes maintain attention on threat or bias attention away from threat, whereas motivational processes are related to threat evaluation and detection, thus biasing attention towards threat (Mogg & Bradley, 2016). Nevertheless, there is a general agreement that selective attention in anxiety is associated with an automatic processing of threatening information in the environment, but due to a number of methodological variations and inconsistencies across empirical research, the exact neurocognitive mechanisms underpinning this association remains unclear.

1.1.4.7 **Co-morbidity between ADHD and anxiety**. Comorbidity between ADHD and anxiety is approximately 25-40% among clinically referred children (Jarrett & Ollendick, 2008; Jarrett, Wolff, & Ollendick, 2007). Despite the high comorbidity rates, only a few studies have aimed to understand cognitive characteristics in individuals with ADHD and

anxiety. While anxiety is characterised by internalizing (i.e., excessive worry and tension) and ADHD by externalizing (i.e*.,* outward expression of distress) symptoms, the two disorders share symptoms including restlessness, sleep problems, increased distractibility and difficulty concentrating (Jarrett & Ollendick, 2008). Some researchers have found that the presence of anxiety in ADHD is associated with challenges in the school setting (Hammerness et al., 2010) including increased rejection and less acceptance by peers (Lee, Falk, & Aguirre, 2012) as well as poorer social skills (Graziano, Geffken, & McNamara, 2011).

Early theoretical frameworks examined the link between biological and environmental factors that contribute to the behaviour of ADHD and anxiety. For example, the functions of two brain systems; the Behavioural Inhibition System (BIS) and the Behavioural Activation System (BAS) have been associated with both internalising symptoms and anxiety (Gray, 1982) as well as with externalising symptoms such as ADHD and conduct disorder (Quay, 1997). The BIS controls the inhibition of an ongoing behaviour, the increase in vigilance, arousal and passive avoidant behaviour, related to stimuli sensitive to punishment and non- reward. The BAS has been associated with approach and goal-motivated behaviour, positive feelings and it is sensitive to stimuli of reward, novelty and non-punishment. The two systems were initially introduced in the reinforcement sensitivity theory (RST; Gray, 1982); a neuropsychological model of anxiety. According to this model, increased activity in the BIS and reduced activity in the BAS have been linked to internalising symptoms and feelings of anxiety, whereas the reversed has been associated with the expression of externalising problems such as ADHD (Quay, 1988, 1997), where individuals are engaged in an impulsive and reward-seeking behaviour characterised by lack of inhibition.

Empirical research has examined the impact of anxiety in ADHD with regard to symptom presentation and neurocognitive functioning but there is no strong evidence supporting either an additive or a compensatory effect. With regard to the neuropsychological profile, an additive effect would suggest that the cognitive control processes that underlie each disorder would be exacerbated for individuals characterised by both ADHD and anxiety symptoms, whereas a compensatory effect would suggest that the attentional mechanisms of each disorder would be attenuated in the case of comorbidity.

With regard to the symptom profile, there is not consistent evidence to suggest that increase levels of anxiety alter the clinical symptomatology in ADHD (Tannock, 2009). More specifically, some evidence shows that there is no difference on the number of anxiety and depression symptoms and rates of anxiety disorders diagnosis between children with comorbid ADHD/anxiety and anxiety only (Jarrett, Wolff, Davis, Cowart, & Ollendick, 2012). Evidence also suggests that children with ADHD and children with comorbid ADHD/anxiety show similar levels of ADHD-related symptoms, ADHD symptom severity and impairment levels (review by Jarrett, 2013). In addition, another study showed similar attentional deficits between ADHD children with and without comorbid anxiety, whereas anxious children showed fewer attentional difficulties (Jarrett et al., 2012).

Considering the cognitive profile, some studies have shown that the presence of anxiety in ADHD is associated with increased verbal and visual working memory difficulties (Bloemsma et al., 2013; Tannock, Ickowicz, & Schachar, 1995) and slower reaction time in response to external cues and motor/self-generated speed assessment (Bloemsma et al., 2013). However, some studies showed that the presence of anxiety might reduce impulsivity in ADHD, such that children with comorbid ADHD/anxiety show better response inhibition (review by Schatz & Rostain, 2006). This finding has also been supported in studies that have employed the stop-signal paradigm (e.g. Manassis, Tannock, & Barbosa, 2000), whereas other studies showed that presence of anxiety in ADHD was not associated with differences in response inhibition during a Go/No-Go task (e.g. Vloet, Konrad, Herpertz-Dahlmann, Polier, & Günther, 2010). It has been suggested that in situations where task demands are high, anxious individuals show enhanced response inhibition (Oosterlaan, Logan, & Sergeant, 1998).

Furthermore, some studies showed better sustained and selective attention for children with comorbid ADHD/anxiety compared with ADHD-only, but worse performance than typically developing children (Rodríguez, González-Castro, García, Núñez, & Alvarez, 2014; Vloet et al., 2010). Nevertheless, it is important to mention that the majority of the studies that have examined comorbidity in ADHD and anxiety did not compare performance separately for symptoms of ADHD and anxiety or clinical groups (i.e. ADHD-only and anxiety –only), as well as with healthy controls.

Understanding the neurocognitive processes underlie both ADHD and anxiety will have important implications for the prognosis and treatment of these conditions, especially

in the case of a potentially distinctive cognitive profile that might characterise comorbidity that could inform the development of novel treatment interventions. This area needs further investigation. Inconsistent and limited findings also come from studies on treatment response in ADHD and anxiety. For example, some studies suggest that ADHD/anxiety comorbidity shows differential response to pharmacological and psychological treatment than either disorder alone. More specifically, some studies showed that children with co-morbid ADHD/anxiety showed less robust response to psychostimulant medication than children with ADHD only (Blouin, Maddeaux, Stanley Firestone, & van Stralen, 2010; Pliszka, 1989;Tannock et al., 1995). However, more recent studies showed that that psychostimulants reduced anxiety symptoms in both children (Abikoff et al., 2005; Golubchik, Sever, & Weizman, 2014) and adults (Bloch et al., 2017) with ADHD. In addition, data from the Multimodal Treatment Study of Children with ADHD (MTA) showed that children with co-morbid ADHD/anxiety were more responsive to medication management, behavioural treatment and combined treatment than children with ADHD-only (Jensen et al., 2001). The majority of the studies that examined treatment response in ADHD have not considered comorbidities with other disorders and therefore, it is not yet clear whether comorbid ADHD/anxiety should be treated as a separate condition (Ollendick, Jarrett, Grills-Taquechel, Hovey, & Wolff, 2008).

Overall, the evidence regarding the mechanisms underpinning the co-occurrence of anxiety and ADHD, and their effects, is unclear and this is probably due to the different diagnostic and assessment criteria used across studies, the differences in the sample characteristics (i.e., a lack of control for other comorbidities) as well as methodological variations. The high comorbidity rate, the symptom overlap and heterogeneity in ADHD and anxiety, complicates diagnosis that allows the development and implementation of targeted and effective treatment protocols. Therefore, a better understanding of the cognitive mechanisms linked to comorbidity between ADHD and anxiety will lead in better diagnostic and classification standards and it will help in elucidating etiological factors linked to the evaluation of existing as well as the development of new therapeutic treatments.

Chapter 2 Orientation to the Current Thesis

2.1 Thesis Motivation

Difficulties with cognitive control and emotion regulation are two core features associated with both ADHD and anxiety. Empirical evidence has highlighted attentional and inhibitory control deficits in individuals with ADHD and anxiety, with further evidence supporting challenges in emotional processing (e.g. Hwang et al., 2015). Research has found that individuals with ADHD show difficulties supressing automatic, prepotent responses in order to execute those that are more consistent with immediate goals. In addition, ADHD has been linked to reduced accuracy in attentional control tasks (review by Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005). ADHD has also been associated with poor emotional functioning, including attentional challenges associated with orienting towards and shifting attention away from emotional stimuli (Shaw et al., 2014), and difficulty recognising emotional facial expressions (i.e. Pelc et al., 2006), particularly threat-related facial expressions (e.g. Kochel et al., 2013; Köchel et al., 2012).

Increased anxiety has been linked to difficulty with cognitive control and increased attentional biases towards threat-related information (review by Cisler & Koster, 2010). Enhanced sensitivity towards threat involves faster engagement towards threat-related stimuli, difficulty to disengage attention from threat (Koster et al., 2004), increased hypervigilance (broadening of attention) in the presence of threat (Richards, Benson, Donnelly, & Hadwin, 2014) and avoidance (Koster et al., 2006). Despite the increased comorbidity levels between ADHD and anxiety (Biederman, 2005; Jarrett & Ollendick, 2008), research on the neuropsychological mechanisms underlie the ADHD/anxiety comorbidity is still very limited.

In addition, few studies have examined EFs in both ADHD and anxiety while incorporating emotionally charged stimuli, and evidence is mainly concentrated on behavioural paradigms. Eye-movement measurements provide effective measures of on-line cognitive processing and thus provide more sensitive information about the underpinning neurocognitive mechanisms that characterise psychopathology (Bittencourt et al., 2013; Hutton, 2008), and developmental change (Luna, Velanova, & Geier, 2008). Saccadic eye-movements are defined as quick, ballistic movements of the eyes that are

made to bring central, high acuity to the visual target (Walker, Walker, Husain, & Kennard, 2000). For example, eye-movement measurements can provide more accurate and sensitive measurement of cognitive processing on task performance, compared with simple manual (i.e., button press) reaction times and accuracy.

2.2 Project Scope and Thesis Structure

The present programme of research examined how symptoms of ADHD and anxiety associated with attentional processes related to inhibition of eye-movement responses, sustained attention and attentional orienting in the presence of emotional and non-emotional stimuli. Given the similar but distinctive profiles of these disorders, we aimed to understand whether increased symptoms of anxiety in ADHD, have an effect on attentional processes especially in the face of emotionally charged stimuli and whether the effect is a compensatory, additive effect or synergistic effect.

Moreover, evidence from taxonomic studies support that psychiatric disorders and psychopathology more broadly should be examined dimensionally rather than categorically (Hyman, 2010; Shear, Bjelland, Beesdo, Gloster, & Wittchen, 2007). In support, empirical studies that adapted dimensional measures in ADHD and anxiety support a continuity in the underlying neuro-cognitive risk with increasing severity of symptoms (Haslam et al., 2012; McLennan, 2016). Therefore, statistical analyses across all the empirical studies in the current research have used symptom count dimensions of ADHD and anxiety.

Following the General Introduction (Chapter 1) and the Orientation to the Current Thesis (Chapter 2), the empirical section of the thesis is divided across four empirical chapters (Chapters 3-6) and a General Discussion (Chapter 7). We initially considered non-clinical symptoms of ADHD and trait anxiety on attentional control and orienting, across children/adolescents and adults to also explore potential developmental differences. We then, extended this work on a bigger sample of both community and clinically-referred children and adolescents across a wider ADHD and anxiety symptom spectrum. For the latter, anxiety levels were measured through symptoms of Generalised Anxiety Disorder (GAD).

Specifically, Chapter 3 examined the interactive effects of ADHD symptoms and trait anxiety as well as potential developmental differences between typically developing

children/adolescents and healthy adults, on attentional control in an eye-movement version of the Go/No-Go task. Chapter 4 employed the same Go/No-Go task and expanded findings from Chapter 3 to consider the interactive effects of ADHD symptoms and GAD symptoms in a mixed sample (clinical and community) of children and adolescents. Chapter 5 examined the interactive effects of ADHD symptoms and trait anxiety (in the same sample used in Chapter 3) on attentional orienting processes using an eye-movement version of the Spatial Cueing paradigm. Subsequently, Chapter 6, expanded on the findings from Chapter 5, to explore attentional orienting and the interactive effects of ADHD and GAD symptoms (in the same sample used in Chapter 4) in the Spatial Cueing Paradigm.

2.2.1 Recruitment and Changes in Thesis Focus

The current programme of research was initially designed to compare attentional performance on four groups of children and adolescents, including those with ADHD, anxiety, comorbid ADHD/anxiety and typically developing children and adolescents based on the criteria of the Diagnostic Interview Schedule for Children (DISC-IV) (Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000). Following a number of challenges with the recruitment processes and the limited number of young people meeting the diagnostic criteria for each categorical group, the focus of the current thesis was adjusted to examine the dimensions of Generalised Anxiety Disorder (GAD) and ADHD symptoms of the total sample of children and adolescents that were recruited as part of this thesis that consisted of both clinical cases of ADHD and anxiety and typically developing children and adolescents. GAD was previously reported as the most prevalent anxiety disorder among children and adolescents with ADHD (Souza, Pinheiro, & Mattos, 2005) and has directly been associated with high levels of trait anxiety when compared to other anxiety disorders that general worry might not be a central characteristic, such Panic Disorder (Hirsch, Mathews, Lequertier, Perman, & Hayes, 2013). Therefore, this thesis is partly focused on comparing the effects of GAD and ADHD symptoms on attentional performance in young people.

Furthermore, an additional study was added to this thesis to examine the potential developmental differences between typically developing children/adolescents and healthy adults, in relation to symptoms of ADHD and trait anxiety on attentional performance. This study involved the recruitment of a healthy adult sample that was compared with the

typically developing children and adolescents recruited as part of the initial research protocol.

2.2.2 Experimental Paradigms

We designed two eye-movement experimental paradigms to consider sustained attention and inhibitory control (Go/No-Go paradigm) as well as attentional orienting and emotional interference control (Central Spatial Cueing paradigm). For both paradigms we considered saccadic eye-movement measurements (latency and accuracy) as outcome measures. Eye movements allow us to distinguish between different manifestations of attentional impairments including an inability to suppress reflexive saccades (failure to maintain fixation) in response to a centrally presented stimulus as well as difficulties disengaging from those stimuli.

2.2.3 Go/No-Go Task

The Go/No-Go task has been widely used to examine EC and particularly response inhibition (Simmonds, Pekar, & Mostofsky, 2008). In this paradigm, participants are required to respond to the presentation of Go trials (typically presented in the majority of the trials), usually with a manual response. Traditionally, prepotent, automatic responses in the Go/No-Go task are built up during the presentation of the Go trials and response inhibition is measured during the presentation of the No-Go trials, in which participants are asked to withhold their response. The number of commission errors (response during the presence of a No-Go stimulus) is an indication of response inhibition.

Here, we adapted an eye-movement version of the Go/No-Go task using centrally presented non-face stimuli (coloured squares) and facial emotional stimuli (happy and angry faces). Both stimuli were used as Go and No-Go cues across experimental blocks. Each experimental block consisted of 200 trials (80% Go trials and 20% No-Go trials presented in a random order). In this task, participants were asked to move their eyes/disengage attention from a centrally presented face/non-face cue to a target on Go trials and to inhibit eye-movements on No-Go trials. The paradigm provides two indices of sustained attention on Go trials as measured by: (1) saccade onset latency (time taken to make a correct eye-movement towards a target (i.e., on correct “hits”)), and (2) task effectiveness or performance as indicated by attentional lapses (as measured by the

absence of a saccade to the target when one is required, i.e., an omission error). This paradigm provides also a measure of (3) inhibitory control via the number of incorrect saccades (commission errors) to a target on No-Go trials. For a more detailed description of the task, see Chapter 3.

2.2.4 Central Spatial Cueing Task

In the classical spatial cueing paradigm (Posner, 1980), participants are presented with a central cue which is either congruent (valid cue), incongruent (invalid cue) or neutral (no-cue) with the location of a peripheral target. In this paradigm, individuals are required to detect an eccentric target quickly and accurately without being distracted by the direction of a central cue distractor. Posner (1980) reported that RTs to respond to the target were facilitated by valid cues and delayed by invalid cues. That is, *cueing* or *validity effect* is typically produced, which involves faster and more accurate responses on trials that central cues point towards the location of the eccentric target (i.e. valid trials) and slower and less accurate responses on trials that cues point to the opposite direction of target location (i.e. invalid trials).

Here, we adapted this paradigm using emotional facial expressions (angry, happy, fearful and neutral) with three possible eye positions (direct gaze, averted left, averted right) and non-emotional stimuli (arrow pointing left, arrow pointing right and horizontal bar). We measured saccadic attentional orienting through (1) saccade onset latency (time taken to make an eye-movement towards the target) and (2) saccade accuracy via saccadic directional errors (saccades made away from the target) during valid, invalid and no-cue trials. For a more detailed description of this task, see Chapter 5.

2.3 Aims and Hypotheses

The aim of the current programme of research is to develop a theoretical framework that defines and explores the cognitive phenotype linked to comorbid ADHD and anxiety. Particularly, we aimed to understand whether the co-occurrence of ADHD and anxiety symptoms, (1) have an effect on attentional processes, (2) whether the effect is a compensatory, additive effect or synergistic effect and (3) whether this effect is moderated by the emotional valence of the stimuli used.

Considering the impact of increased ADHD and anxiety symptoms, we predicted that the ADHD symptoms would be associated with disrupted EC and attentional processing across non-emotional and emotional tasks. In addition, we predicted that individuals with elevated ADHD symptoms would demonstrate difficulties in effectively using social emotional cues (e.g. Marotta et al., 2014, 2017), resulting in slower saccade latencies of the centrally presented emotional faces compared to the non-emotional cues of the Go/No-Go task. In the same task, increased symptoms of ADHD are expected to be associated with increased number of omission and commission errors in the presence of emotional facial expressions compared to the non-emotional stimuli. For the spatial cueing task, increased symptoms of ADHD are anticipated to be associated with less effective use of eye-gaze cues, especially in the presence of emotional facial expressions compared to direct gazes and symbolic/arrow stimuli (Marx et al., 2011; Villemonteix et al., 2017). This is expected to manifest with increased saccade latency and errors for valid compared to invalid eye-gaze cues.

In comparison, we predicted that increased anxiety levels would be associated with reduced attentional control (Eysenck et al., 2007). We expected evidence of an attentional bias to threat in anxious individuals, leading to attentional disengagement difficulties from centrally presented presence of task-relevant threat (vs. non-threat). Disengagement difficulties in high anxiety, are expected to be associated with improved task performance on inhibitory control in threat contexts. That is, for centrally presented threatening stimuli in the Go/No-Go task, increased anxiety levels are expected to be associated with increased saccade latencies, increased omissions and fewer commission errors. We also anticipated anxiety to be associated with impaired performance in the presence of task-irrelevant threat (vs. non-threat) (i.e., increased distractibility as previously evidenced by Fox, Mathews, Calder, & Yiend (2007)). Based on attentional biases previously reported for threat-related, social stimuli (such as angry and fearful faces) in anxiety (Fox, Mathews, Calder, & Yiend, 2007), we predicted that angry faces with direct gaze will be associated with slower saccade latencies and increased saccadic errors compared to other emotional facial expressions, for individuals with elevated anxiety symptoms. We also predicted that elevated anxiety symptoms will be associated with enhanced cueing effect (i.e., faster saccade latencies and fewer saccadic errors for valid relative to invalid trials) for averted gaze of fearful faces compared to happy, angry and neutral averted eye-gaze cues.

Considering elevated symptoms of both anxiety and ADHD, we predicted that together will be associated with increased levels of inattention for the Go/No-Go task, manifested with slower saccade latencies and increased number of omission errors, compared with the elevated anxiety symptoms -only and the elevated ADHD-symptoms-only, suggesting an additive effect. However, we hypothesized that the anxiety experienced by individuals with ADHD symptoms will lower behaviour that reflect impulsivity (Schatz & Rostain, 2006) (i.e., inhibitory control measured by the number of commission errors), thus we expected anxiety-related attentional processing to prevail in the presence of threat for individuals high in both ADHD and anxiety symptoms, leading to an attentional bias to threat (as manifested with fewer commission errors in the Go/No-Go task). For the spatial cueing task, we anticipated that attentional biases towards threatening stimuli associated with elevated anxiety symptoms to prevailed when both ADHD and anxiety symptoms are elevated. This is expected to manifest with improved cueing effect and thus faster saccade latencies and fewer saccadic errors for valid relative to invalid trials, for averted gaze of fearful faces compared to happy, angry and neutral gaze cues as well as slower saccade latencies and increased saccadic errors for direct gaze of angry faces compared to other emotional facial expressions. Further detail on individual hypotheses of each experimental task are provided in each empirical chapter of this thesis.

2.4 Ethics Procedures and Approvals

The recruitment process for young people required both internal (ERGO; Ethics and Research Governance Online) and NHS (IRAS; Integrated Research Application System) ethics application procedures. Ethical approvals were obtained from the Research Ethics Committee of the Psychology Academic Unit at the University of Southampton and the South Central Berkshire Research –B Ethics Committee.

To refine and enhance recruitment strategies for young people, the current project underwent two NHS Ethics Amendments. *Figure 2.1* illustrates the stages of the recruitment processes. Based on the initial study protocol, typically developing children and adolescents were recruited via study adverts and posters placed around the Southampton city, whereas identification and recruitment of children and adolescents with a research (and potentially clinical) diagnosis with ADHD and/or anxiety was undertaken through the South Hampshire ADHD Register (SHARe). The SHARe is a clinical database for

children and adolescents with ADHD living in the South Hampshire area and has been a source of well-characterised patients for a number of neuroscience studies conducted in the department of Psychology at the University of Southampton. The SHARe steering group committee approved the recruitment process (through the SHARe database), for the current study.

Due to limited sample size, the recruitment process was refined with the first ethics amendment and involved recruitment of young people with or without a clinical diagnosis of ADHD and anxiety via study adverts and posters that were distributed in primary and secondary schools in the Hampshire, and other places and charity organisations including the Child and Adolescent Mental Health Services (CAMHS). For the second ethics amendment we aimed to identify children and adolescents with ADHD using the self-report Strengths and Difficulties Questionnaire (SDQ; (Goodman, Ford, Simmons, Gatward, & Meltzer, 2000)) and children and adolescents with anxiety using the short version of the self-report Spence Children's Anxiety Scale (SCAS; Spence, 1997, 1998), that were distributed in local primary and secondary schools.

2.4.1 SHARe Recruitment

Children and adolescents recruited via the SHARe database fall into a number of inclusion criteria that were provided in the SHARe protocol[1] and thus also applied in the current study. Children and adolescents were eligible for inclusion in the current study if they: were currently on the SHARe register and their parent(s)/legal guardian(s) provided Level 6 consent (e.g. permission to be contacted about future research linked to SHARe), were aged between 8 and 15 years old, met a Diagnostic Interview Schedule for Children (DISC-IV) diagnosis for ADHD (including all subtypes) and/or the following Anxiety

[1] Young people were recruited into SHARe via clinician referral or self-referral. A number of exclusion criteria were provided in the SHARe protocol: 1) The child has a paediatric condition which could lead to major neurological disorders and/or children with severe learning delay (e.g. Autism, Down Syndrome, Smith-Magenis syndrome, Cri du Chat Syndrome, Lesch-Nyhan Syndrome, or children with mucopolysaccharide disorders); 2) The parent and child are not able to speak and understand English. Children and their parents recruited into SHARe can consent to participate in all or some of the elements of SHARe ranging from consent to basic identifiable information to be included on the SHARe research register (Level 1), to providing permission to be contacted about future research linked to SHARe (Level 6). The current project falls within the area of new research linked to SHARe at Level 6. The SHARe protocol required new NHS ethics permission for all new research projects and access to SHARe participants required approval from the SHARe steering group committee approval, and the appropriate NHS R&D departments and University of Southampton which were all obtained.

disorders: Specific Phobia, Social Phobia, Separation Anxiety Disorder, Panic Disorder, Generalised Anxiety Disorder, did not meet a diagnosis for Conduct Disorder (CD) (the diagnosis for Oppositional Defiant Disorder- ODD, was not excluded from the ADHD group but it was excluded from the Anxiety group), did not take any long-acting stimulant medication (in case of short-acting psychostimulants participants were required not to take their medication 48 hours prior to testing); gave written assent to participate and had a parent or legal guardian to provide written consent to participate.

2.4.2 School Recruitment

Children and adolescents that were recruited from local primary and secondary schools in Hampshire, were screened for symptoms of inattention and/ or hyperactivity using the self-report Strengths and Difficulties Questionnaire (SDQ; (Goodman et al., 2000)) and for the generalised anxiety symptoms using a short version of the self-report Spence Children's Anxiety Scale (SCAS; Spence, 1997, 1998). This screening procedure was carried out to facilitate identification of potential participants for our experimental groups. Following the screening procedure, the eligible participants were then invited to take part in the main project.

As part of the main project, participants were assessed for ADHD (all subtypes) and anxiety disorders (Specific Phobia, Social Phobia, Separation Anxiety Disorder, Panic Disorder, Generalised Anxiety Disorder) according to the DISC-IV (Shaffer et al., 2000).

The comorbidities with other disorders were determined according to the *Conners Comprehensive Behaviour Rating Scale-Parent* (CBRS-P; Conners, 2008), which is a parent report that includes subscales for conduct disorder (CD), oppositional defiant disorder (ODD), major depressive episode, manic episode and Autism Spectrum Disorder (ASD). Participants with co-morbid CD and ASD were excluded from the study. A potential diagnosis of ODD was included for young people meeting the DISC-IV criteria for ADHD but not for those who met the DISC-IV criteria for anxiety disorder(s). Likewise potential diagnosis of depression was included for young people meeting the DISC-IV criteria for but anxiety disorder(s) but not for those who met the DISC-IV criteria for ADHD.

Finally, children that were eligible for inclusion into the typically developing control group did not meet the criteria for ADHD and anxiety disorders according to the DISC-IV,

did not meet the criteria (for both *T*-scores and symptom count) for other mental health disorders according to CBRS parent report (including ADHD, anxiety disorders, depressive disorder, ODD, CD and ASD), did not take any psychoactive medication and had no severe learning difficulties or special educational needs. Finally, inclusion criteria required that the participants were able to speak and understand English, the children gave written assent to participate and had a parent or legal guardian who provided written consent to participate.

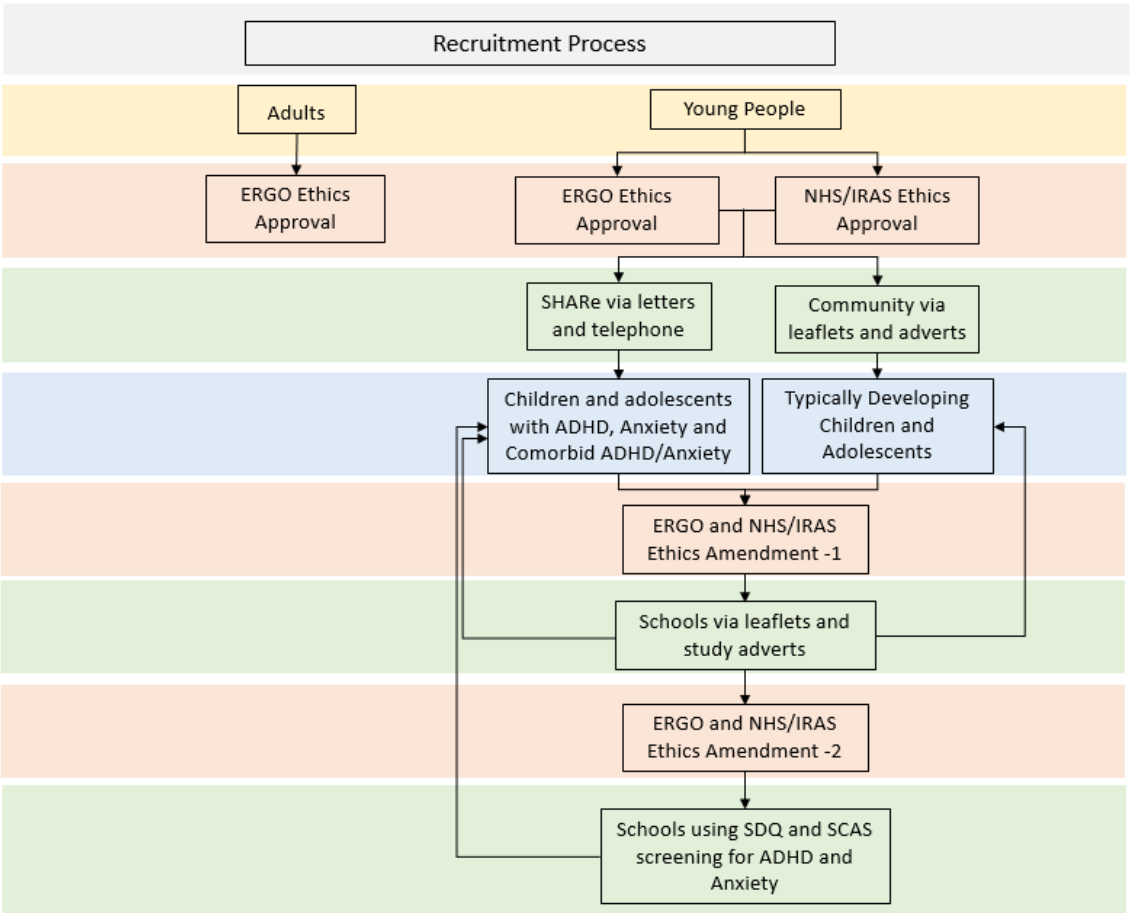

Figure 2.1: Recruitment process for young people and adults.

2.5 General Testing Procedure

2.5.1 Young people

Following the school screening procedure and participants' identification from the SHARe database, participants were invited to take part to the main project.

Parents of eligible participants were informed and invited to take part in the study either via email (electronic invitation letters), or via invitation letters (Appendix A1) that were sent by post. Parents who were willing and agreed to take part in the study completed a short demographics form for the young person (Appendix A2). Upon receiving replies, we contacted the parents to arrange a convenient time for the testing session with both parents and young people that was carried out at the Psychology Academic Unit at the University of Southampton.

The testing session began with the researcher explaining the purpose and procedure of the study and providing separate information sheets for the parent (Appendix A3i) and the young person (Appendix A3ii). The young person was then asked to sign a written assent form (Appendix A4) and the parent/guardian was asked to sign a written consent form (Appendix A5). Once assent and consent were obtained, the young person completed the experimental part of the study in a separate room (i.e., eye-tracking laboratory) with one researcher and the parent was asked to complete the parent-report measures (i.e., questionnaires and a short diagnostic interview) in a separate room with another researcher. Prior to starting the first experimental task, the young person was familiarised with the laboratory and the eye tracking equipment. Throughout the testing session, the young person was encouraged to take short breaks. The experimental paradigms were designed in a way that allowed participants to also take breaks within the blocks of experimental trials. After completing the first experimental task, the young people took a longer break (around 10 minutes) during which was offered snacks and refreshments. This break was followed by the second experimental task. Young people completed the self-report questionnaires after completing the eye-tracking paradigms and spent an additional 20 – 30 - minute short assessment on cognitive ability (i.e., two short test that estimated IQ) before the end of the testing session.

Upon completion, both young people and parents/guardians were debriefed (both verbally and by giving written debriefing statements) (Appendix 6i & Appendix 6ii) and were reimbursed with the total of £25 (young person was offered £10 and parents were offered £15) for their participation and the time spent for the study. In total, the testing session took approximately 3 hours.

2.5.2 Adults

The young adults were recruited via study adverts placed in different places in the Southampton city including the University of Southampton- Highfield campus. The adult study was also advertised online in different social networks (e.g. Facebook and Twitter) and via University's eFolio site to give the opportunity to Psychology students to take part and receive course credits in return.

Young adults that responded to the study adverts were asked to complete a short demographics form (Appendix B1). Following that, at the beginning of the testing session, participants were provided with the study's information sheet (Appendix B2) to read and ask questions. The researcher explained the procedure of the study and provided further information and instructions about the tasks. Participants who agreed to take part, signed a consent form (Appendix B3).

In total, the testing session lasted approximately 1 hour and 30 minutes. Between the first and the second experimental paradigm, participants took a 10-minute break. Following completion of the eye-tracking tasks, participants completed the self-report questionnaires.

At the end of the study, participants were debriefed (Appendix B4) and reimbursed with the total of £10 for their participation and the time spent. Undergraduate psychology students that took part in the study were offered the option to receive course credits in return.

Chapter 3 The Interaction between Anxiety and ADHD Symptoms on Emotional Go/No-Go Performance: An Eye-Tracking Study of Adults and Young People

3.1 Introduction

Attention Deficit/Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder affecting around 5% of children and 2.5 % of adults (American Psychiatric Association; APA, 2013). Theoretical models emphasise a causal role for executive dysfunction in the pathophysiology of ADHD (Willcutt et al., 2005) - with inhibitory control (IC) deficits at their central (Barkley, 1997). The effects of poor IC are also thought to underpin emotion dysregulation (Graziano & Garcia, 2016; Shaw, Stringaris, Nigg, & Leibenluft, 2014; Van Cauwenberge, Sonuga-Barke, Hoppenbrouwers, Van Leeuwen, & Wiersema, 2015). Studies, have shown that IC is further disrupted in ADHD when tasks include emotionally-charged stimuli (i.e. threat-related social cues), in both childhood (Kochel et al., 2013) and adulthood (Köchel et al., 2012). There is also evidence that individuals with ADHD have difficulties recognising emotional expression in faces (e.g. Pelc, Kornreich, Foisy, & Dan, 2006).

ADHD has been associated with several comorbid disorders and it can be difficult to disentangle the psychological challenges associated with ADHD from those which underpin other disorders. For example, ADHD frequently co-occurs with elevated symptoms of anxiety (Jarrett & Ollendick, 2008), that are often associated with disrupted patterns of attention to emotional stimuli, especially in the context of perceived or actual threat. Increased anxiety has been associated with attentional control difficulties that are most evident in the context of threat-related information (review by see Richards, Benson, Donnelly, & Hadwin, 2014). These cognitive biases have been demonstrated with respect to enhanced attention towards, as well as difficulty disengaging attention from, threatening stimuli (such as angry faces and negative words) (e.g., Pavlou, Benson, & Hadwin, 2016). In addition, anxious individuals also show more effort in the completion of complex cognitive

tasks, as reflected in increased pupillary responding (Hepsomali et al., 2017). This set of findings raises the question of whether effects of emotional content of stimuli presented during executive control tasks in ADHD are most evident in the context of co-occurring symptoms of anxiety.

A number of studies have explored the impact of comorbid anxiety and ADHD during cognitive and emotional processing, and have found inconsistent results. Some studies have shown that children with comorbid ADHD and anxiety (vs. ADHD-only) showed improved response inhibition (e.g. Rodríguez, González-Castro, García, Núñez, & Alvarez, 2014; for a review, see Schatz & Rostain, 2006), suggesting that anxiety ameliorates impulsivity in ADHD. Other studies have not found a moderating effect of comorbid anxiety on inhibitory difficulties in ADHD (e.g. Vloet, Konrad, Herpertz-Dahlmann, Polier, & Günther, 2010). Further research has suggested that comorbid anxiety may exacerbate the difficulties in inhibitory and emotional control in ADHD (Sørensen, Plessen, Nicholas, & Lundervold, 2011). One study, for example, showed that the combination of adult ADHD and anxiety symptoms increased difficulties of self-regulation of emotions, compared with elevated symptoms of either ADHD-only or anxiety-only (Jarrett, 2016).

Increasingly studies in development and psychopathology support a conceptualisation of both ADHD and anxiety as continuous dimensions rather than discrete categories. For instance, taxonomic studies find no evidence of taxa for ADHD or anxiety in terms of a discontinuity in underlying neuro-cognitive risk with increasing severity of symptoms (Haslam, Holland, & Kuppens, 2012; McLennan, 2016). This view is supported by recent studies that have found difficulties with executive processes in individuals who reported elevated symptoms of trait anxiety (Derakshan, Smyth, & Eysenck, 2009) and inattention/hyperactivity symptoms (Salum et al., 2014; Shaw et al., 2011), who do not show a clinical symptom profile.

The current study aimed to examine the interactive effects of subclinical symptoms of ADHD and anxiety on sustained attention and response inhibition using emotional (happy and angry faces) and non-emotional stimuli (coloured squares) in an eye-tracking version of a Go/No-Go task. In this task, automatic responses are built up during the presentation of Go trials (80% of the trials) and response inhibition is measured during the presentation of the No-Go trials (20% of the trials), in which participants are asked to withhold an eye-movement response. A high proportion of eye-movement (saccadic)

commission errors (response during the presence of a No-Go stimulus) is an indication of poor response inhibition.

Measuring saccadic eye-movements in behavioural paradigms provides an effective on-line measure of attentional processes that is sensitive to the neurocognitive mechanisms that underpin psychopathology (Hutton, 2008) and development more broadly (Luna et al., 2008). We utilised an eye-movement Go/No-Go paradigm with angry and happy faces, and non-face cues. Participants were asked to move their eyes from a centrally presented face/ non-face cue to a target on Go trials and to inhibit eye-movements on No-Go trials. This paradigm provides two indices of sustained attention on Go trials as measured by; (1) "hits" - saccade onset latency (time taken to make a correct eye-movement towards a target), and (2) task effectiveness or performance as indicated by attentional lapses (as measured by the absence of a saccade to the target when one is required, i.e., an omission error). In addition, it provides a measure of (3) inhibitory control via the number of incorrect saccades (commission errors) to a target on No-Go trials.

We predicted that more ADHD symptoms would be associated with poorer sustained attention as reflected in reduced monitoring of task goals (i.e., slower saccade latencies and more attentional lapses through increased omission errors), and more commission errors, indicating difficulty suppressing reflexive saccades. We anticipated that these effects would be exacerbated in the presence of emotional stimuli compared to non-face stimuli. We anticipated that higher levels of anxiety would be associated with disrupted processing of angry face (vs happy and non-face) stimuli. Following previous research with young children (Pavlou et al., 2016) and adults (Richards et al., 2012), we predicted that elevated anxiety would be manifest in the current task as slower disengagement, that is, slower saccade onset latencies on angry and fewer saccadic commission errors in response to centrally presented angry faces. Finally, we expected that the increased anxiety symptoms would exacerbate the predicted negative effects of ADHD symptoms as evidenced by reduced attentional control, resulting in slower saccade latencies, and increased omission and fewer commission errors specifically for angry face (compared with happy and non-face) stimuli.

We explored these effects in both children/adolescents and adults, in order to examine broad developmental differences. We anticipated that performance would be reflected with better accuracy (i.e. fewer saccade errors) and efficiency (i.e. faster saccade

onset latency) for adults compared to children. We further investigated the impact of individual differences of ADHD and anxiety symptoms on attentional performance in these age groups.

3.2 Method

3.2.1 Participants

Fifty-four participants, including 27 adults (12 males) aged between 18-34 years old (*M*= 21.44, *SD*= 3.93) and 27 children and adolescents (12 males) aged between 8-15 years old (*M*= 11.84, *SD*= 2.22) participated in the current study. The young people were recruited from primary and secondary schools in the South of England, as well as from study adverts distributed in the local community. Because the focus of our study was on cognitive effects in the non-clinical range we excluded individuals if they met criteria for ADHD (inattention and hyperactivity/impulsivity subscales) or anxiety disorders (specific phobia, social phobia, separation anxiety disorder, panic disorder, generalised anxiety disorder) scales of the Diagnostic Interview Schedule for Children (DISC-IV) (Shaffer et al., 2000). We also excluded participants who met the criteria for depressive disorder, oppositional defiant disorder (ODD) and conduct disorder (CD) on the parent-reported Conners Comprehensive Behaviour Rating Scale (CBRS-P; Conners, 2008; across both symptom count and standardised *T*- score[2]). Exclusion criteria also included taking psychoactive medication or the recognition of severe learning difficulties or special educational needs. Young people were also required to be able to speak and understand English; the young person gave written assent to participate and a parent or legal guardian had to be present to provide written consent to participate.

Adult volunteers were recruited via a study advert that was placed around the university campus. Adults undertook a short structured mini neuropsychiatric interview based on the DSM-IV criteria (Mini International Neuropsychiatric Interview, MINI; Sheehan et al., 1998). They were excluded if they had a diagnosis of depression, mania, anxiety,

[2] Results of the DSM-5 Symptom Counts contribute to consideration of whether a particular DSM-5 diagnosis might be appropriate. A *T*-score for each DSM-5 diagnosis facilitates comparison of individual's symptoms with his or her peers. When both scores are average or below (i.e., DSM-5 Symptom Count probably not met, DSM-5 *T*-score < 65): it is unlikely that the diagnosis is currently present (Conners, 2008).

obsessive compulsive disorder, and post-traumatic stress disorder, addiction to drugs and alcohol and strong family history of mood disorder, including panic disorder or panic attacks) (Appendix D).

3.2.2 Questionnaires

3.2.2.1 **Trait anxiety.** We used the State - Trait Anxiety Inventory for children (STAIC; Spielberger, Edwards, Montuori, & Lushene, 1973) and adults (STAI; Spielberger, Gorssuch, Lushene, Vagg, & Jacobs, 1983) to measure symptoms of trait anxiety. The trait anxiety scale includes 20 items and each item is rated on a 3- point Likert response scale for the child version and a 4-point Likert scale for adults. The scale is based on how individuals 'usually feel' (e.g., "I worry too much… hardly ever/sometimes/often" (child scale) or "almost never /sometimes/often/almost always" (adult scale)). Child participant trait anxiety scores ranged from 23-46 (*M*= 32.90, *SD*= 7.17). Adult participants' trait anxiety scores ranged from 20-48 (*M* = 33.85, *SD*=6.58).

3.2.2.2 **ADHD Symptoms.** Child and adolescent symptoms of ADHD were measured using the parent-reported Diagnostic Interview Scale for Children – Fourth Edition (DISC-IV; Shaffer et al., 2000). This is a structured diagnostic interview designed to assess psychiatric disorders (based on the Diagnostic and Statistical Manual; DSM-IV) and symptoms in children and adolescents aged 6–17 years old. Most of the questions are recorded and coded as 'yes' (1), 'no' (0), not applicable (8), or 'don't know' (9). The DISC has moderate to good diagnostic reliability and validity for the parent interview (Schwab-Stone et al., 1996). In particular, test-retest diagnostic reliability of the DISC- parent report for ADHD is .60 for and for any anxiety disorder .56 (κ- statistics). The ADHD-Combined symptom count for young people was taken from both the ADHD- Inattention and Hyperactivity/Impulsivity scales of the DISC- IV, with total symptom count ranging from 0-20, (*M*= 6.10, *SD*= 6.24).

We used the Current Symptoms Scale (CSS) (Barkley & Murphy, 2006) to measure ADHD symptoms in adults (Appendix D1). The scale consists of two parts. The participant filled out the first part and an additional informant known to the participant (i.e., friend or relative), filled out the second one[3], in order to reduce self-report bias (Appendix D2). The

[3] The total score of inattention and hyperactivity symptoms did not differ between adults' self-reports (*M*=1.26, *SD*= 1.43) and 'other' informants (*M*= .69, *SD*= 1.27), *t* (48) = 1.45, *p*=.16.

scale is based on DSM-IV criteria for ADHD and measures the number of symptoms experienced in the last 6 months. It includes 18 items and where each asks the participant to endorse a symptom via a four-point Likert scale (never or rarely (0), sometimes (1), often (2), and, very often (3)). Items are equally divided into inattentive and hyperactive/ impulsive subscales. The items rated as "often" or "more" counted as an indicator of DSM-IV symptom counts, with total symptom count ranging from 0-5 (*M*=1.26, *SD*= 1.43).

3.2.3 Experimental Go/No-Go Task.

The Go/No-Go task was comprised of four blocks including two blocks using non-face stimuli (blue and orange squares that were used both as Go and No-Go cues across the two blocks) and two blocks using facial emotional stimuli (happy and angry faces that were used both as Go and No-Go cues across the two blocks). Emotional face stimuli were modelled by two (one male and one female) individuals from the NimStim face set (Tottenham et al., 2009). In order to reduce variations between images and prevent unwanted effects of chromatic and differently-illuminated images, image pre-processing was carried out using Adobe Photoshop CS6. Images were converted to grayscale, face size was rescaled by keeping a constant aspect ratio for each face, head orientations were adjusted to horizontal plane and centring, hair was removed and intensity was adjusted to obtain images with stable contrast and illumination. Each experimental block consisted of 200 trials (80% Go trials and 20% No-Go trials presented in a random order), with each block preceded by 15 practice trials.

In each trial sequence, participants saw an initial presentation of a black fixation cross that appeared at the centre of the screen (2000ms). This fixation cross was followed by either a Go or a No-Go cue, along with an eccentric target (a white square) that was presented at 8 degrees eccentricity either to the left or to the right of fixation (600ms). Participants were instructed to look at the central fixation cross until they saw a Go cue, during which they had to move their eyes towards the eccentric white square as quickly as possible and then bring their eyes back to the centre after the central fixation cross appeared back again. Participants were also asked to maintain central fixation in the presence of No-Go cues. A randomised inter-trial interval (ITI) of 1500 – 2500ms was

added between the initial fixation cross and the target screen. An automatic recalibration was added every 25 trials throughout each block. This was added to minimise data loss due to the continuous presentation of the trial sequences[4]. The coloured squares subtended 3 x 3 degrees of visual angle, whereas the targets (white squares that subtended 1.5 x 1.5 degrees of visual angle). The faces subtended 4.2 degrees horizontally and 6.5 degrees vertically (see *Figure 3.1).*

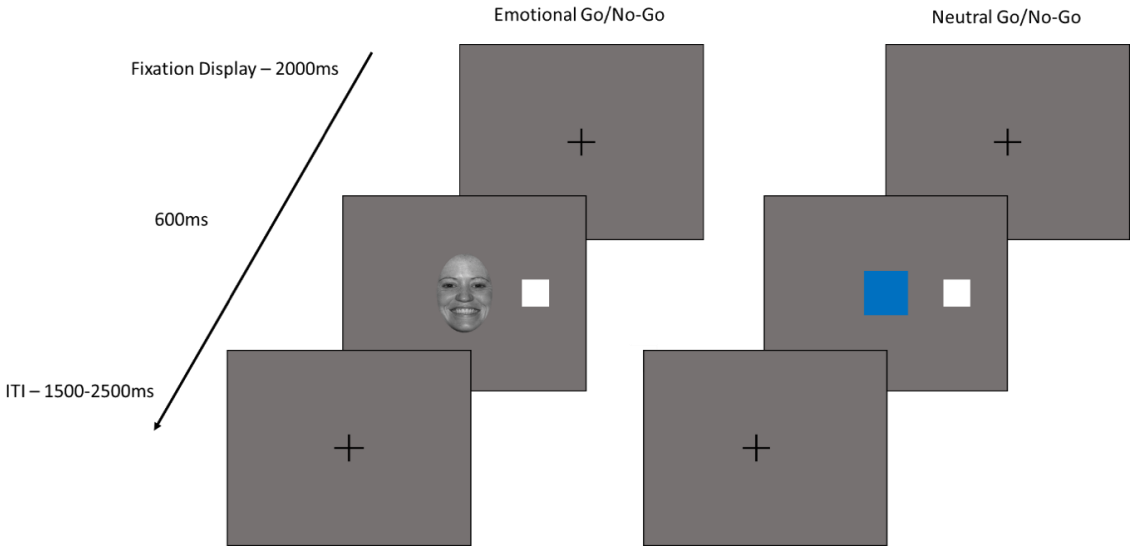

Figure 3.1: Trial Sequence of the Go/No-Go Task.

Eye movements were recorded using an EyeLink 1000 Plus Desk Mount eye tracking system (SR Research Ltd) housed in a department research laboratory. The experiments were created and implemented using Experiment Builder software (SR Research Ltd.) and presented on a 23-inch monitor (1920 x 1080 resolution). Although viewing was binocular, the vertical and horizontal movements of the right eye were sampled monocularly at a rate of 1000 Hz. The eye-movement data were extracted in the form of saccadic reports the EyeLink Data Viewer software (SR Research Ltd).

[4] Data visualisation indicated noise in the first trial following automatic recalibration and thus it was removed from the dataset for all the participants.

3.2.4 Data Analyses

We performed linear mixed effects models (LMMs) using the lmer function from the lme4 package (Bates, Mächler, Bolker, & Walker, 2015) in R (R, Core Team, 2017) to examine the effects of anxiety and ADHD symptoms and Age (children vs adults) on saccade onset latency in the presence of emotional and non-emotional stimuli. The saccade onset latency was measured on correct Go trials ("hits") and it was defined as the time elapsed from the presentation of the Go cue until the first correct saccade landed to the interest area of the target. Saccade latencies below 80ms were excluded from the dataset. Data were screened for the assumptions of normality, linearity, homogeneity. The data loss due to outliers was approximately 1%.

We performed generalised linear mixed effects models (gLMMs) using the glmer function from the lme4 package in R to examine the effects of anxiety and ADHD symptoms in saccadic accuracy (saccadic error rates; binary variables: 1 = error, 0 = no error) in the presence of emotional and non-emotional stimuli between children and adults. Saccadic accuracy was considered in relation to (1) omission errors, defined as the number of misses (absence of a saccade) in the presence of a Go cue, and (2) commission errors, defined as the number of incorrect saccades executed in the presence of a No-Go cue. Analyses revealed a very low number of saccadic omission errors, therefore the results are only reported for "hit" saccade latency and saccadic commission errors (Table 3.2).

We used the participants' age group (adults vs. children), the cue condition (happy face, angry face and non-face stimuli), anxiety and ADHD symptoms (continuous variables) as fixed factors across all the analyses. We considered two- and three-way interactions between ADHD symptoms, anxiety symptoms and cue condition.

The random effect of the models resolves the non-independence that stems from having multiple responses by the same participant and multiple trials across each experimental block. Therefore, Participant and Trial number were used as random factors in a maximal random structure including random intercepts and slopes for the cue condition. The models were trimmed in a top-down method until convergence (Barr, Levy, Scheepers, & Tily, 2013). In this case, the random structure of the first model was reduced first by removing the correlations, then the interactions between the slopes and then the random effects explaining the least variance until the maximal converging model was identified. The random structure of the final model for used for "hit" saccade latency

included different intercepts and slopes for the cue condition for the random effect of participants and trials. The final model used for commission errors included different intercepts and slopes for the cue condition for the random effect of participants trials. The saccade latencies for "hits" were log transformed to ensure normal distribution. The continuous variables were mean centred to reduce collinearity between main effects and interactions.

3.3 Results

3.3.1 Sample characteristics

There was no main effect of gender on the outcome measures ("hit" saccade latency (β = -.05, SE = .04, t = -1.45, p= .15), omission errors (β = -.48, SE = .32, z = -1.50, p= .13), commission errors (β = .24, SE = .19, z = 1.27, p= .20)).

3.3.2 Effects of Age and Emotional Content of Cues

There was a significant effect of age, with adults having faster "hit" saccade latencies and fewer saccadic commission errors than children (Tables 3.1, 3.2 and 3.3). There was also a significant effect of cue condition on both outcomes. Non-face cues elicited faster "hit" saccade latencies and more commission errors, compared to face cues. Angry faces elicited slower "hit" saccade latencies than happy faces (i.e., slower stimulus disengagement). No difference in saccadic commission error rates were observed for this contrast. There were no interactions between age and condition.

Table 3.1*: Mean Saccade Latency (ms) during Hits in Children and Adults for each Cue Condition.*

	Saccade Latency		
	Children	Adults	All
Cue Condition			
Square	360.07 (134.81)	304.01 (104.63)	331.18 (123.42
Happy face	448.67 (146.76)	392.08 (118.97)	419.74 (136.24)
Angry face	467.43 (154.13)	398.78 (116.33)	431.83 (140.11)

Note: Standard deviations shown in the parentheses

Table 3.2: *Mean Saccade Accuracy during Hits and Commission Errors in Children and Adults for each Cue Condition.*

	Saccadic Accuracy					
	Children		Adults		All	
	OE	CE	OE	CE	OE	CE
Cue Condition						
Square	.04 (.21)	.56 (.50)	.03 (.18)	.37 (.48)	.04 (.19)	.46 (.50)
Happy face	.08 (.27)	.42 (.49)	0.5 (.21)	.30 (.46)	.06 (.24)	.36 (.48)
Angry face	.09 (.28)	.37 (.48)	.05 (.21)	.29 (.45)	.07 (.25)	.33 (.47)

Note: Standard deviations shown in the parentheses

3.3.3 Effects of ADHD Symptoms

There was no main effect of ADHD symptoms on either outcome (saccade latency and commission errors). However, there were a number of interaction effects between ADHD and condition, suggesting ADHD processing was disrupted in the context of angry faces. ADHD symptoms were positively correlated with saccadic commission errors for angry relative to happy faces ((β = -.27, SE = .11, z = -2.49, p < .05) *see Figure 3.2*) and showed marginally significant increase in "hit" latencies for angry (vs. happy) faces (β =

-.02, SE = .01, *t* = -1.82, *p* = .07). In addition, elevated symptoms of ADHD were associated with slower "hit saccade latencies" in adults and faster saccade latencies in children, although this effect was just under statistical significance (*β* = .07, SE = .04, *t* = 1.76, *p* = .08). This finding shows that disrupted attentional processing (as reflected through slower saccade latencies) was greater in adults with increased ADHD symptoms compared to young people. This findings was further modulated by the cue condition, showing a marginally significant effect on saccade latency in which, adults relative to young people with elevated symptoms of ADHD was increased in response to angry faces (vs non-face stimuli) (*β* = .05, SE = .03, *t* = 1.96, *p* = .06).

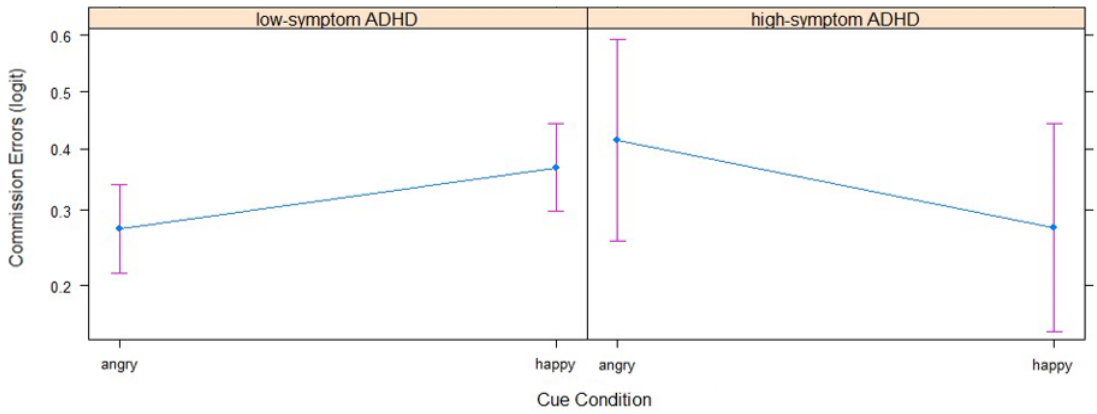

Figure 3.2: Two- way interaction from the gLMMs on commission errors made on No-Go trials, as a function of ADHD symptoms, anxiety symptoms and emotional (happy/angry) faces. For a better visualisation ADHD and anxiety symptoms were divided in low-and – high symptom based on the lower and upper quartiles. The number of commission errors is shown in logit (log-odds) values. Error bars represent 95% confidence *intervals*

3.3.4 Effects of Anxiety Symptoms

There was no significant main effect of anxiety on any outcome measure. There were however, interactions between anxiety symptoms and cue condition with regard to "hit" saccade latency, suggesting that attentional processing was affected by the presence of negative Go stimuli. Anxiety symptoms were associated with faster "hit" saccade latency for angry compared to happy faces (*β* = .03, SE = .01, *t* = 2.43, *p* < .05), and non-face stimuli (*β* = -.02, SE = .01, *z* = -1.76, *p* = .08).

3.3.5 ADHD x Anxiety Interaction

There were no two-way interactions between anxiety and ADHD symptoms for any outcomes. However, there was a significant three-way interaction among symptoms of ADHD, anxiety and cue condition, showing that that the presence of high levels of anxiety and ADHD symptoms were linked to faster "hit" saccade latencies for angry (versus happy) faces (β = .02, SE = .01, t = 2.11, p < .05; *see Figure 3.3*). No other effects were significant (Table 3.3).

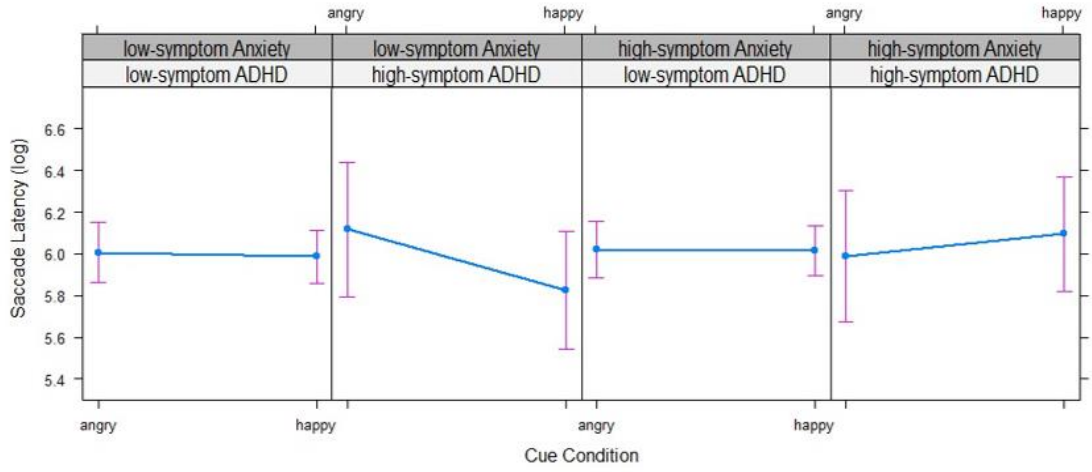

Figure 3.3: Three- way interaction from the LMMs on saccade latency during hits (Go trials) as a function of ADHD symptoms, anxiety symptoms and emotional (happy/angry) faces. For a better visualisation ADHD and anxiety symptoms were divided in low-and – high symptom based on the lower and upper quantiles. Saccade latency is shown in log values. Error bars represent 95% confidence intervals.

Table 3.3: *LMMs of Group, Cue Condition, ADHD and Anxiety, and Interactions on Saccade Latency during Hits and gLMMs on Saccade Accuracy of Commission Errors.*

		Saccade Latency				Saccade Accuracy			
		Hits				CE			
		β	*SE*	*t*	Sign.	*β*	*SE*	*z*	Sign.
Intercept		5.92	.02	311.42		-.53	.09	-5.76	***
Group	Adults - Children	.15	.04	3.88	***	.54	.20	3.13	**
Cue Condition									
	Angry-Happy	-.03	.01	-2.78	**	-.20	.11	-1.77	ns
	Happy-Square	-.24	.01	-18.61	***	.70	.10	6.70	***
	Square-Angry	.28	.01	20.19	***	-.50	.10	-4.86	***
Anxiety		.01	.02	.57	ns	-.06	.09	-.70	ns
ADHD		.001	.02	.04	ns	.01	.09	.13	ns
Anxiety * Cue Condition									
	Angry-Happy	.03	.01	2.43	*	.06	.18	.34	ns
	Happy-Square	-.003	.01	-.22	ns	-.13	.09	-1.41	ns
	Square-Angry	-.02	.01	-1.76	.	.01	.10	.08	ns
ADHD * Cue Condition									
	Angry-Happy	-.02	.01	-1.82	.	-.27	.11	-2.49	*
	Happy-Square	.02	.01	1.23	ns	.10	.10	.98	ns
	Square-Angry	.004	.01	.29	ns	.17	.10	1.67	.
Anxiety*ADHD*Cue Condition									
	Angry-Happy	.02	.01	2.11	*	.14	.11	1.25	ns
	Happy-Square	-.01	.01	-.92	ns	.01	.11	.10	ns
	Square-Angry	-.01	.01	-.82	ns	.14	.11	1.25	ns

Note: Commission Errors (CE), *beta*-coefficients (*β*), Standard Errors of Estimates (SE), $p<.001$ (***), $p<.01$ (**), $p<.05$ (*), $p<.1$ (.) non-significant (ns)

3.4 Discussion

This study examined the effects of anxiety and ADHD symptoms on attentional control in children and adults using emotionally-loaded (happy and angry faces) and non-face stimuli. Elevated ADHD symptoms were associated with an increased impairment in IC and specifically when processing threat stimuli (as reflected in more saccadic commission errors for angry faces) and reduced sustained attention (as reflected in slower "hit" saccade latencies for angry faces). In contrast, increased levels of anxiety were associated with faster "hit" saccade latencies in response to angry compared to happy faces. Moreover, when anxiety and ADHD symptoms were elevated the effect of elevated anxiety symptoms on saccade latency remained, while those associated with symptoms of ADHD were no longer evident.

Individuals who reported increased ADHD symptoms showed greater inability to suppress reflexive saccades in the context of angry compared to happy faces and showed reduced efficiency in executing voluntary saccades in response to angry compared to happy faces. This finding is consistent with previous studies that showed reduced IC for angry (vs. happy and neutral) faces in children with ADHD (Kochel et al., 2013). In addition, behavioural IC in response to angry faces, has been previously accompanied by reduced right parietal ERP (Event-Related Potential) amplitudes in both children (Kochel et al., 2013) and adults (Köchel et al., 2012) with ADHD, highlighting a reduced sensitivity in recognising negative emotional stimuli relative to positive or neutral stimuli. Further, children with ADHD showed reduced prefrontal activity (i.e., in ventrolateral, orbitofrontal and medial prefrontal cortices) when angry faces were used in a working memory task and increased prefrontal activity in the presence of happy faces, when compared to healthy controls, thus highlighting attentional control difficulties in the presence of emotional stimuli ADHD (Passarotti, Sweeney, & Pavuluri, 2010b). Similarly, reduced ventrolateral prefrontal activation was previously shown in adolescents with ADHD when negative words were used in an emotional Stroop task, highlighting reduced attentional engagement in the presence of negative stimuli (Passarotti, Sweeney, & Pavuluri, 2010a). In support, the current study showed similar findings in regard to IC in the presence of negative compared to positive emotional faces, supporting previous accounts that emotion dysregulation is a core diagnostic feature in ADHD (Shaw et al., 2014).

The reduced sensitivity during IC of angry faces in individuals with high ADHD and low anxiety was also supported by the reduced sustained attention (i.e. slower saccade latency) in response to angry (vs. happy) faces. Interestingly, this effect suggests that increased ADHD symptoms were associated with difficulties disengaging from angry faces (slowing a required response to move the eyes away from an angry face). In support, disrupted processing of angry (but not happy) faces in ADHD were previously shown with reduced haemodynamic response during recognition of angry faces and typical (increased) response during recognition of happy faces (Ichikawa et al., 2014). Other studies, have also shown that challenges with emotion identification in ADHD is specific to negative stimuli (including anger, sadness and fear) (e.g. Pelc et al., 2006; Singh et al., 1998; Williams et al., 2008).

Individuals with elevated levels of anxiety showed better processing efficiency (i.e. faster "hit" saccade latencies) in response to angry facial expressions relative to happy faces and non-face stimuli. Previous evidence showed that increased vigilance facilitates attention towards threatening information (i.e. with faster responses towards threatening stimuli) (review by Cisler & Koster, 2010) in both high trait anxiety (Bradley, Mogg, & Millar, 2000) and clinical anxiety (Chen, Ehlers, Clark, & Mansell, 2002), that might subsequently lead to increased avoidance and thus responses made away from threating stimuli (Mogg et al., 2004). However, other studies have also shown that anxiety is associated attentional disengagement difficulties from negative stimuli in children and adults (Ladouceur et al., 2009; Pavlou et al., 2016; Richards et al., 2012). However, in these studies, threatening stimuli were irrelevant to the task goals (i.e., used as distractors) and increased distractibility by those stimuli was reflected through disengagement difficulties. Contrary to our predictions, the results showed that elevated anxiety levels were associated with facilitated attentional processing for negative (vs positive and non-face) stimuli, rather than disengagement difficulties. Considering that attention was already directed and engaged by the central cues, attentional disengagement would have been evident if high anxious individuals needed more time (i.e., exhibit slower saccade latencies) to direct attention away from angry faces, compared to the other stimuli. However, the opposite was found (i.e. saccade latencies were only slower for happy and non-face stimuli compared to angry faces). This finding is also in line with other studies used centrally presented emotional cues and found faster attentional disengagement from centrally presented angry faces,

when compared to neutral and happy faces in clinical anxiety (i.e., GAD) (Yiend et al., 2015).

Although some studies have reported that comorbid anxiety disorders can positively moderate IC deficits in ADHD (for a review, see Schatz & Rostain, 2006), our results show that the presence of increased anxiety symptoms in ADHD did not affect the number of IC errors. In support, a study that examined emotional interference in children with ADHD aged between 8-13 years old, showed that trait anxiety had no effect in the relationship between ADHD and emotional interference (Villemonteix et al., 2017). In addition, even though we did not find any moderating effects of anxiety on impulsive behaviour and response inhibition in ADHD, increased anxiety symptoms when ADHD symptoms were high affected sustained attention when processing of emotional stimuli (i.e., through saccade latencies). This finding supports previous accounts on the association between anxiety and reduced processing efficiency (in this case, saccade latency during response execution), but not performance accuracy (i.e. saccade inhibition errors) (Eysenck, Derakshan, Santos, & Calvo, 2007). Reduced efficiency was previously explained due employment of compensatory strategies, such as increased effort, that individuals with trait anxiety use to achieve performance similar to that of low anxious individuals (Berggren & Derakshan, 2013).

Considering the impact of comorbid ADHD and anxiety symptoms on performance, the results showed that while the association between anxious affect and processing remained, the links between symptoms of ADHD and processing of angry faces were no longer evident. This result suggests that anxiety counteracted the effect of ADHD symptoms on emotional processing. Previous evidence have shown a similar effect, with anxiety counteracting impairments in emotion recognition in children with comorbid conduct disorder (CD) (Short, Sonuga-Barke, Adams, & Fairchild, 2016). In this study, Short et al. (2016) examined emotion recognition of anger, fear, happiness, sadness and disgust using a five-alternative-forced-choice task in adolescents with CD, anxiety, comorbid CD/anxiety and typical controls. Interestingly, the comorbid group was characterised by more worry-based anxiety disorders (i.e., GAD) rather than fear-related ones and results showed that emotion recognition (across all emotions) of comorbid CD/anxiety was similar to that of the control group, suggesting that emotion processing in anxiety counteracted the impairments associated with CD.

In summary, the current study examined the synergistic effects of ADHD and anxiety symptoms on attentional control and emotional processing using saccadic eye-movement measurements. The interaction between ADHD and anxiety showed that the effect of anxiety symptoms led to a reduction of the effect of ADHD symptoms on sustained attention during processing negative emotional information, when both symptom levels were elevated. These findings indicate that subclinical ADHD and anxiety have differential effects on cognitive performance when emotional processing is involved with the effects of anxiety prevailing when both symptoms are elevated. Increased anxiety symptoms in individuals with elevated ADHD symptoms may act as a 'protective' factor for disrupted emotional processing in negative contexts for ADHD. The current findings should stimulate future research to further investigate the interaction between cognition and emotion across a wider spectrum of ADHD and anxiety symptoms including clinical levels. This research enables the disentanglement of the psychological challenges associated with ADHD from those underpinning comorbid disorders (i.e. anxiety) and has implications on diagnostic criteria currently used for those conditions as well as interventional approaches including attention and bias modification training that focus on reducing negative attentional biases through attention training that involves processes such as orienting attention away from threat or towards non-threatening stimuli (Mogg & Bradley, 2016, 2018).

Chapter 4 The Interaction between Symptoms of GAD and ADHD on Performance in a Go/No-Go Task. Effects of Emotional Context in Eye-Movements Measurements

4.1 Introduction

ADHD is a heterogeneous disorder underpinned by a range of complex etiological factors (including genetic, environmental, neurobiological and cognitive factors; Steinhausen, 2009). The heterogeneity in symptoms and aetiology may, in part, be explained by the high comorbidity rates between ADHD and other internalising and externalising disorders (with comorbidity estimates ranging from 13-93%; Jarrett and Ollendick, 2008). Previous research in this area has predominantly focused on the comorbidity between ADHD and externalising disorders (e.g., conduct disorder and oppositional defiant disorder), with relatively little research considering the comorbidity between ADHD and anxiety. Anxiety disorders are highly comorbid in children and adolescents with ADHD; with around 25% prevalence rate (Jarrett & Ollendick, 2008), and where Generalised Anxiety disorder (GAD) is reported as the most prevalent (Souza et al., 2005). Developing a conceptual understanding of the impact of comorbidity between ADHD and anxiety may lead to the identification of important etiological factors that are involved in its development.

Studies have shown that comorbid anxiety disorders in young people with ADHD have been associated with challenges in school performance, lower social competence and more attentional difficulties compared to those without anxiety (Bowen, Chavira, Bailey, Stein, & Stein, 2008). For example, several studies found better inhibitory control in a comorbid group compared to children having ADHD only (Schatz & Rostain, 2006), suggesting that anxiety might moderate impulsive behaviour in ADHD. Indeed, some studies have found improved response inhibition for clinical (Grillon et al., 2017) and non-clinical (Grillon et al., 2017; Robinson, Krimsky, & Grillon, 2013) anxiety. Taken together, these findings fit with theoretical propositions linking lowered behavioural inhibition in

ADHD with increased impulsivity and poorer inhibitory control (Quay, 1988,1997) and increased behavioural inhibition in anxiety (Gray & McNaughton, 2003). Consistently, a recent study that examined the effects of trait anxiety on cognitive performance in adolescents with ADHD showed improved inhibitory control (with faster stop signal reaction time in the stop signal task), fewer omission errors, improved reaction time and fewer variable responses in a continuous performance test, suggesting that anxiety may play a 'protective' role to counteract cognitive deficits in ADHD (Ruf, Bessette, Pearlson, & Stevens, 2017). However, further evidence has shown no effect of anxiety on response inhibition in children and adolescents with ADHD (e.g., Korenblum, Chen, Manassis, & Schachar, 2007; Manassis, Tannock, & Barbosa, 2000).

Increased anxiety has been linked to sensitivity for threat-related stimuli, including faster attentional engagement with threat, difficulties with disengagement from threat, and attentional avoidance of threat(see review by Barry, Vervliet, & Hermans, 2015) and biases involving interpretation of neutral or ambiguous faces as threatening (Richards et al., 2002). ADHD has been associated with disrupted processing of emotions more broadly, including orienting towards or allocating attention to emotional stimuli (Shaw et al., 2014) and impairments with facial emotion recognition (Boakes, Chapman, Houghton, & West, 2008; Pelc et al., 2006); particularly negative facial expressions such as anger and fear (Williams et al., 2008). In the context of both ADHD and anxiety have been linked to challenges in the emotional processing, it is important to explore the interactive effects of ADHD and anxiety symptoms on cognitive performance in the presence of emotional stimuli.

Extending previous evidence on trait anxiety (e.g. Ruf, Bessette, Pearlson, & Stevens, 2017), we considered measures of dimensional symptom count of GAD and ADHD in children and adolescents on cognitive and emotion processing using eye-movement measurements in a modified version of the Go/No-Go task (see Method section of Chapter 3). Eye movement measurements allow us to distinguish between different manifestations of attention including an inability to suppress eye-movements in response to a stimulus and difficulties disengaging from stimuli presented to central vision. Our findings in subclinical symptoms of ADHD and anxiety from Chapter 3, showed that the effects of trait anxiety on emotional processing, prevailed over the effects of ADHD in young people and

adults. Here, we extend those previous findings in a larger sample of children and adolescents with ADHD and GAD symptoms.

Considering the inattention difficulties that characterise ADHD, and following the results of Chapter 3, we predicted that more ADHD symptoms would be associated with poorer sustained attention (i.e., slower saccade latencies and more saccadic omission errors), and reduced inhibitory control (i.e., more saccadic commission errors). We anticipated that these effects would be exacerbated in the presence of emotional stimuli and particularly, angry faces compared to non-face stimuli. In regard to the effects of anxiety, we hypothesised that GAD symptoms would be associated with faster processing in the presence of angry faces (vs happy and non-face stimuli). We also expected that increased GAD symptoms would improve the predicted negative effects of ADHD symptoms in response to angry facial expressions, resulting in faster saccade latencies, and fewer saccadic omission (i.e., failed to move away) and potentially commission errors (i.e., poorer inhibitory control) for angry faces (compared with happy and non-face) stimuli.

4.2 Method

4.2.1 Participants

A total sample of 71 (38 males) children and adolescents aged between 8-15 years old were recruited in the current study. Participants were both community and clinically-referred sample, recruited from local primary and secondary schools in Hampshire, from study adverts and posters that were put around the Southampton city, via the SHARe (South Hampshire ADHD Register; which is a clinical database for children and adolescents with ADHD living in the South Hampshire area) as well as from Child and Adolescent Mental Health Services (CAMHS) in Southampton[5].

Three participants were excluded for meeting above cut-off scores on comorbid disorders on the Conners Comprehensive Behaviour Rating Scale (CBRS-P; Conners, 2008). The remaining 68 (36 males) children and adolescents (M_{Age} = 11.28, SD_{Age} = 2.04) took part in the current study. Estimated IQ score was measured using the block design and

[5] For a detailed description of the recruitment stages, procedures and criteria is included in Chapter 2, page 30.

vocabulary check subscales of the Wechsler intelligence scale for children (WISC- IV; *4th Ed*, 2003) with *M*= 105.92 (*SD*= 12.80), and all participants had an estimated IQ score > 70.

4.2.2 ADHD and GAD symptoms

Child and adolescent symptoms of ADHD and GAD were measured using the parent-reported DISC-IV (Shaffer et al., 2000). This is a structured diagnostic interview designed to assess psychiatric disorders (based on the Diagnostic and Statistical Manual; DSM-IV, year) and symptoms in children and adolescents aged 6–17 years old. Most of the questions are recorded and coded as 'yes' (1), 'no' (0), not applicable (8), or 'don't know' (9). The DISC has moderate to good diagnostic reliability and validity for the parent interview (Schwab-Stone et al., 1996). In particular, test-retest diagnostic reliability of the DISC- parent report for ADHD is .60 for and for any anxiety disorder .56 (κ- statistics). The ADHD-Combined symptom count for young people was taken from both the ADHD- Inattention and Hyperactivity/Impulsivity scales, with total symptom count ranging from 0-20 (*M*= 6.99, *SD*= 6.59). The GAD symptom count was ranged from 0-10 (*M*= 3.16, *SD*= 3.04).

Participants were assessed for ADHD (including all subtypes) and/or the following Anxiety disorders: Specific Phobia, Social Phobia, Separation Anxiety Disorder, Panic Disorder and Generalised Anxiety Disorder, using the Diagnostic Interview Schedule for Children (DISC-IV; Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000). According to the DISC-IV criteria, 11 participants (9 males) met the criteria for a research diagnosis of ADHD; 19 (9 males) met the criteria for a research diagnosis of at least one anxiety disorder, 9 (5 males) participants met the criteria for a research diagnosis of co-morbid ADHD/anxiety and 28 (12 males) participants did not meet the criteria for either ADHD or any anxiety disorder (for a summary of diagnostic criteria across the individual groups comprised the total sample, see Table 4.1). We excluded three participants who met the criteria (for both *T*-scores and symptom count) of Conduct Disorder (CD) and Autism Spectrum Disorder (ASD) on the Conners Comprehensive Behaviour Rating Scale-Parent (CBRS-P; Conners, 2008). Potential comorbidity of ODD on the Conners CBRS-P was included for participants meeting ADHD but not anxiety criteria of the DISC-IV and likewise, potential comorbidity of depression on the Conners CBRS-P was included for participants meeting anxiety but not ADHD criteria in the DISC-IV. Potential comorbidities of depression and /or ODD were also included for participants meeting both ADHD and anxiety criteria in the DISC-IV. The

current study considered dimensional measures of ADHD and GAD in the total sample. *Figure 4.1* shows GAD and ADHD symptom distribution across the individual group of participants.

Table 4.1: Research Diagnostic Criteria, according to the DSM- IV for ADHD and Anxiety Disorders and the CBRS-Parent Criteria for CD, ODD and Depression Comorbidities

TD (*N*= 27)	ADHD (*N*= 11)	Anxiety (*N* = 19)	Co-morbid (*N* = 9)
• no diagnosis of ADHD, anxiety disorders, depressive disorder, ODD or CD) • no severe learning difficulties or special educational needs • able to speak and understand English	• primary diagnosis of ADHD (including all subtypes) • possible diagnosis of ODD • no diagnosis of anxiety, CD, Depression • do not take long-acting stimulant medication • no severe learning difficulties or special educational needs • able to speak and understand English	• primary diagnosis of at least one anxiety disorder (GAD: *n*= 11, SAD: *n*=5, PD: *n*= 4, SP: *n*= 15, SoAD: *n*= 5) • possible diagnosis of Depression • no diagnosis of ADHD, CD, ODD • no severe learning difficulties or special educational needs • able to speak and understand English	• diagnosis of co-morbid ADHD and anxiety ((GAD: *n*= 4, SAD: *n*=4, PD: *n*= 2, SP: *n*= 7, SoAD: *n*= 5) • possible diagnosis of ODD and depression • no diagnosis of CD • do not take long-acting stimulant medication • no severe learning difficulties or special educational needs • able to speak and understand English

Note: GAD = Generalised Anxiety Disorder, SAD= Separation Anxiety Disorder, PD= Panic Disorder, SP= Social Phobia, SoAD= Social Anxiety Disorder

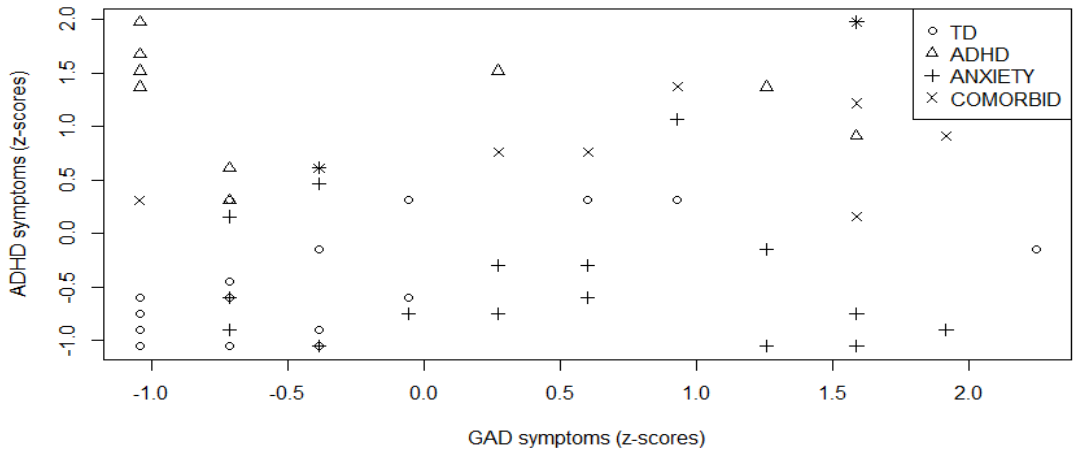

Figure 4.1: The scatterplot represents symptoms of ADHD and GAD across participants' group diagnostic (DICS) criteria.

4.2.3 Experimental Go/No-Go Task

This paradigm is described in Chapter 3, section 3.2.3.

4.2.4 Data Analyses

We performed linear mixed model (LMMs) effects using the lmer function from the lme4 package (Bates et al., 2015) in R (R, Core Team, 2017) to examine the effects of GAD and ADHD symptoms on saccade onset latency in the presence of emotional and non-emotional stimuli. The saccade onset latency was measured on correct Go trials ("hits") and it was defined as the time elapsed from the presentation of the Go cue until the initiation of the first correct saccade to the target.

We performed generalised linear mixed model (gLMMs) effects using the glmer function from the lme4 package in R to examine the effects of anxiety and ADHD symptoms in saccade accuracy (saccadic error rates; binary variables: 1 = error, 0 = no error) in the presence of emotional and non-emotional stimuli between children and adolescents. Saccade accuracy was considered in relation to (1) omission errors, defined as the number of misses (absence of a saccade) in the presence of a Go cue, and (2) commission errors, defined as the number of incorrect saccades executed in the presence of a No-Go cue.

ADHD and GAD symptoms (continuous variables) along with the cue condition (happy face, angry face and non-face stimuli), were used as fixed factors across for each outcome measure. We considered two- and three-way interactions between ADHD symptoms, GAD symptoms and cue condition. Participant and Trial number were used as random factors in a maximal random structure. The models were trimmed in a top-down method until convergence (Barr et al., 2013). The random structure of the final model for used for "hit" saccade latency included different intercepts and slopes for the cue condition for the random effect of participants and random intercepts for the random effect of trial number. The final model for the effect of omission and commission errors included separate intercepts and slopes for the cue condition for the random effect of participants and trials. The saccade latencies for "hits" were log transformed to ensure normal distribution. The continuous variables were mean centred to reduce collinearity between main effects and interactions. Saccade latencies below 80ms were excluded from the dataset. Data were screened for the assumptions of normality, linearity, homogeneity. The outliers were removed from the dataset (0.5%).

4.3 Results

4.3.1 Sample Characteristics

There was no main effect of gender on the outcome measures ("hit" saccade latency (β = .03, SE = .04, t = .74, p= .45), omission errors (β = -.35, SE = .25, z = -1.39 p= .16), commission errors (β = -.18, SE = .18, z = -1.00, p= .32)).

There was also no effect of estimated IQ on the outcome measures ("hit" saccade latency (β = -.00, SE = .001, t = -.33, p= .74), omission errors (β = -.001, SE = .01, z = -.14, p= .88), commission errors (β = -002, SE = .01, z = .36, p= .72)). There was a negative association between symptoms of ADHD and estimated IQ, r = -.20, p< .001 and between symptoms of GAD and estimated IQ, r = -.11, p< .001, showing a small effect size.

4.3.2 Effects of Emotional Content of Cues

There was a significant effect of cue condition on all outcomes (Tables 4.2 and 4.3). "Hit" saccade latency was faster for non-face cues compared to face stimuli (happy and

angry faces) and slower for angry faces relative to happy faces. The number of omission errors was increased for happy and angry faces relative to non-face stimuli, but did not differ between happy and angry faces. The number of commission errors were higher for non-face stimuli than both happy and angry faces. Commission errors were also fewer for angry relative to happy faces.

Table 4.2: *Mean Saccade Latency (ms) during Hits and Mean Omission and Commission Error Rates in for each Cue Condition.*

	Saccade Latency	Saccadic Accuracy	
	Hits	Omission Errors	Commission Errors
Cue Condition	*M (SD)*	*M (SD)*	*M (SD)*
Square	370.02 (148.79)	0.06 (0.23)	0.63 (0.48)
Happy face	463.97 (155.74)	0.11 (0.32)	0.49 (0.50)
Angry face	480.59 (158.41)	0.13 (0.34)	0.45 (0.50)

Note: Standard deviations are shown in the parentheses

4.3.3 Effects of ADHD Symptoms

There was no main effect of ADHD symptoms on "hit" saccade latency (β = -.001, SE = .02, t = -.07, p = .94) and commission errors (β = .05, SE = .10, z = .52, p =.60). There was, however, a significant main effect of ADHD symptoms on the number of omission errors, showing that elevated ADHD symptoms were associated with increased omission errors (β = .26, SE = .13, z = 2.01, p <.05), thus poor sustained attention (Table 4.3).

4.3.4 Effects of GAD Symptoms

There was no main effect of GAD symptoms on "hit" saccade latency (β = .02, SE = .02, t = 1.00, p = .32), saccadic omission (β = .15, SE = .13, z = 1.16, p = .24) and commission (β = .08, SE = .10, z = .87, p <.52) errors (Table 4.3).

4.3.5 ADHD x GAD interactions

There was no significant interaction of ADHD and GAD symptoms on "hit" saccade latency (β = .00, SE = .02, t = .25, p = .80) and saccadic commission errors (β = -.03, SE = .09, z = -.15, p =.78). However, there was a significant interaction between ADHD and GAD symptoms on saccadic omission errors, showing that elevated symptoms of both ADHD and GAD symptoms were associated with fewer omission errors, compared to elevated ADHD symptoms with lower GAD symptoms ((β = -.23, SE = .12, z = -2.00, p <.05) see *figure 4.2*).

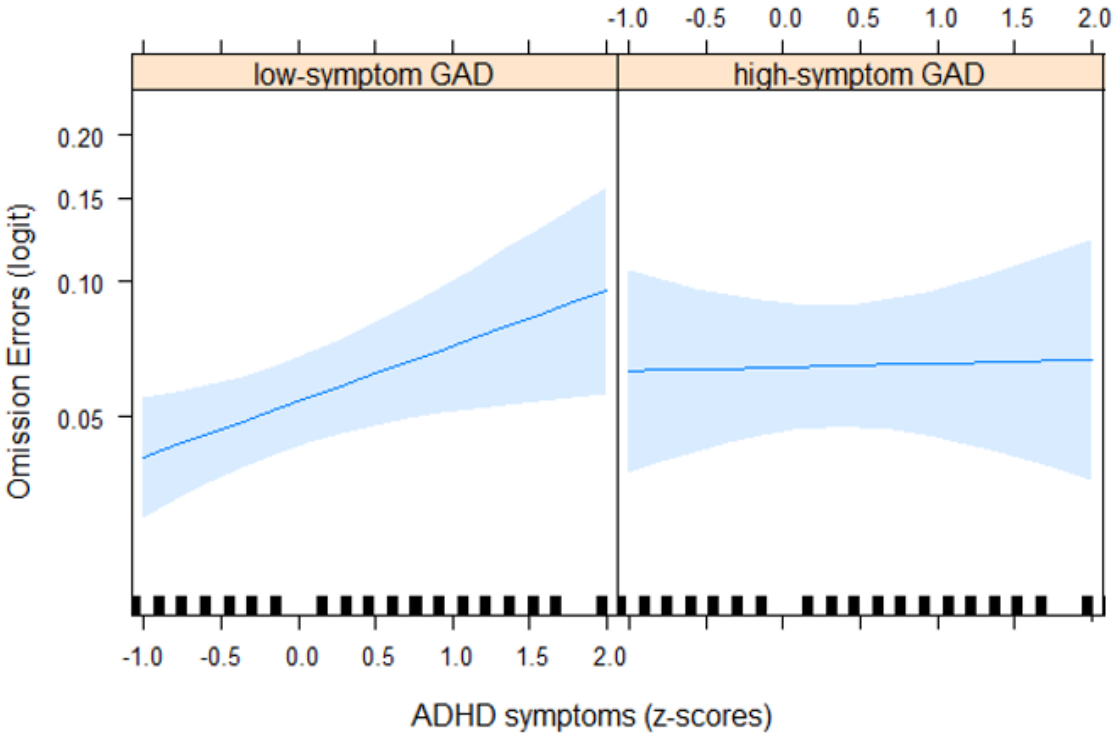

Figure 4.2: Two-way interaction from the gLMMs on omission errors made on Go trials, as a function of ADHD and GAD symptoms. For a better visualisation GAD symptoms were divided in low-and – high symptom based on the lower and upper quartiles. The number of omission errors is shown in logit (log-odds) values. Shaded error bands represent 95% confidence intervals.

There were three-way interactions among GAD symptoms, ADHD symptoms and cue condition (see *Figure 4.3*). The first interaction showed that elevated ADHD symptoms and lower GAD symptoms were associated with slower saccade latencies for angry relative to happy faces but when both ADHD and GAD symptoms were elevated, saccade latency was faster for angry relative to happy faces (β = .03, SE = .01, t = 2.11, p < .05). A marginally significant interaction showed that elevated ADHD symptoms and lower GAD were associated with slower "hit" saccade latency for non-face stimuli, compared to happy faces, but with elevated GAD symptoms (with high ADHD symptoms), "hit" saccade latency for happy faces (vs. non-face stimuli) was increased (β = -.03, SE = .01, t = -1.96, p =.06). These results indicate that symptoms of GAD counteracted the effects of ADHD on emotional processing.

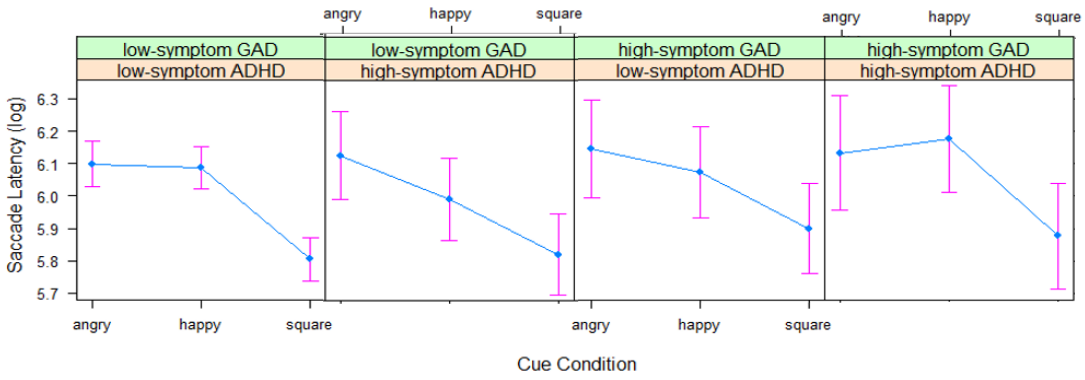

Figure 4.3: Three- way interactions from the LMMs on saccade latency during hits (Go trials) as a function of ADHD symptoms, GAD symptoms and cue condition. For a better visualisation ADHD and GAD symptoms were divided in low-and – high symptom based on the lower and upper quantiles. Saccade latency is shown in log values. Error bars represent 95% confidence intervals.

Table 4.3*: LMMs Cue Condition and Interactions with ADHD and GAD on Saccade Latency during Hits and gLMMs on Saccade Accuracy of Omission and Commission Errors*

		Saccade Latency				Saccade Accuracy							
		Hits				OE				CE			
		β	*SE*	*t*	Sign.	*β*	*SE*	*z*	Sign.	*β*	*SE*	*z*	Sign.
Intercept		6.01	.02	323.38	***	-2.73	.13	-21.61	***	-.33	.13	-2.48	*
Cue Condition													
	Angry-Happy	.04	.01	3.35	**	-.77	.11	-6.68	***	-.29	.14	-2.11	*
	Happy-Square	.24	.01	16.05	***	.10	.12	.81	ns	-.93	.12	-7.70	***
	Square-Angry	.28	.01	19.09	***	.77	.11	6.68	***	-.93	.12	-7.71	***
GAD		.02	.02	1.00	ns	.15	.13	1.16	ns	.08	.10	.87	ns
ADHD		-.00	.02	-.07	ns	.26	13	2.01	*	.05	.10	.52	ns
GAD*ADHD		.00	.02	.25	ns	-.23	.12	-1.99	*	-.01	.09	-.15	ns
GAD * Cue Condition													
	Angry-Happy	-.01	.01	-.46	ns	.08	.11	.75	ns	-.01	.13	-.07	ns
	Happy-Square	-.01	.01	-.68	ns	.00	.11	.03	ns	.01	.11	.07	ns
	Square-Angry	-.02	.01	-1.10	ns	-.08	.11	-.75	ns	.01	.11	.07	ns
ADHD * Cue Condition													
	Angry-Happy	.01	.01	1.07	ns	-.05	.10	-.45	ns	.07	.13	.60	ns
	Happy-Square	-.01	.01	-.74	ns	.08	.11	.74	ns	-.08	.11	-.75	ns
	Square-Angry	.00	.01	.25	ns	.05	.10	.45	**ns**	-.08	.11	-.75	ns
GAD*ADHD*Cue Condition													
	Angry-Happy	-.03	.01	-2.11	*	-.02	.10	.21	ns	-.06	.12	-.47	ns
	Happy-Square	.03	.01	1.96	.	-.01	.10	-.12	ns	-.00	.10	-.03	ns
	Square-Angry	-.00	.01	-.01	ns	.02	.10	21	ns	-.00	.10	-.03	ns

4.4 Discussion

The current study examined the interactive effects of ADHD and GAD symptoms on attentional control via saccadic performance, in children and adolescents using emotional faces and non-face stimuli. Elevated ADHD symptoms in young people were associated with reduced sustained attention (i.e., more attentional lapses/ omission errors) regardless of the emotional valence of the stimuli. However, attentional lapses were reduced with elevated symptoms of GAD (in the context of elevated ADHD symptoms). In addition, the interactive effects between ADHD and GAD symptoms showed that elevated symptoms of ADHD, but lower GAD symptoms were associated with disrupted processing (i.e., slower saccade latencies) for non-face stimuli and angry faces relative to happy faces, but this effect was reversed with elevated GAD symptoms.

Young people with increased in both GAD symptoms and ADHD symptoms had improved attentional performance (i.e., fewer attentional lapses) compared to those with elevated ADHD symptoms only, regardless of the emotional nature of the stimuli. This finding suggests that anxiety has a potential compensatory effect on the attentional difficulties seen in ADHD that are not specific to the emotional context of the task. Previous studies have shown similar effects of anxiety in ADHD in attentional processes that did not involve emotionally charged stimuli. For example, Ruf et al. (2017) found that high trait anxiety, in adolescents with ADHD, was associated with fewer attentional lapses, improved sustained performance, faster reaction times and fewer variable responses in a continuous performance task, suggesting that anxiety improves attentional engagement in tasks in ADHD. In addition, previous studies showed that even though anxiety did not improve impulsive behaviour and response inhibition in individuals with ADHD (Korenblum, Chen, Manassis, & Schachar, 2007), improved sustained attention (on a continuous performance test) and divided attention (as measured through visual and acoustic discrimination task) (Vloet et al., 2010). These findings indicate that elevated anxiety symptoms may act as a 'protective' factor for disrupted attentional processes in ADHD.

Furthermore, the effects of anxiety on emotional processing counteracted the effects of ADHD. Individuals with elevated symptoms of ADHD and reduced symptoms of GAD showed slower processing (i.e., slower saccade latency) for angry compared to happy faces; an effect that was reversed with elevated GAD symptoms (i.e. presence of GAD

symptoms was associated with faster saccade latencies for angry versus happy faces). This finding shows that the elevated anxiety symptoms improved disrupted processing associated with negative relative to positive stimuli in ADHD, and it is consistent with our previous findings on subclinical (trait) anxiety and ADHD symptoms found in Chapter 3. These findings indicate that previously reported effects of high trait anxious subclinical individuals, may be directly generalizable to clinical groups, however, these evidence were specific in the context of emotional processing. The synergistic effects between increased GAD and ADHD symptoms on sustained attention, regardless of the emotional context of the task were not previously found in our subclinical (trait) anxiety groups of young people and adults (Chapter 3). Even though, we did not directly compare the effects of trait anxiety and GAD symptoms, this finding may indicate that clinical symptoms of anxiety have generally protective role in disrupted attentional processes in ADHD, beyond the emotional context of the task. In addition, this finding is in line with other studies showing that anxiety counteracted impairments in emotion recognition in children with comorbid externalising disorders, such as CD (Short et al., 2016). In line with the effects of elevated ADHD symptoms, previous studies showed that children with ADHD had deficits recognising facial emotional expressions (Tehrani-Doost et al., 2017) and some of them found more difficulties in the recognition of threat-related faces (i.e. fear and anger) (Corbett & Glidden, 2000; Pelc et al., 2006; Williams et al., 2008).

Furthermore, elevated levels of anxiety in ADHD might also be associated with optimal levels of arousal that lead to improved attentional performance (Arnsten, 2009). Attenuation in PFC function (Rubia et al., 1999) and reduced prefrontal connectivity (Casey et al., 2007; Sowell et al., 2003) has been implicated in individuals with ADHD, which further derives from weaker noradrenaline production leading to impairments with sustained attention (Bellgrove, Hawi, Gill, & Robertson, 2006). Therefore, the increased anxiety levels in ADHD might be associated with moderate levels of catecholamine (i.e. noradrenaline and dopamine) release that in turn improve prefrontal cortex (PFC) function (i.e. attentional processes) (Arnsten, 2009).

Overall, the current study shows that the effects of GAD symptoms in ADHD led to improvements in sustained attention and counteracted effects associated with emotional processing. The findings from the current study extend our previous findings on the same paradigm, on the effects of trait anxiety in ADHD in children/adolescents and adults

(Chapter 3). Together these findings suggest that the presence of clinical and subclinical symptoms of anxiety counteracted the effects of ADHD on attentional processing and particularly in the presence of emotional stimuli.

Chapter 5 Attentional Orienting to Emotional "Eye-gaze" Stimuli: The relationship with ADHD and Anxiety Symptoms in Adults and Young People

5.1 Introduction

Following other people's eye–gaze develops during infancy and it is important for social learning and communication (Csibra & Gergely, 2006). A number of studies examined this phenomenon experimentally and have shown that in typical populations social (i.e., eye gaze) and non-social (i.e., arrows) cue types can elicit automatic orienting effects following the direction of these cues (Kuhn & Benson, 2007; Tipples, 2002), with some evidence suggesting that social cues produce stronger orienting effects (Ricciardelli, Bricolo, Aglioti, & Chelazzi, 2002), as they are biologically relevant.

Studies have shown that direct gazes (i.e., eyes directed at the observer) are detected faster and more accurately than averted gaze cues (i.e., eyes looking left or right) (Conty, Tijus, Hugueville, Coelho, & George, 2006). Further evidence found that when participants were required to detect peripheral targets while fixating at central direct gazes were slower than when fixating at faces with averted eye-gazes (e.g. Senju & Hasegawa, 2005). These findings suggest that direct eye-contact holds attention more than averted gaze cues, making the direct eye-contact critical for social communication , as it provides information about the gazer's intentions, whereas averted gazes provide information about the environment (such as presence of potential threats or rewards). If these were true then one would expect the emotional content of the face to modulate attentional orienting (i.e., an averted gaze in the context of a fearful face can signal potential threat in the environment).

Research evidence on whether the emotional valence of the facial cues modulate the orienting of attention following the eye-gaze direction has provided mixed findings. A number of studies showed that the emotional facial expressions, such as happy, angry and fearful faces did not modulate attentional orienting based on the gaze direction of the faces (Graham, Kelland Friesen, Fichtenholtz, & LaBar, 2010; Hietanen & Leppänen, 2003).

Other studies showed that attentional shift was benefitted from the gaze direction of fearful, angry and surprised faces when compared to happy and neutral faces (Lassalle & Itier, 2013). Further evidence showed that attentional orienting following emotionally informative eye-gazes was affected by the participant's search goals of such that when individuals were searching for unpleasant/threatening pictures were more likely to follow fearful eye-gaze cues but not happy facial cues and vice versa, during a visual search paradigm (Kuhn & Tipples, 2011). Another study showed that in a typical adult population, high cognitive load (i.e., counting backwards in steps of 7) enhanced gaze cueing effects for task-irrelevant angry faces, but reduced gaze cueing for neutral faces, whereas gaze cueing for happy faces was not affected by the cognitive load of the task (Pecchinenda & Petrucci, 2016). These findings suggest that cognitive control processes can interact and modulate the gaze cueing according to the emotional valence of the cues.

Furthermore, empirical evidence showed that anxiety levels can also modulate attentional orienting in response to emotional "eye-gaze" cues (Frischen, Bayliss, & Tipper, 2007). For example, trait anxiety in adults has been previously associated with enhanced attentional orienting (faster RTs to identify peripheral targets when the eye gaze was directed towards the peripheral target than when the eye gaze was directed opposite to the peripheral target) for fearful eye gaze cues compared to happy, angry and neutral faces (Fox, Mathews, Calder, & Yiend, 2007; Mathews, Fox, Yiend, & Calder, 2003). Moreover, individuals with high levels of anxiety showed slower attentional orienting away from direct eye-gaze of angry compared to fearful faces, suggesting a double dissociation between the effects triggered by fearful and angry faces as social cues (Fox et al., 2007). In addition, differences between fearful and angry faces in high anxious individuals were also found in studies used cone of direct gaze (CoDG); an index of measuring the range of gaze directions that participants perceive as being directed at them. A wider CoDG found for angry than fearful faces (Ewbank, Jennings, & Calder, 2009; Hu, Gendron, Liu, Zhao, & Li, 2017), indicating that angry faces associated with greater perception of being directed at the observer (i.e. individuals with high trait anxiety).

Anxious individuals are characterised by increased attentional preference and hypervigilance towards negative stimuli (such as threating faces or pictures) (Armstrong & Olatunji, 2012; Barry et al., 2015) as well as increased susceptibility to interference in the presence of negative stimuli. Anxiety often co-occurs with ADHD in both clinical (Kessler et

al., 2006) and community populations (Das, Cherbuin, Butterworth, Anstey, & Easteal, 2012; Prevatt, Dehili, Taylor, & Marshall, 2015), and studies have shown that the presence of ADHD with anxiety can exacerbate social impairments (Karustis, Power, Rescorla, Eiraldi, & Gallagher, 2000). Therefore, findings related to the levels of anxiety and attentional orienting in response to social cues such as eye-gaze of emotional expressions become complicated in the case of co-occurring symptoms of anxiety with conditions such as ADHD. Furthermore, individuals with ADHD are characterised by disrupted emotion regulation, including impaired emotion recognition processing (Shaw et al., 2014). Further studies, showed that both children (e.g. Villemonteix et al., 2017) and adults (e.g. Marx et al., 2011) with ADHD are characterised by reduced emotional interference control that further disrupted cognitive processes (i.e., working memory). However, the interactive deficits underpinning ADHD and anxiety co-occurrence on attentional orienting in response to socially relevant stimuli are yet unclear.

Considering the use of social cues in ADHD, evidence that examined attentional orienting to symbolic (arrows) and social cues (eye-gazes) found that children and adolescents with ADHD showed a reduced tendency to reflexively respond to eye-gaze cues, while orienting to non-social stimuli (i.e. directional arrows) was comparable to TD peers. More recently, a study examined interference control in children and adolescents with ADHD using a word classification task (Marotta et al., 2017). In this study, participants were required to indicate the side of the word presented ('left' or 'right') and ignore eye-gaze and arrow cue distractors that appear above the target stimuli. Young people with ADHD showed no interference effect for eye-gaze cue distractors but showed typical (i.e., similar to peer controls) interference effect in the presence of arrow distractors (Marotta et al., 2017).

While empirical evidence suggests differential processing of symbolic versus social cues in ADHD, no study has explored whether this is impacted by the use of emotional stimuli. Moreover, the results of the Go/No-Go task presented in this thesis indicated that disrupted emotional processing in ADHD is specific to negative emotional expressions, such as angry faces rather than positive emotional expressions (i.e., happy faces), whereas the opposite effect was found for elevated anxiety levels. This study aims to investigate the effects of ADHD and anxiety symptoms on attentional orienting in the presence of symbolic

and eye-gaze cues of emotional facial expressions.

Previous studies have adapted the classical spatial cueing paradigm (Posner, 1980) to examine attentional orienting in response to social (i.e., eye-gaze cues) and non-social (i.e. arrows) stimuli. In this task, a centrally presented cue (e.g. an arrow or a face looking to the left or right) predicts the location of a peripheral target on valid trials, that is compared to invalid trials; where the central cue is pointing to the opposite direction of the peripheral target. In this task, participants are required to identify the peripheral target as soon as it appears. Typical performance in this task results in what is called; the *cue validity* or *cueing effect*, where valid cues lead to better performance (i.e., faster RTs and fewer errors) and invalid cues are associated with poorer performance (i.e., slower reaction times and more errors). In addition, using spatially neutral cues (i.e., where the central cue does not provide either valid or invalid information about the target location), allow a measurement of observed attentional effects caused by benefits/facilitation of attentional orienting to the valid location, and/or costs of attentional orienting to the invalid location. Attentional benefits refer to faster RTs and fewer errors for valid relative to no-cue trials, while attentional costs refer to slower RTs and increased errors for invalid than for no-cue trials (Chica, Martín-Arévalo, Botta, & Lupiáñez, 2014).

Chapters 3 and 4 showed that emotional facial expressions affect monitoring and inhibitory control in ADHD and anxiety, and specifically when individuals had to interpret these stimuli and make an eye-movement response away from it (i.e., attentional disengagement). The results from the Go/No-Go task showed that symptoms of ADHD were associated with disrupted attentional processing of angry (i.e., difficulty to disengage) relative to happy faces, whereas elevated levels of anxiety in ADHD were associated with attenuation of this effect, showing improved attentional processing for angry relative to happy faces. The spatial cueing task extends our previous Go/No-Go task and allows us to explore more reflexive (exogenous) orienting to targets via socially relevant cues. Specifically, it will enable further exploration of attentional responses to socially relevant cues such as eye-gazes and whether different emotional expressions interfere with orienting of attention in relation to symptoms of ADHD and anxiety.

In the current study, we designed an eye-movement version of the Posner central cueing task to examine the effects of trait anxiety and ADHD symptoms on attentional

orienting to eye-gaze cue from emotional faces (happy, angry, fearful and neutral) and symbolic (arrows) cue distractors on valid (i.e., central cue correctly indicates target location), invalid i.e., central cue points to the opposite direction of the target location), and no-cue trials. In this task, we measured attentional orienting through (1) saccade onset latency (time taken to make an eye-movement towards a peripheral target) and (2) saccade accuracy via saccadic directional errors (first saccade made away from a peripheral target) across valid, invalid and no-cue trials. We anticipated that our results would demonstrate a typical validity effect across face and non-face stimuli and specifically that 1) valid cue distractors (i.e. central cue pointing to the target location compared to invalid cue distractors) would elicit faster saccade latencies and fewer saccadic errors than invalid cue distractors, and 2) we explored whether interference effect following eye-gaze cues is modulated by facial emotional expressions.

With regard to symptoms of anxiety and ADHD we predicted that symptoms of ADHD would be associated with a reduced cueing effect following social (eye-gaze cues) versus non-social cues (Marotta et al., 2014, 2017). We anticipated that reduced cueing effect (i.e., slow saccade latency and errors for valid compared to invalid cues) will be exacerbated in the presence eye-gaze cues of emotional face expressions compared to neutral faces, due to reduced emotional interference control previously found in ADHD (Marx et al., 2011; Villemonteix et al., 2017). In addition, based on our previous findings from the Go/No-Go task, we anticipated that interference control for negative eye-gaze cues (i.e., eye-gaze of angry faces) will be poorer and thus participants will not follow eye-gaze cues of angry compared to happy faces. Based on attentional biases previously reported for threat-related, social stimuli (such as angry and fearful faces) in anxiety (Fox, Mathews, Calder, & Yiend, 2007), we predicted that angry faces with direct gaze will be associated with slower saccade latencies compared to happy, fearful and neutral faces with direct gaze, for individuals with elevated anxiety symptoms. We also predicted that elevated anxiety symptoms will be associated with enhanced orienting effect (i.e., faster saccade latencies and fewer saccadic errors for valid relative to invalid trials) for averted gaze of fearful faces compared to happy, angry and neutral averted eye-gaze cues. Based on our previous findings from Chapter 3 and 4 on the interactive effects between ADHD and anxiety, we anticipated that elevated symptoms of anxiety in individuals with elevated symptoms of ADHD to be associated with improved/typical cueing effect. We also

anticipated negative emotional expressions (i.e., fearful and angry faces) to be associated with faster disengagement and better accuracy compared to happy and neutral faces.

Finally, we examined differences in attentional orienting between children and adults. Studies that considered the development of reflexive and volitional orienting in response to central target in children and adults found that children show adult-like reflexive orienting at an early stage during childhood but volitional orienting is supported by a more protracted development that continues to develop until late adolescence (Luna et al., 2008; Ristic & Kingstone, 2009). Considering that reflexive orienting in response to directional (either symbolic or eye-gaze) cues requires minimal cognitive control, we predicted that there will be no differences between children and adults and that both groups will demonstrate validity effect (i.e. faster saccade latencies for valid vs. invalid cues). Based on the trend we showed in Chapter 3, showing slower responses in adults with elevated ADHD symptoms compared to young people, we anticipated that elevated ADHD symptoms would be associated with poorer cueing effect for adults relative to young people.

5.2 Method

5.2.1 Participants

The participants' characteristics is included in Chapter 3, section 3.2.1.

5.2.2 Questionnaires

Measures of anxiety and ADHD symptoms are described in Chapter 3, section 3.2.2.

5.2.3 Experimental Spatial Cueing Task

The spatial cueing task was made up of two experimental blocks; one non-social block (with arrows and horizontal bars) and one social block (with facial emotional expressions). For the non-emotional/neutral block, participants saw a black fixation cross, followed by a black horizontal bar. Then a centrally presented distractor cue appeared, which was a black horizontal bar or an arrow pointing left or right and that was either congruent with the

position of the subsequent target (correctly indicated the position of the target) (valid trials) or was incongruent with the position of the target (invalid trials). The distractor cue was then followed by the presentation of a peripheral target- a white square or diamond. The task consisted of 144 trials presented in one block (48 trials with a horizontal bar, 48 trials with a valid arrow, and 48 trials with an invalid arrow).

In the non/social (arrow) condition, the left and right pointing arrows appeared with equal frequency. The horizontal bar subtended 4.2 degrees horizontally and 1.5 degrees vertically; the arrows subtended 4.2 degrees horizontally and 2.5 degrees vertically. The target stimulus subtended 1.5 x 1.5 degree of visual angle and was presented at 8 degrees eccentricity on the horizontal axis to the left or right of central visual fixation.

In the social block, the central distractor cue was a face (angry, happy, fearful or neutral) with three possible eye positions (direct gaze, averted left, averted right). The eye-gaze was directed either to the position of the subsequent target (congruent trials) or to the side opposite to the subsequent target (incongruent trials) on equal frequency. The block consisted of 192 trials that were divided in equally probable combinations of facial expressions and validity trials (48 trials for happy, 48 angry, 48 fearful and 48 neutral faces). In total 64 trials were with direct gaze, 64 trials with valid averted gaze and 64 trials with invalid averted gaze. The total number of trials in the experimental blocks was previously used in studies used a similar paradigm (e.g. Fox et al., 2007; Pecchinenda, Pes, Ferlazzo, & Zoccolotti, 2008) The face stimuli were generated from 16 colour photographs from the NimStim face set (Tottenham et al., 2009); these included four models (two male and two female) with an angry, fearful, happy or neutral expression with eyes directed straight ahead. Each photograph was digitally modified using Adobe Photoshop CS6 in order to create two new versions with a leftward and rightward-averted gaze. The faces subtended 4.2 degrees horizontally and 6.5 degrees vertically.

Each block of experimental trials was preceded by 15 practice trials. A trial sequence consisted of: 1) a drift correction (this is to ensure central fixation before the presentation of each trial sequence), 2) the presentation of a central fixation cross (1000ms), 3) the presentation of the initial fixation stimulus (700ms; this is a face (neutral, happy, angry or fearful) with eyes directed straight ahead in the face task or a horizontal bar in the

arrow/bar task), 4) the central cue stimulus (300ms; a face with direct or averted gaze in the face task and an arrowhead or horizontal bar in the arrow/bar task), 5) a peripheral target stimulus (a white square or diamond) presented with the central cue until a response is made or for a further 2500ms (whichever occurred earliest). Participants used a response box and were asked to use one of two response buttons to indicate whether the target was a square or diamond as quickly and accurately as possible. Participants were informed that the directional cues were not predictive of target location and, therefore, the optimal strategy in relation to eye movement behaviour was to maintain fixation on the central cue until the target appears (see *Figure 5.1*).

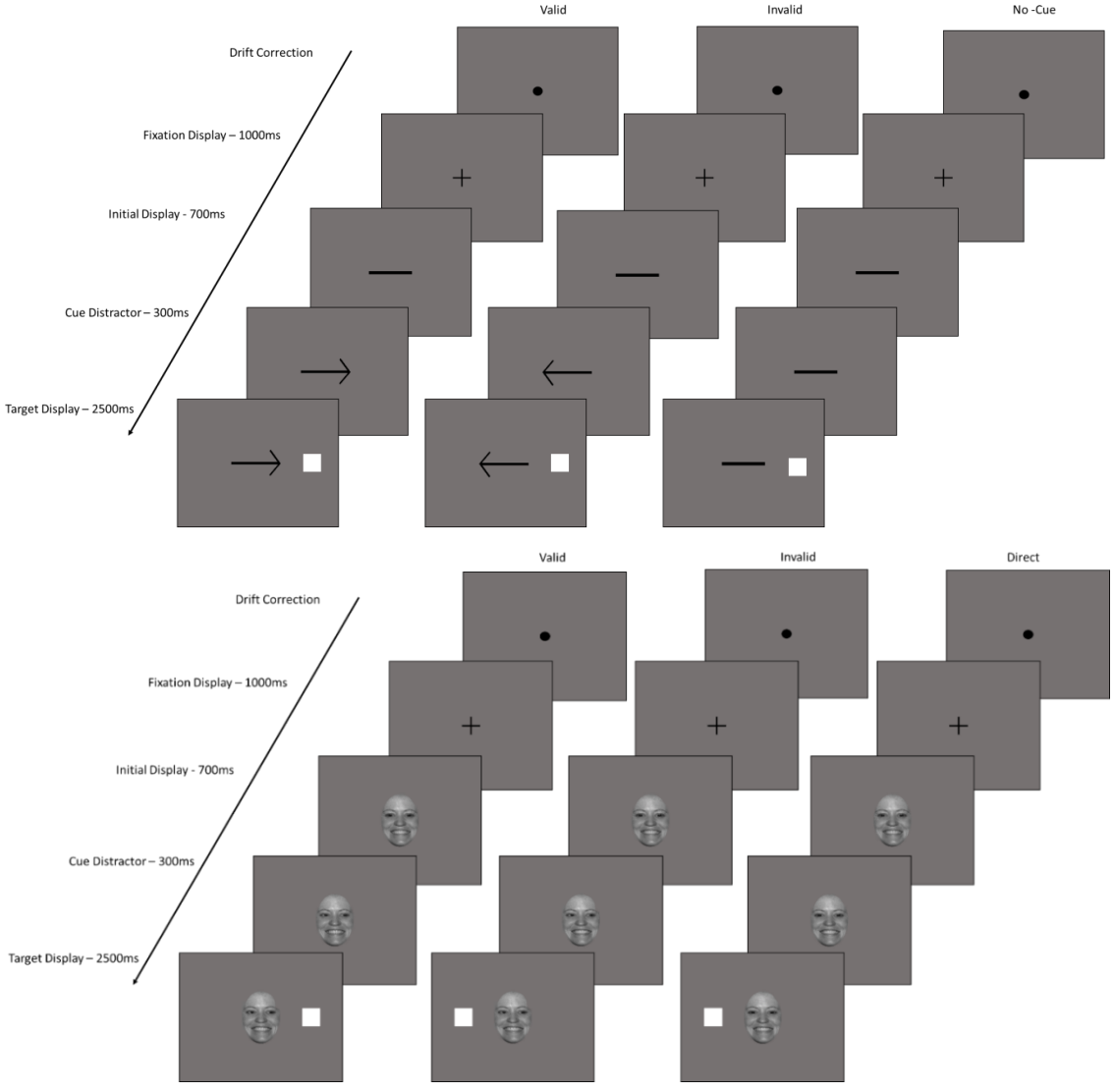

Figure 5.1: Trial Sequence of the Spatial Cueing Task. The top panel shows the non-social/arrow block for the valid, invalid and no-cue trials and the bottom panel shows an example of the social block, with a happy face used as a cue distractor across valid, invalid and direct eye-gaze trials.

5.3 Data Analyses

We performed linear mixed effects models (LMMs) using the lmer function from the lme4 package (Bates et al., 2015) in R (R, Core Team, 2017), to examine the effects of anxiety and ADHD symptoms on saccade onset latency in the presence of eye-gaze cue distractors and arrow cue distractors across validity trials (valid, invalid, no-cue) in children and adults. The saccade onset latency was defined as the time elapsed from the presentation of the cue distractor until the first correct saccade to the target.

We also performed generalised linear mixed effects models (gLMMs) using the glmer function from the lme4 package in R to examine the effects of anxiety and ADHD in saccadic errors (binary variable: 1 = error, 0 = no error) between children and adults and between eye-gaze cues and arrow cues across validity conditions (valid, invalid, no-cue). The saccadic errors were defined as the number of saccades made away from the target.

We ran two separate analyses including first: the participants' age group (adults vs. children), validity trials (valid, invalid, and no-cue), cue condition (eye-gaze vs. arrows), anxiety and ADHD symptoms (continuous variables) as fixed factors and second: emotional face cue distractors (happy, angry, fearful, and neutral faces), validity trials (valid averted gaze, invalid averted gaze and direct gaze), anxiety and ADHD symptoms as fixed factors, for both saccade latency and saccadic errors.

Participants were included as a random factor in a full random structure, including separate slopes and intercepts for validity and cue distractors. The full random structure for saccade accuracy model was trimmed down (due to 'failure to converge') until achieving the best- fitting model. The random structure for both saccade latency and accuracy included separated intercepts and slopes for cue condition and validity trials for the random effects of participants. Saccade latencies were log transformed to ensure normal distribution. All continuous variables were centred to reduce collinearity between main effects and interactions and the outliers were removed from the dataset (1%).

5.4 Results

5.4.1 Sample Characteristics

There was a significant effect of gender of saccade latency (*β* = -.12, SE = .03, *t* = -3.48, *p*< .01), showing that female had slower saccade latencies than males. There was no effect of gender on saccadic errors (*β* = -.01, SE = .08, *z* = -.01, *p*= .93).

5.4.2 Basic Task Performance

There was a significant validity effect on both saccade latency and saccadic errors. Saccade latency was faster for valid compared to invalid (*β* = -.11, SE = .01, *t* = 7.20, *p* < .001) and no-cue trials (*β* = -.10, SE = .02, *t* = -4.59, *p* < .001). Similarly, saccadic errors were fewer for valid than invalid (*β* = -2.68, SE = .07, *z* = -39.38, *p* < .001) and no-cue (*β* = -1.27, SE = .07, *z* = -17.98, *p* < .001) trials. There were also more saccadic errors for invalid compared to no-cue trials (*β* = 1.41, SE = .07, *z* = 19.17, *p* < .001).

5.4.3 Effects of Age, ADHD and Anxiety on Basic Task Performance

There was no significant main effect of age group (adults vs. children/adolescents) on either saccade latency (*β* = .07, SE = .04, *t* = 1.67, *p* = .10) or saccadic errors ((*β* = .11, SE = .06, *t* = 1.77, *p* = .08); Tables 5.1 and 5.2). There was also no main effect of ADHD or anxiety symptoms on saccade latency (ADHD: *β* = -.002, SE = .02, *t* = -.08, *p* = .93, anxiety: *β* = -.01, SE = .02, *t* = -.73, *p* = .47) and saccadic errors (ADHD: *β* = -.05, SE = .03, *z* = -1.79, *p* = .07, anxiety: *β* = .01, SE = .03, *z* = -.18, *p* = .85). However, there was a two-way interaction between ADHD symptoms and age group on saccade latency, showing that adults with elevated symptoms of ADHD had slower saccade latencies relative to children with elevated ADHD symptoms (*β* = -.12, SE = .04, *t* = -2.91, *p* < .01). Furthermore, ADHD symptoms interacted with validity trials and age group on saccadic errors. Increased ADHD symptoms in adults, compared to children, were associated with reduced saccadic errors for no-cue trials and increased saccadic errors for both valid (*β* = -.36, SE = .14, *z* = -2.50, *p* < .05) and invalid (marginally significant effect: *β* = .27, SE = .14, *z* = 1.90, *p* =.06) trials (see *Figure 5.2*). These findings suggest that symptoms of ADHD were associated poorer attentional processing and increased attentional costs in adults compared to children.

There was also a three-way interaction among anxiety symptoms, validity trials and age group on saccadic errors. Increased anxiety symptoms in adults, compared to children, were associated reduced saccadic errors for valid and increased errors for no-cue trials (β = .43, SE = .14, z = -3.08, p < .01), suggesting that adults with increased anxiety showed attentional facilitation to directional cues relative to children and adolescents (see *Figure 5.3*).

Table 5.1: *Mean Saccade Latency (ms) for Social and non-Social Cue Distractors across Validity Trials in Children and Adults.*

Saccade Latency						
	Children		Adults		All	
	Social	Non-Social	Social	Non-Social	Social	Non-Social
Valid	197.07 (87.38)	175.30 (68.51)	170.57 (64.63)	162.36 (63.14)	183.47 (77.66)	168.65 (66.10)
Invalid	210.99 (83.20)	200.02 (77.82)	191.06 (71.37)	181.73 (62.92)	201.37 (78.32)	190.49 (71.02)
No-Cue	211.70 (109.58)	198.92(85.30)	189.84 (78.87)	191.70 (90.10)	199.34 (94.03)	194.58 (88.22

Table 5.2: *Mean Saccadic Accuracy (saccadic directional error rates) for Social and non-Social Cue Distractors across Validity Trials in Children and Adults.*

Saccadic Accuracy						
	Children		Adults		All	
	Social	Non-Social	Social	Non-Social	Social	Non-Social
Valid	.46 (.50)	.11 (.33)	.42 (.49)	.17 (.38)	.44 (.50)	.14 (.35)
Invalid	.77 (.42)	.90 (.30)	.73 (.44)	.84 (.36)	.75 (.43)	.87 (.34)
No-Cue	.54 (.50)	.58 (.49)	.56 (.50)	.49 (.50)	.55 (.50)	.52 (.50)

Note: Standard deviations are shown in the parentheses

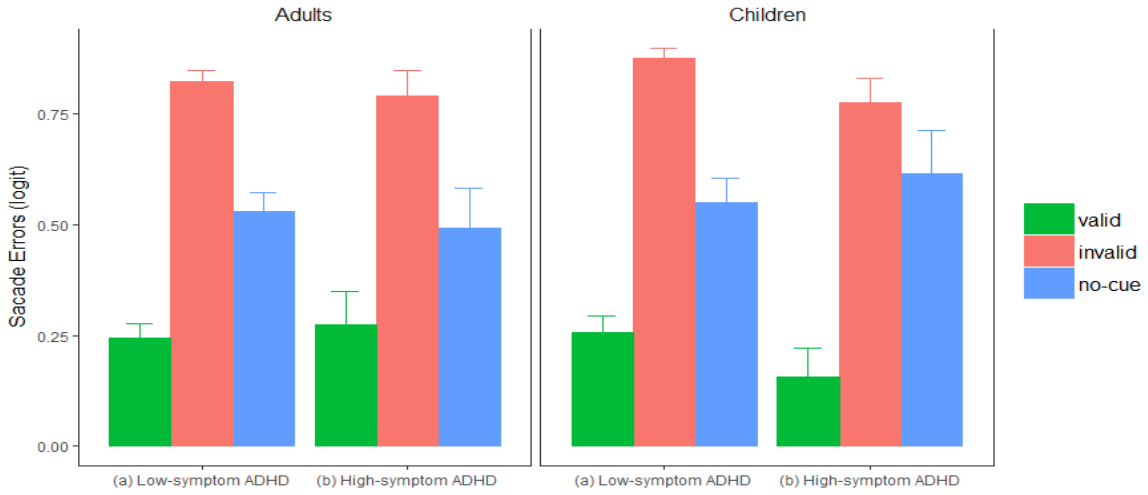

Figure 5.2: Saccadic Errors (shown in logit values) as a function of ADHD symptoms, age group (adults vs children) and validity trials. For a better visualisation, ADHD symptoms were divided in low-and – high symptom based on the lower and upper quartiles. Error bars represent 95% confidence intervals.

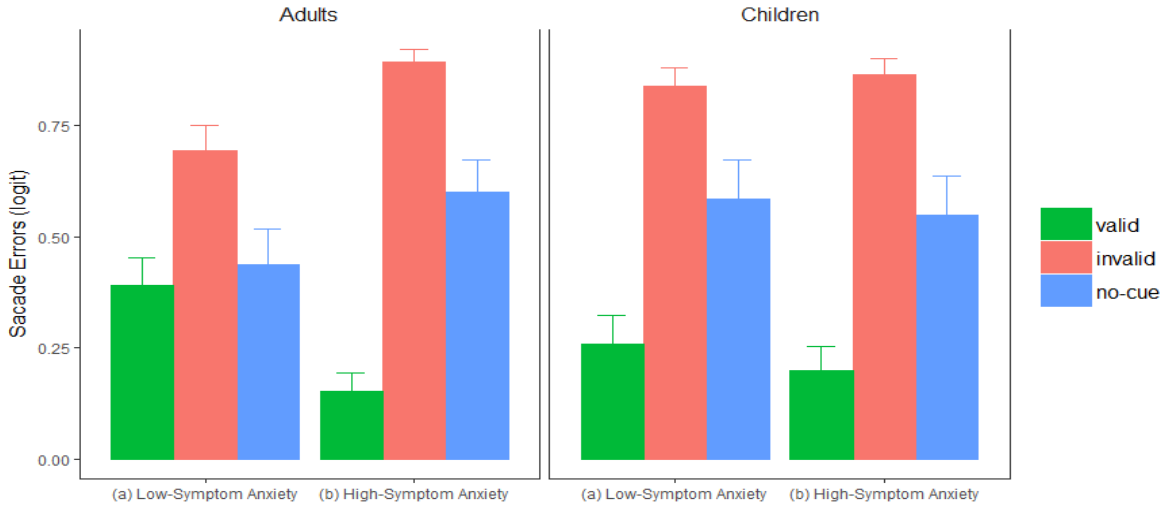

Figure 5.3: Saccadic Errors (shown in logit values) as a function of anxiety symptoms, age group (adults vs children) and validity trials. For a better visualisation anxiety symptoms were divided in low-and – high symptom based on the lower and upper quartiles. Error bars represent 95% confidence intervals.

In addition, there was no significant interaction between anxiety symptoms or ADHD symptoms and validity trials, on saccade latency. However, increased anxiety symptoms were associated with fewer saccadic errors for valid relative to no-cue (β = -.24, SE = .12, z =

-2.07, $p < .05$) and invalid ($\beta = .31$, SE = .17, $z = 1.84$, $p = .06$) trials). In contrast, increased symptoms of ADHD were associated with fewer errors for invalid relative to no-cue trials ($\beta = .24$, SE = .11, $z = 2.10$, $p < .05$).

5.4.4 Effects of Eye-Gaze Cues vs Arrow Cue Distractors

Eye-gaze cues were associated with slower saccade latencies ($\beta = .06$, SE = .02, $t = 2.67$, $p < .05$) and more saccadic errors ($\beta = .28$, SE = .06, $z = 4.84$, $p < .001$) compared to arrow cue distractors. There was a better cueing effect for arrows compared to eye-gaze cue distractors as manifested through slower saccade latency for valid averted gaze cues than invalid (marginally significant effect:$\beta = .04$, SE = .02, $t = 1.97$, $p = .05$, and direct ($\beta = .06$, SE = .02, $t = 2.85$, $p < .01$) gaze cues relative to arrow cues. Similar result was also found for saccadic errors. There was a reduction in saccadic errors for invalid (vs. direct) gaze ($\beta = -1.04$, SE = .15, $z = -7.12$, $p < .001$) gaze cues and increased saccadic errors for valid (vs. direct) gaze ($\beta = 1.59$, SE = .14, $z = 11.21$, $p < .001$) relative to arrow cues. These results indicated that cueing effect was larger for arrows compared to eye-gazes.

5.4.5 Effects of Facial Emotional Expressions on Saccadic Performance

There was a significant main effect of emotional facial expressions on saccade latency, showing that fearful faces were associated with slower saccade latencies relative to angry faces ($\beta = -.04$, SE = .02, $t = -2.56$, $p < .05$). There was no other significant effect of emotional facial expressions on neither saccade latency nor saccadic errors.

5.4.6 Effects of Facial Emotional Expressions and Eye-Gaze Cues on Saccadic Performance

Saccade latencies were faster for valid gaze of fearful relative to happy faces and slower for direct gaze of fearful (vs. direct happy) faces ($\beta = .10$, SE = .04, $t = 2.94$, $p < .05$), suggesting attentional benefits for fearful (vs happy) faces. Better cueing effect and attentional facilitation for fearful gaze cues was also found for saccadic errors. Saccadic errors were fewer for valid fearful compared to valid angry faces but increased for both direct ($\beta = -.71$, SE = .26, $z = -2.76$, $p < .01$), and invalid gaze ($\beta = -.62$, SE = .24, $z = -2.60$, $p < .01$) of fearful compared to direct and invalid angry faces, respectively. In addition, saccadic errors increased for valid angry (vs valid happy) faces and reduced for invalid angry relative to invalid happy faces ($\beta = .49$, SE = .24, $z = 2.05$, $p < .05$), suggesting better cueing

effect for eye –gaze cues of happy (vs angry) faces. Collectively, these results showed that emotional facial expressions modulated eye-gaze cueing effect with better cueing effect found for fearful relative to angry and happy faces, and happy faces relative to angry faces.

5.4.6.1 **Effects of anxiety symptoms and "emotional eye-gaze" cues.** Anxiety symptoms interacted with emotional facial expressions on saccadic performance. Increased anxiety symptoms were associated with increased saccadic errors for angry faces and reduced saccadic errors for fearful (β = -.23, SE = .12, z = -2.00, p < .05) and happy (a marginally significant effect: β = -.21, SE = .11, z = -1.88, p = .06) faces.

Increased anxiety symptoms were also associated with faster saccade latency for invalid happy compared to neutral face trials and slower saccade latency for direct happy compared to direct neutral faces (β = .09, SE = .04, t = 2.02, p < .05), suggesting higher attentional costs for neutral (vs happy) eye-gaze cues (see *Figure 5.4*). Increased anxiety symptoms were generally associated with better gaze cueing and attentional benefits on saccade latency for angry faces compared to other facial expressions (see *Figure 5.4*), however, these effects were just under statistical significance (contrasts comparisons for a) angry/neutral with valid/direct (β = -.08, SE = .04, t = -1.90, p = .06), b) angry/happy faces with valid/invalid (β = -.07, SE = .04, t = -1.89, p = .06), and c) angry/fearful with valid/invalid (β = .07, SE = .04, t = 1.85, p = .06)).

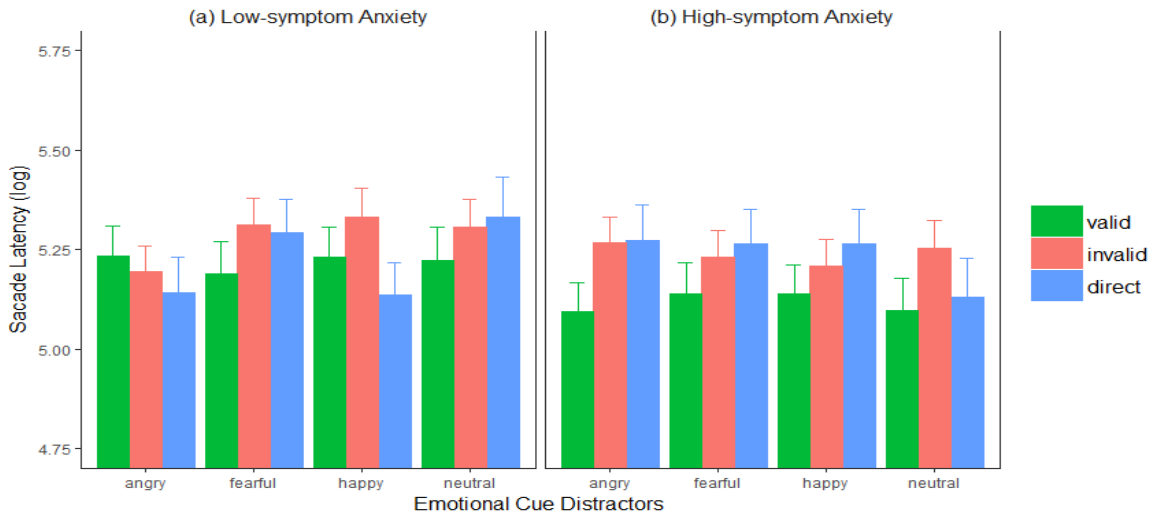

Figure 5.4: Saccade onset latency (shown in log values) as a function of anxiety symptoms, validity trials and emotional cue distractors. For a better visualisation, anxiety symptoms were divided in

low-and – high symptom based on the lower and upper quartiles. Error bars represent 95% confidence intervals.

5.4.6.2 **Effects of ADHD symptoms and "emotional eye-gaze" cues.** Interactions among ADHD symptoms, eye-gaze validity trials and emotional cue distractors on saccade latency, showed that ADHD symptoms were associated with a general poorer cueing effect for angry faces. Increased ADHD symptoms were associated with faster saccade latencies for valid averted gaze of neutral compared to valid angry faces and slower saccade latency for invalid averted gaze of neutral compared to invalid angry faces (β = -.07, SE = .03, t = -2.04, p < .05) (see *Figure 5.5*).

Increased symptoms of ADHD were associated with fewer saccadic errors for direct angry (β = .69, SE = .27, z = 2.57, p < .05) and direct neutral (β = -.72, SE = .27, z = 2.68, p < .01) face compared to direct fearful face trials and more saccadic errors for invalid gaze of invalid angry and neutral (vs invalid fearful) faces (*Figure 5.6*). These findings suggest that eye-gaze cues of angry and neutral (relative to fearful) faces were associated with greater emotional interference and increased attentional costs for individuals with elevated ADHD symptoms.

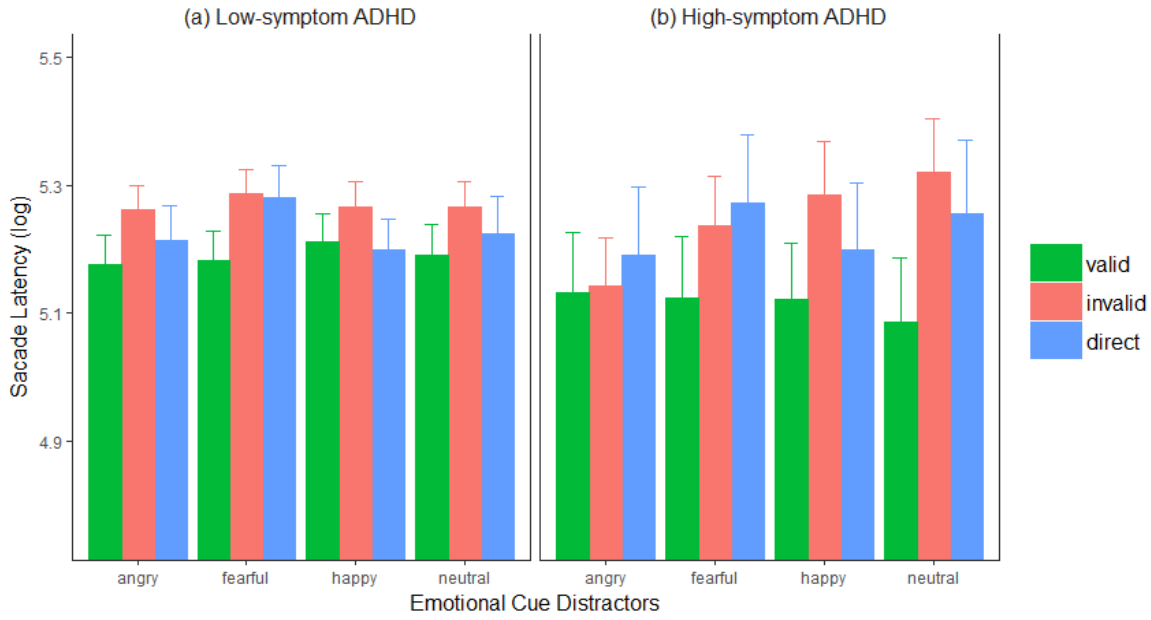

Figure 5.5: Saccade onset latency (shown in log values) as a function of ADHD symptoms, validity trials and emotional cue distractors. For a better visualisation ADHD symptoms were divided in low-and – high symptom based on the lower and upper quartiles. Error bars represent 95% confidence intervals.

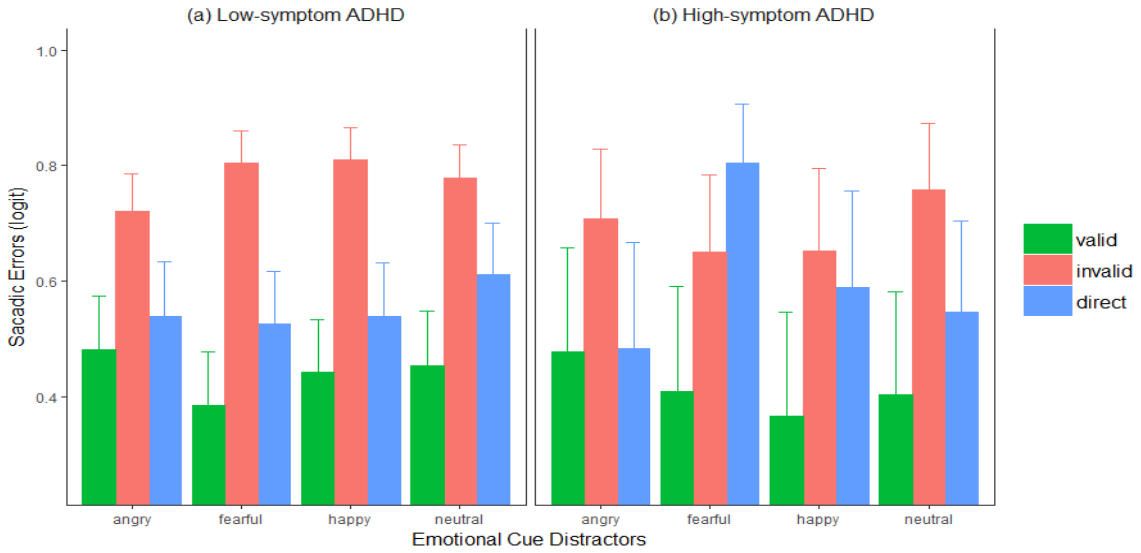

Figure 5.6: Saccadic Errors (shown in logit values) as a function of ADHD symptoms, validity trials and emotional cue distractors. For a better visualisation ADHD symptoms were divided in low-and – high symptom based on the lower and upper quartiles. Error bars represent 95% confidence intervals.

5.4.6.3 **The interaction between ADHD and anxiety symptoms.** There were three way interactions among symptoms of ADHD, anxiety and eye-gaze validity trials on both saccadic errors (see *Figure 5.7)* and saccade latency[6]. The results showed reduced cueing effect for elevated ADHD symptoms that was improved with elevated symptoms in both ADHD and anxiety. Specifically, elevated ADHD symptoms and fewer anxiety symptoms were associated with increased saccadic errors for valid compared to invalid averted (β = .39, SE = .18, z = 2.20, p < .05) and direct gazes (β = -.44, SE = .16, z = -2.70, p < .01)), whereas increased in both ADHD and anxiety symptoms were associated with reduced saccadic errors for valid compared to invalid and direct gaze cues.

[6] Similar to saccadic accuracy, there was a marginally significant interaction on saccade latency showed that increased ADHD symptom but fewer anxiety symptoms were associated with slower saccade latencies for valid compared to direct eye-gaze cues. Increased in both ADHD and anxiety symptoms were associated with faster saccade latencies for valid-averted gazes and slower saccade latency for direct eye-gaze cues (β = .05, SE = .02, t = 1.82, p = .08).

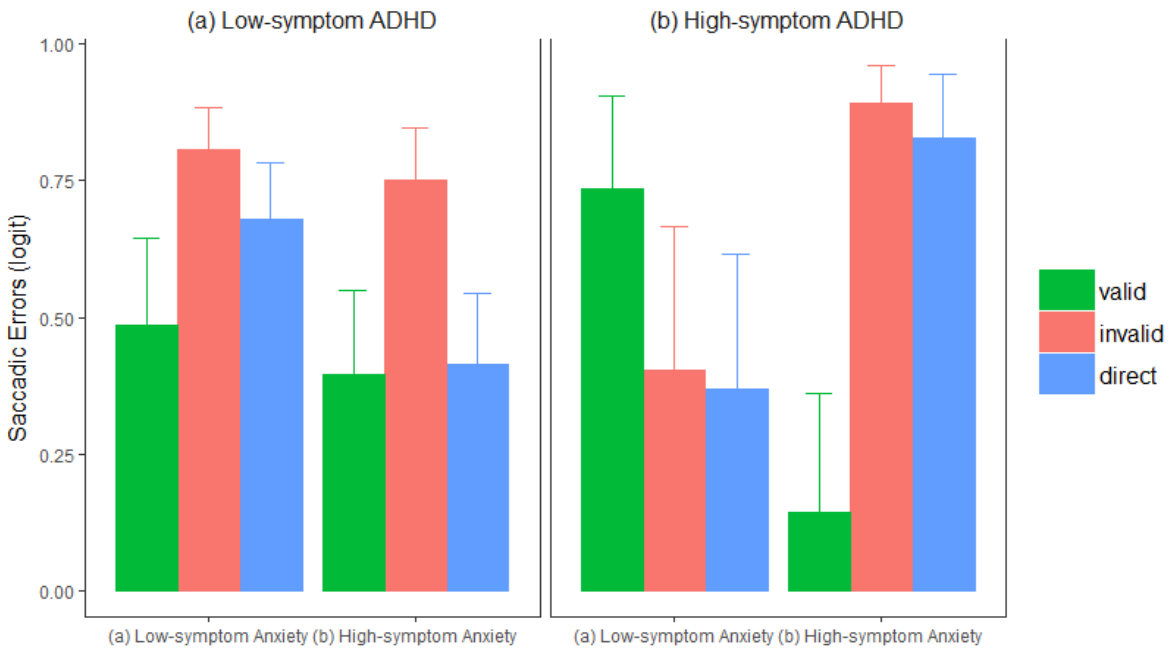

Figure 5.7: Saccadic Errors (shown in logit values) as a function of ADHD and anxiety symptoms and validity (valid vs. invalid) trials. For a better visualisation ADHD and anxiety symptoms were divided in low-and – high symptom based on the lower and upper quartiles. Error bars represent 95% confidence intervals.

Finally, three-way interactions among symptoms of ADHD, anxiety and emotional facial expressions on saccade latency showed that increase in both ADHD and anxiety symptoms was associated with difficulties disengaging attention (i.e., slower saccade latencies) from fearful compared to angry (β = .04, SE = .02, t = -2.17, p < .05) and happy (β = .04, SE = .02, t = 1.97, p = .05) faces; effect that was opposite with elevated ADHD symptoms and fewer anxiety symptoms (see *Figure 5.8*).

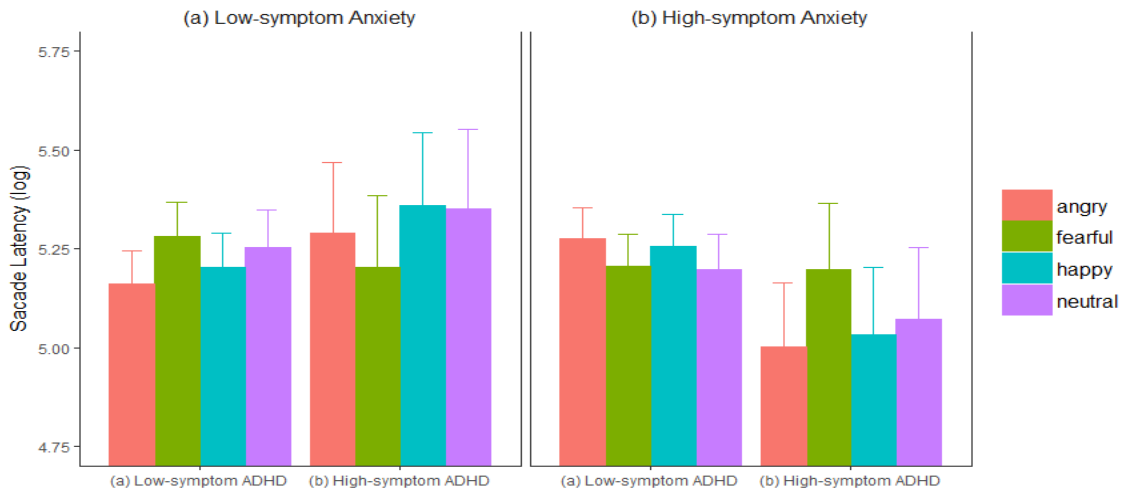

Figure 5.8: Saccade onset latency (shown in log values) as a function of ADHD and anxiety symptoms and emotional cue distractors. For a better visualisation ADHD and anxiety, symptoms were divided in low-and – high symptom based on the lower and upper quartiles. Error bars represent 95% confidence intervals.

5.5 Discussion

This study examined the effects of ADHD and anxiety symptoms on attentional orienting following symbolic and eye-gaze cue distractors from emotional faces (happy, angry, fearful and neutral) in children/adolescents and adults. First, we found that arrows were associated with stronger validity effect compared to eye-gaze cues. Saccadic errors were reduced for invalid (vs direct) gaze cues and increased for valid (vs. direct) gazes. Second, the emotional valence of the facial cues modulated the gaze cueing effect. Eye gaze cueing for fearful faces was associated with attentional benefits (i.e., faster saccade latency for valid fearful and slower saccade latency for direct fearful (vs. happy faces) and better cueing effect (i.e., fewer saccadic errors for valid fearful more errors for direct and invalid fearful compared to direct and invalid angry faces). Better cueing effect was also found for happy relative to angry faces gaze cues (i.e., increased errors for valid angry and reduced for invalid angry compared to happy faces). Third, symptoms of anxiety and ADHD modulated gaze cueing differently in young people and adults. Increased anxiety symptoms in adults were associated with attentional facilitation following directional cues, relative to younger people with increased anxiety symptoms. In contrast, increased ADHD symptoms in adults were associated with slower saccade latencies and fewer saccadic errors for no-

cue trials and increased saccadic errors for both valid and invalid trials, when compared to younger people. Fourth, high ADHD symptoms were associated with poorer gaze cueing effect (i.e., reduced errors for invalid relative to no-cue trials). Fifth, anxiety symptoms were associated greater emotional interference for angry faces (i.e., increased saccadic errors) compared to the other facial emotional expressions (regardless of the validity condition of the gaze direction), but better cueing effect and attentional facilitation following gaze cueing for angry compared to neutral and fearful faces. In contrast, ADHD symptoms were associated with poorer gaze cueing and higher attentional costs for angry faces compared to other emotional expressions. Finally, the interactive effect between ADHD and anxiety symptoms showed that elevated symptoms of both ADHD and anxiety, were associated with better cueing effect (i.e., fewer saccadic errors for valid compared to invalid and direct gaze cues) and increased disengagement difficulties (i.e., slower saccade latencies) for fearful (vs angry and happy) faces. This effect was opposite to that found with increased symptoms of ADHD (and fewer anxiety symptoms).

Attentional orienting following symbolic/arrow cues was associated with stronger validity effect compared to gaze cueing effect. This finding is in line with previous work supporting automatic orienting following arrow cues (Ricciardelli et al., 2002), but is not consistent with some accounts arguing that biologically-relevant cues such as eye-gazes, produce similar automatic orienting effects with that of symbolic cues, such as arrows (e.g. Kuhn et al., 2009; Kuhn & Kingstone, 2009). However, it may be possible that the current findings related to poorer gaze cueing effect, are attributed to the emotional valence of the stimuli, since facial expressions were presented prior to the presentation of the eye-gaze cues, in the trial sequence of the task.

We showed that gaze cueing effect for fearful faces was stronger compared to that for happy and angry faces. Better gaze cueing effect was also found for happy relative to angry faces. A number of studies, has previously demonstrated that gaze direction for fearful faces produced stronger cueing effect (Carlson, 2016; Kuhn & Tipples, 2011; Pecchinenda et al., 2008), however evidence on gaze cueing benefit for happy relative to angry faces is less consistent. Previous studies demonstrated an earlier processing facilitation for happy faces compared to neutral faces (e.g. Fichtenholtz, Hopfinger, Graham, Detwiler, & LaBar, 2007), supporting a motivational approach-oriented behaviour for happy faces, that can emerge in social circumstances associated with the presence of

potential reward. Overall, our findings highlight that negative emotional expressions are more likely to modulate gaze cueing effect to elicit automatic orienting compared to positive emotions, with fearful gaze cues to be associated with greater effects on attentional orienting, probably due to their high salience to indicate the presence of potential threat in the environment.

Adults with elevated anxiety levels showed attentional facilitation (i.e., fewer saccadic errors for valid cue distractors versus no-cues), compared to children with elevated anxiety. This finding suggests that anxiety symptoms interfere with attentional orienting in response to directional cues more for children relative to adults. Previous studies demonstrated similar findings, with young people high in trait anxiety showing greater interference, with slower reaction times for fearful face distracters in a 2-back working memory task, compared to adults with high trait anxiety (Ladouceur et al., 2009). Although there is limited research in the development of attentional processes in high anxious individuals in the absence of emotional information, our findings suggest that there are developmental differences on interference control and attentional orienting processes in anxious individuals. In addition, considering the fact that non-directional cues require employment of voluntary/endogenous attentional resources compared to spatially predictive cues (i.e., valid cues), this finding supports previous evidence on impaired voluntary attentional control in adults with increased anxiety levels (Eysenck & Derakshan, 2011; Eysenck et al., 2007).

In contrast, adults with increased ADHD showed poorer cueing effect and slower responses following directional cues, compared to children/adolescents with increased ADHD symptoms. This finding suggests symptoms of ADHD have a greater, negative impact on attentional orienting processes in adults relative to children. Children with ADHD may rely more on automatic attentional processes when orient their attention to the target compared to adults with ADHD. This is in line with previous studies showed that children with ADHD show intact exogenous attentional orienting but impaired endogenous attentional orienting (Gupta & Kar, 2009; Jonkman, 2005). In addition, since more endogenous attentional orienting is required in the presence of no-cue conditions compared to directional cues (that elicit more automatic responses), slower saccade latencies for no-cue trials in adults with ADHD could be attributed to disrupted executive control processes (review by Willcutt et al., 2005).

Elevated anxiety symptoms were associated with increased number of errors for angry faces compared to fearful and happy faces, regardless of the eye-gaze cues. This effect might be associated with greater interference and increased distractibility associated with angry facial emotional expressions and anxious individuals. However, this was not found for saccade latency, which contrasts previous accounts supporting that anxious individuals show disengagement difficulties from threat related stimuli (such as angry faces) compared to non-threating stimuli (such as neutral faces), when used similar paradigms (Fox, Russo, Bowles, & Dutton, 2001; Fox, Mathews, Calder, & Yiend, 2007) and other paradigms (e.g. Richards et al., 2012). However, increased anxiety symptoms were associated with attentional facilitation following gaze cues for angry relative to neutral, happy and fearful faces. In line with these findings, the results from our Go/No-Go task showed faster attentional disengagement in response to centrally presented angry relative to happy faces. As discussed, in Chapter 3, increased vigilance in high anxious individuals is associated with attention facilitation towards threatening information (i.e. with faster responses towards threatening stimuli) (review by Cisler & Koster, 2010); evidence found in both high trait anxiety (Bradley et al., 2000) and clinical anxiety (Chen et al., 2002).

In addition, even though results did not reach statistical significance, our findings supported a dissociation on attentional orienting following eye-gaze cues from angry and fearful faces. That is, with increased anxiety, the gaze cueing effect for angry faces was associated with faster saccade latencies for valid and slower for invalid cues, when compared to the cueing effect elicited by fearful gazes. This finding however, contradicts previous evidence on eye-gaze cue in response to fearful and angry faces in individuals with high trait anxiety (Fox et al., 2007). The differences between our findings and the results by Fox et al. (2007) could be attributed to a number of methodological issues. For example, in the study by Fox et al. (2007), direct and averted gaze cues were separately analysed, and thus a direct comparison between the two cue conditions as well as potential interactive effects were not directly examined. In addition, in the study by Fox et al. (2007) averted gaze cues were collapsed and analysed across 300ms and 700ms SOAs (stimulus onset asynchronies), during which cueing effect may have elicited different effect. Evidence shows that stronger cueing effect for central cues is elicited within 300ms (Frischen et al., 2007), and that reflexive cueing effects decline at longer SOAs (*see* also Friesen & Kingstone, 1998). In the current study, we also examined attentional orienting effects

based on saccadic performance instead of manual RTs, that allow a more accurate measure of temporal attentional effects for target detection and we considered interactions between validity cues from emotional expressions across averted and direct gazes within the same analysis at SOA of 300ms.

Individuals with increased anxiety levels showed increased difficulty to disengage attention from happy direct faces and faster attentional orienting following invalid averted gaze of happy compared to neutral faces. In line, a previous study that examined attentional biases in the presence of angry, happy and neutral faces using a central cueing task, showed that adults with high trait anxiety showed slower responses for both happy and angry faces compared to neutral faces (Mogg, Holmes, Garner, & Bradley, 2008). Similarly, preferential attentional allocation was previously found for both angry and happy relative to neutral stimuli in socially anxious individuals (e.g. Garner, Mogg, & Bradley, 2006). These findings suggest that attentional biases for emotional stimuli in anxiety might not be unique to threat-related information (such as angry faces), but disrupted attentional processes and interference effect might be influenced by also positive task-irrelevant stimuli.

Contrary to the effects of anxiety symptoms, eye-gaze cues of angry faces constituted a weaker social cue for individuals with more ADHD symptoms compared to eye-gaze cues of neutral faces. The current findings showed that individuals with high levels of ADHD had fewer saccadic errors for direct gaze angry and neutral faces and fewer errors for invalid angry and neutral compared to fearful gaze cues, showing higher attentional costs for angry and neutral relative to fearful faces. These findings suggest that angry and neutral faces are associated with greater emotional interference for individuals with ADHD. Previous studies found that individuals with ADHD showed more difficulties encoding angry compared to happy and neutral faces (e.g. Ichikawa et al., 2014; Pelc, Kornreich, Foisy, & Dan, 2006). In addition, our results from Chapter 3 showed that elevated symptoms of ADHD were associated with disrupted attentional processing in response to angry relative to happy faces Overall, these findings support that individuals with higher symptoms ADHD are characterised by an increased difficulty to reflexively orient attention following social cues such as eye-gaze and this difficulty becomes greater in the presence of angry faces, compared to neutral faces

The interactive effect between symptoms of ADHD and anxiety showed that performance accuracy for individuals with more ADHD symptoms but fewer anxiety symptoms was associated with poor cueing effect, whereas increased anxiety symptoms in ADHD were associated with improved cueing effect. This finding suggests that elevated anxiety symptoms may act as a 'protective' factor for attentional orienting deficits in ADHD. This is in line with previous studies demonstrated that the presence of anxiety in ADHD was associated with better attentional control (Rodríguez et al., 2014; Schatz & Rostain, 2006), however evidence specific to attentional orienting processes in ADHD and anxiety is still limited. One study that examined attentional networks in children with anxiety disorders, non-clinical anxiety and ADHD showed that executive attention (i.e., difference between invalid and valid cue distractors) did not differ between anxiety disorders and comorbid ADHD (Mogg et al., 2015). However, children with ADHD were benefitted more from the spatial information of cue (showing the location of target presentation) compared to children with anxiety disorders and typically developing children, suggesting that attentional orienting might be more compromised in ADHD than in anxiety. Consistently, Chapters 3 and 4 showed that the anxiety symptoms in individuals with ADHD were associated with compensatory effect to the disrupted attentional processing found in individuals with elevated ADHD and lower anxiety symptoms.

Finally, our results showed that regardless of the eye-gaze cues, elevated symptoms of both ADHD and anxiety were associated with faster attentional disengagement from angry and happy faces relative to fearful faces. However, increased ADHD but lower anxiety symptoms were associated with slower disengagement (i.e., slower saccade latencies) of angry and happy faces compared to fearful faces. This finding shows that increased anxiety symptoms counteracted the effects associated with elevated ADHD specific to emotional interference control. In addition, faster saccade latencies for angry relative to fearful faces were found in the current study, regardless of the individual differences in ADHD and anxiety symptoms. Therefore, it could be argued that the elevated of both anxiety and ADHD symptoms relative to emotional interference, was associated with typical performance.

In summary, the current study provides evidence on the effects of ADHD and anxiety symptoms and their interaction on attentional orienting in the presence of social and non-social cue distractors. This study demonstrates differential effects between symptoms of

ADHD and anxiety that are associated with attentional orienting. Individuals with more ADHD symptoms showed difficulty to follow social directional cues and challenges to control emotional interference specific to angry faces. Individuals with increased anxiety levels showed typical performance on attentional orienting following directional cues but increased disengagement difficulties from angry faces compared to other neutral expressions. In addition, angry faces acted as a stronger cue for individuals with increased anxiety compared to other emotional expressions, which may reflect adaptive behaviour towards potential threats. In terms of the interactive effects between ADHD and anxiety symptoms, increased anxiety counteracted the effects of ADHD on attentional orienting in response to directional cues and emotional cue distractors. Increase in both ADHD and anxiety symptoms showed disengagement difficulties from fearful compared to angry and happy faces, emphasising increased sensitivity to environmental threat; an effect that reflected typical performance and was opposite to that observed with increased ADHD symptoms and fewer anxiety symptoms.

Chapter 6 The Effects of ADHD and GAD Symptoms on Attentional Orienting following Emotional "Eye-Gaze" Cues

6.1 Introduction

A number of studies have examined the influence of emotional expression typical populations, following eye-gaze cues and found that fearful expressions can enhance gaze cueing and lead to faster responses on valid compared to invalid trials, when compared to neutral faces in (Carlson, 2016), indicating that attention is enhanced by a signal for potential threat. Other studies showed that gaze cueing does not differ across emotional expressions (Graham et al., 2010; Hietanen & Leppänen, 2003). Further research has found than following gaze cues automatically for fearful faces is most evident in individuals with high anxiety levels (Fox, Mathews, Calder, & Yiend, 2007; Holmes, Richards, & Green, 2006; Mathews, Fox, Yiend, & Calder, 2003). However, a number of studies demonstrated that individuals with high levels of anxiety did not show a similar gaze cueing effect for angry faces, but instead, showed slower attentional disengagement from angry faces when looking straight ahead (with a direct gaze) (e.g. Fox et al., 2007; Hu, Gendron, Liu, Zhao, & Li, 2017), suggesting that direct gaze enhances perception of angry faces, whereas gaze cueing is facilitated be fearful ones. Our evidence from the spatial cueing task used in Chapter 5 on children/adolescents and adults with trait anxiety showed better gaze cueing effect and attentional facilitation for angry faces compared to fearful, happy and neutral gaze cues.

Although extensive research has examined attentional biases in anxiety, the majority of existing studies have focused on individual differences in subclinical (typically trait) anxiety. One recent study examined attentional orienting in the presence of emotional facial cue distractors in adults with Generalised Anxiety Disorder (GAD) (Yiend et al., 2015), and found faster attentional disengagement from centrally presented angry faces, when compared to neutral and happy faces. The same study showed that individuals with GAD demonstrated faster disengagement from fearful, compared to neutral faces, but eye-gaze cueing effect did not interact with the emotional valence of the facial cues. These findings

may indicate that individuals with GAD showed attentional avoidance in the presence of threatening stimuli and thus, contradict previous evidence on gaze cueing from emotional faces in subclinical anxiety (Fox et al., 2007; Mathews et al., 2003).

In addition, previous studies that examined the effects of anxiety levels on attentional orienting in response to gaze cues and emotional expressions did not consider or controlled for comorbid conditions, such as ADHD (Jarrett & Ollendick, 2008; Souza et al., 2005). Evidence on attentional orienting, in the context of eye-gaze cues in ADHD, is also scarce with mixed findings. For example, individuals with ADHD showed reduced tendency to reflexively respond to eye-gaze cues but they show typical orienting effect to non-social stimuli (i.e. directional arrows) (Marotta et al., 2014, 2017), thus highlighting challenges specific to social communication and interactions for individuals with ADHD.

This chapter extends on previous work from Chapter 5 on attentional orienting and interference control using social and non-social cues while considering the effects of ADHD and GAD symptoms. Chapter 5 showed that trait anxiety was associated with greater interference for angry faces (i.e., more saccadic errors), regardless of the eye-gaze cue conditions, compared to the other facial emotional expressions (i.e., happy, fearful and neutral), but better cueing effect following eye-gaze cues of angry faces compared to other facial expressions. We also showed that ADHD symptoms were associated with poorer cueing effect for angry faces compared to other neutral expressions. The synergistic effects between trait anxiety and ADHD showed that increased anxiety symptoms in ADHD were associated with better cueing effect and faster disengagement (i.e., faster saccade latencies) for angry and happy faces relative to fearful faces; effect that was opposite to that found with increased symptoms of ADHD (and fewer anxiety symptoms).

Here, we extend these findings on trait anxiety and ADHD symptoms and we examined the effects of GAD and ADHD symptoms in attentional orienting in children and adolescents using the same paradigm on the effects of: (1) eye-gaze and arrow cue distractors on valid, invalid and no-cue trials and (2) eye-gaze cues from emotional face (happy, angry, fearful and neutral) cue distractors on valid, invalid and direct eye-gaze trials.

Based on our previous finding, we predicted that symptoms of ADHD will be associated with reduced validity effect, especially for eye-gaze cues of angry facial

expressions. This will manifest with slower disengagement (slower saccade latencies) and increased emotional interference (increased saccadic errors) for angry eye-gaze cues compared to neutral and other facial emotional expressions (fearful and happy faces). We hypothesised that the effect of emotion in attentional orienting during which angry faces with direct gaze will be associated with slower disengagement (i.e. slower saccade latencies) towards the target compared to happy, fearful and neutral faces with direct gaze, for individuals with more GAD symptoms. We also hypothesised that more GAD symptoms will be associated with better cueing effect following eye-gaze cues of angry faces (i.e., faster saccades and fewer saccadic directional errors towards the target for valid compared to invalid and direct eye-gazes) compared to averted gaze of fearful, happy and neutral eye-gaze cues. We also, predicted that that young people with elevated in both GAD and ADHD symptoms will be associated with better cueing effect compared to young people with elevated ADHD symptoms and fewer GAD symptoms.

6.2 Method

6.2.1 Participants

Participants' characteristics and measures of ADHD and anxiety symptoms are described in Chapter 4 in sections 4.2.1 and 4.2.2, respectively.

6.2.2 Experimental Paradigm

The spatial cueing task was described in Chapter 5, section 5.2.3.

6.2.3 Data Analyses

We performed linear mixed effects models (LMMs) using the lmer function and generalised linear mixed effects models (gLMMs) using the glmer function from the lme4 package (Bates, Maechler, Bolker, & Walker, 2015) in R (R, Core Team, 2017), to examine the effects of GAD and ADHD symptoms on saccade onset latency and saccadic errors (binary variable: 1 = error, 0 = no error) respectively in the presence of eye-gaze cue distractors and arrows across validity trials (valid, invalid and no-cue). The saccade onset latency was defined as the time elapsed from the presentation of the cue distractor until

the first correct saccade to the target. The saccadic errors were defined as the number of saccades made away from the target. We used validity trials (valid, invalid, and no-cue), cue distractors (arrows vs eye-gazes), GAD and ADHD symptoms (continuous variables) as fixed factors for both outcome measures. We further examined the effects of GAD and ADHD symptoms on both saccade onset latency and saccadic errors in the presence of eye-gaze cue distractors of emotional faces (happy, angry, fearful, and neutral) across validity conditions. We used validity trials (valid, invalid, and no-cue), cue distractors (happy, angry, fearful and neutral faces), GAD and ADHD symptoms (continuous variables) as fixed factors for both measures.

Participants and Trial number were used as random factors in a maximal random structure. The models were trimmed in a top-down method until convergence (Barr et al., 2013). The random structure for saccade latency included random intercepts for the random effects of participants and trials. The random structure for both saccade accuracy included separated intercepts and slopes for both the cue condition and validity trials for the random effects of participants. The saccade latencies were log transformed to ensure normal distribution. All continuous variables were centred to reduce collinearity between main effects and interactions and around 2% of the data was removed due to outliers.

6.3 Results

6.3.1 Sample Characteristics

There was a significant main effect of gender on saccade latency (β = .08, SE = .04, t = 2.02, p < .05,) showing that females had slower saccade latencies than males. There was no significant effect of gender on saccadic errors (β = .09, SE = .07, z= 1.30, p = .19). There was also no effect of estimated IQ on saccade latency (β = -.002, SE = .002, t = -1.34, p = .18) and saccadic errors (β = -.005, SE = .003, z = -1.73, p = .10).

6.3.2 Basic Task Performance

There was a significant validity effect for both saccade latency and saccadic errors. Valid trials revealed faster saccade latencies (β = -.11, SE = .01, t = -8.23, p < .001) and

fewer saccadic errors (*β* = -2.26, SE = .09, *z* = -24.17, *p* < .001) than invalid trials. In addition, valid trials revealed faster saccade latencies (*β* = -.05, SE = .01, *t* = -3.84, *p* < .001) and fewer saccadic errors (*β* = -1.11, SE = .09, *z* = -11.85, *p* < .001) compared to no-cue trials. There was also slower saccade latency (*β* = .05, SE = .01, *t* = 3.38, *p* < .01) and more saccadic errors (*β* = 1.15, SE = .08 *z* = -14.42, *p* < .001) for invalid compared to no-cue trials (Table 6.1).

Table 6.1*: Mean Saccade Latency (ms) and Saccadic Accuracy (saccadic directional error rates) for Social and non-Social Cue Distractors across Validity Trials.*

	Saccade Latency		**Saccadic Accuracy**	
	Social	Non-Social	Social	Non-Social
Valid	209.10 (99.90)	191.07 (89.54)	.57 (.49)	.20 (.40)
Invalid	228.06 (106.02)	215.17 (98.54)	.77 (.42)	.88 (.32)
No-Cue	219.13 (119.37)	213.01(101.23)	.63 (.48)	.59 (.49)

6.3.3 Effects of ADHD and GAD symptoms on Basic Task Performance

ADHD symptoms were positive associated with saccadic errors (*β* = .09, SE = .05, *z* = 2.01, *p* <.05). ADHD symptoms did not interact significantly with validity trials on saccadic errors (*β* = .07, SE = .06, *z* = 1.26, *p* = .21.) However, higher ADHD symptoms were associated with reduced cueing effect as manifested through increased saccade latency for valid and reduced saccade latency for invalid trials (*β* = -.03, SE = .01, *t* = -2.28, *p* < .05).

Symptoms of GAD interacted significantly with validity trials on saccadic directional errors. Contrasts comparisons showed that increased GAD symptoms were associated with poorer cueing effect and attentional costs, as manifested through increased saccadic errors for valid compared to invalid (*β* = .27, SE = .11, *z* = 2.37, *p* < .001) and no-cue (*β* = .19, SE = .09, *z* = 2.13, *p* < .05) trials. In addition, a marginally significant effect showed that increased GAD symptoms were also associated with reduction in saccadic errors for invalid compared to no-cue trials (*β* = -.13, SE = .08 *z* = -1.78, *p* = .07).

6.3.4 Effects of Eye-Gaze vs Arrow Cue Distractors on Saccadic Performance

There was a main effect of cue condition on outcome measures, showing that there was slower saccade latency (β = .06, SE = .02, t = 3.30, p < .01) and more saccadic errors (β = .38, SE = .06 z = 6.40, p < .001) for eye-gaze cues compared to arrow cues (Table 6.1). Validity trials interacted significantly with cue conditions for both saccade latencies and saccadic errors. The validity effect was reduced for eye-gaze compared to arrow cue distractors, as manifested through increased saccade latency for valid compared to no-cue (β = .07, SE = .02, t = 3.53, p < .001) and invalid trials (β = .04, SE = .02, t = 2.06, p < .05), for eye-gaze relative to arrow cues. Similarly, the cueing effect was reduced for eye-gaze compared to arrow cue distractors on saccadic errors as manifested through reduced saccadic errors on invalid (vs. no-cue) trials for eye-gaze cues (β = 1.04, SE = .15 z = 6.96, p < .001), and increased saccadic errors for valid compared to no-cue (β = 1.53, SE = .15 z = 9.95, p < .001) and invalid (β = -2.57, SE = .15 z = -14.87, p < .001) trials on eye-gaze (vs. arrow) cue distractors. These findings indicate that arrow cue distractors produced stronger cueing effect relative to that of eye-gaze cues.

6.3.4.1 **Effects of GAD symptoms and "emotional eye-gaze" cues.** Symptoms of GAD interacted significantly with emotional face cues on saccade latency. Contrast comparisons showed that individuals with high GAD symptoms showed faster saccade latencies for angry (β = .04, SE = .01, t = 2.89, p < .01), fearful (β = .05, SE = .01, t = 3.29, p < .001) and neutral (β = .03, SE = .01, t = 2.50, p < .05) face cue distractors, relative to happy face cue distractors.

There were also three-way interactions with GAD symptoms interacted significantly with eye-gaze validity trials and emotional cue distractors on saccadic errors (see *figure 6.1).* First, individuals with high GAD symptoms showed increased saccadic errors for direct gaze of fearful compared to angry faces and reduced saccadic errors for invalid fearful compared to invalid angry faces (β = .45, SE = .21, z = 2.12, p < .05), suggesting that increased GAD symptoms were associated with higher costs following angry eye-gaze cues (i.e., participants followed invalid averted gaze of angry faces more than fearful ones).

Second, high GAD symptoms were associated with increased saccadic errors for direct gaze of fearful (β = .42, SE = .20, z = 2.11, p < .05) and neutral (β = .42, SE = .20, z =

2.11, $p < .05$) face cue distractors compared to direct gaze of happy faces, but increased saccadic errors for valid happy compared to valid fearful and valid neutral face cue distractors. These results show that young people with elevated GAD symptoms showed attentional facilitation following fearful and neutral (vs happy) eye-gaze cues.

Third, increased GAD symptoms were associated with increased saccadic errors for valid eye-gazes of happy compared to valid neutral (β = -.39, SE = .19, z = -1.99, $p < .05$) and angry faces (marginally significant effect: β = .38, SE = .20, z = 1.90, p = .06), but reduced saccadic errors for invalid averted gaze of happy compared to invalid neutral and angry faces, respectively. This finding indicated that increased GAD symptoms were associated with better cueing effect for angry and neutral relative to happy eye-gaze cues.

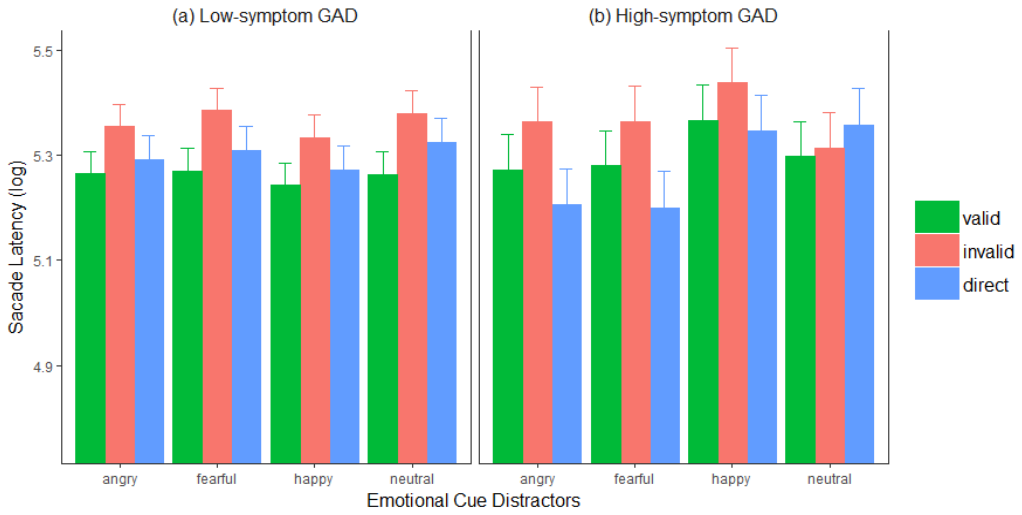

Figure 6.1: LMMs effects on Saccade onset latency (shown in log values) as a function of GAD symptoms, validity trials and emotional cue distractors. For a better visualisation, GAD symptoms were divided in low-and – high symptom based on the lower and upper quantiles. Error bars represent 95% confidence intervals.

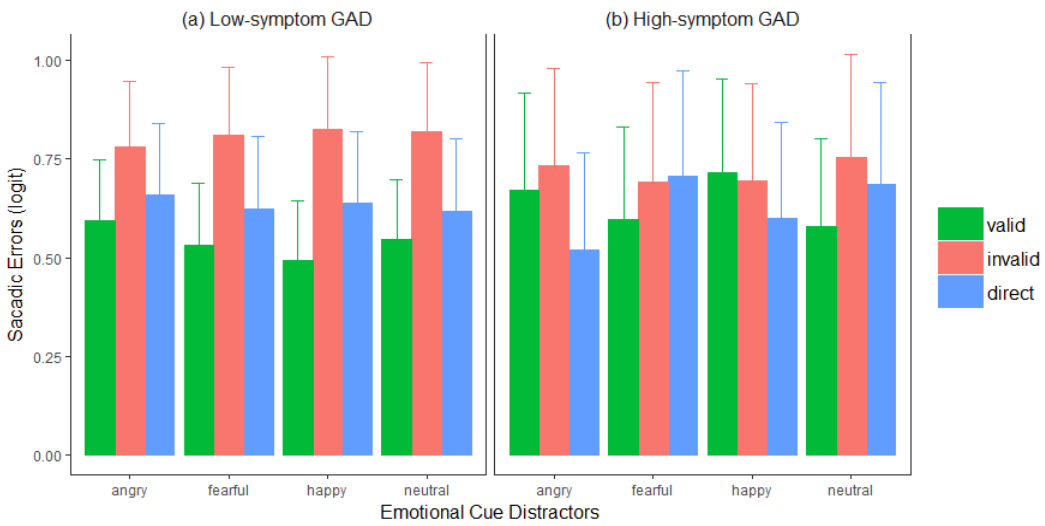

Figure 6.2: GLMMs effects of saccadic errors (shown in logit values) as a function of GAD symptoms, validity trials and emotional cue distractors. For a better visualisation, GAD symptoms were divided in low-and – high symptom based on the lower and upper quantiles. Error bars represent 95% confidence intervals.

6.3.4.2 **Effects of ADHD symptoms and "emotional eye-gaze" cues.** ADHD symptoms interacted significantly with the emotional facial expressions on saccade latency, showing that higher ADHD symptoms were associated with faster saccade latencies for happy compared to neutral (β = .03, SE = .01, t = 1.96, p < .05) face cue distractors, supporting reduced interference from positive emotional expressions. This effect was interacted further with validity trials, such that increased ADHD symptoms were associated with increased saccade latency for direct neutral than happy faces and increased saccade latency for valid averted gaze of happy (vs valid neutral) face cue distractors (β = .08, SE = .04, t = 2.14, p < .05), indicating reduced attentional benefits for neutral relative to happy eye-gaze cues.

In addition, individuals with high ADHD symptoms showed increased saccade latency for direct gaze of neutral compared to fearful face cue distractors and increased latency for valid averted gaze of fearful compared to valid neutral faces (β = -.12, SE = .04, t = -3.22, p < .01), indicating attentional benefits for eye-gaze cues of neutral relative to fearful faces. Similarly, a marginally significant effect showed increased ADHD symptoms were associated with faster saccade latencies for valid gaze of neutral compared to valid fearful and increased saccade latencies for invalid neutral relative to invalid fearful faces (β = .06, SE = .03, t = 1.84, p = .06). These findings indicate that individuals with increased ADHD

symptoms showed poorer cueing effect following eye-gaze cues of fearful compared to neutral faces (see *figure 6.3*).

In addition, increased ADHD symptoms were associated with slower saccade latencies for direct gaze of angry (vs. direct fearful) face cue distractors and slower saccade latency for invalid (β = -.08, SE = .03, t = -2.24, p < .05) and valid (β = .08, SE = .04, t = 2.34, p < .05) gaze cues of fearful compared to invalid and valid eye-gaze cues of angry faces respectively. This finding showed that direct gaze of angry faces was associated with greater disengagement difficulties relative to direct fearful faces and averted eye-gaze of fearful faces were associated with poorer cueing effects relative to those of angry faces, for young people with increased ADHD symptoms.

There were also three-way interactions among symptoms of ADHD, validity trials from eye-gaze cues and emotional facial expressions on saccadic errors, suggesting that negative emotional expressions (angry and fearful faces) were associated with poorer cueing effects compared to eye-gaze cueing from neutral faces. Specifically, increased ADHD symptoms were associated with increased saccadic errors for direct neutral (vs angry) faces and reduced saccadic errors for valid gaze of neutral (vs. angry) faces (β = .62, SE = .20, z = 3.03, p < .01). Similarly, increased ADHD symptoms were associated with increased saccadic errors for direct neutral compared to direct fearful faces and fewer saccadic errors for valid neutral compared to valid fearful faces (β = -.49, SE = .21, z = -2.33, p < .05). A marginally significant interaction showed that increased ADHD symptoms were associated with more errors for valid averted gaze of fearful (vs neutral) faces and invalid averted gaze of neutral (vs fearful) faces ((β = .39, SE = .21, z = 1.88, p = .06), see *figure 6.4))*

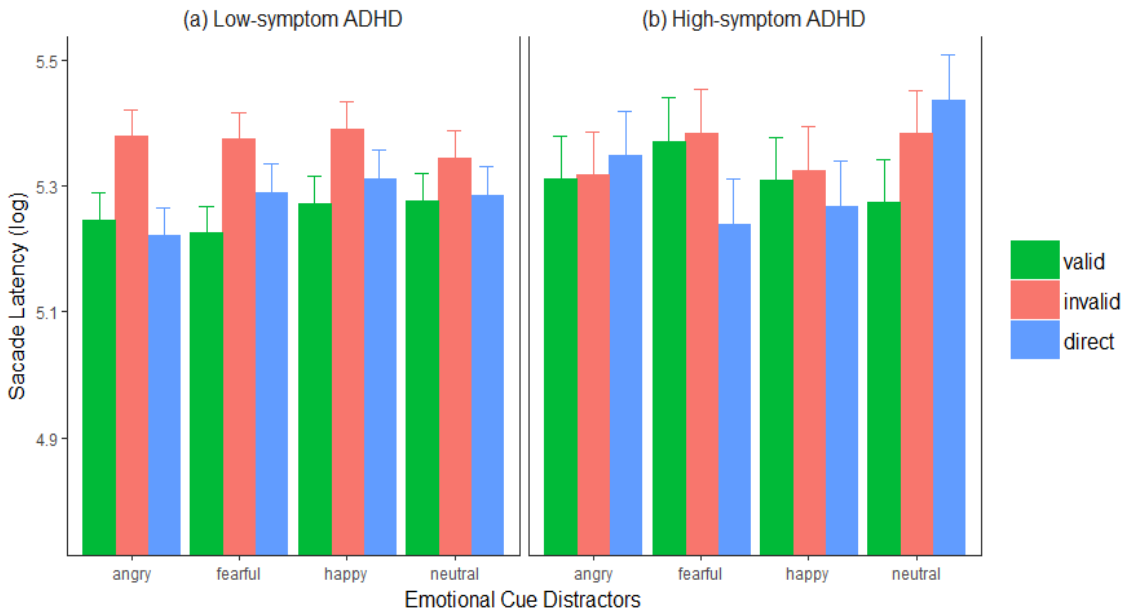

Figure 6.3: LMMs effects of Saccade onset latency (shown in log values) as a function of ADHD symptoms, validity trials and emotional cue distractors. For a better visualisation ADHD symptoms were divided in low-and – high symptom based on the lower and upper quantiles. Error bars represent 95% confidence intervals.

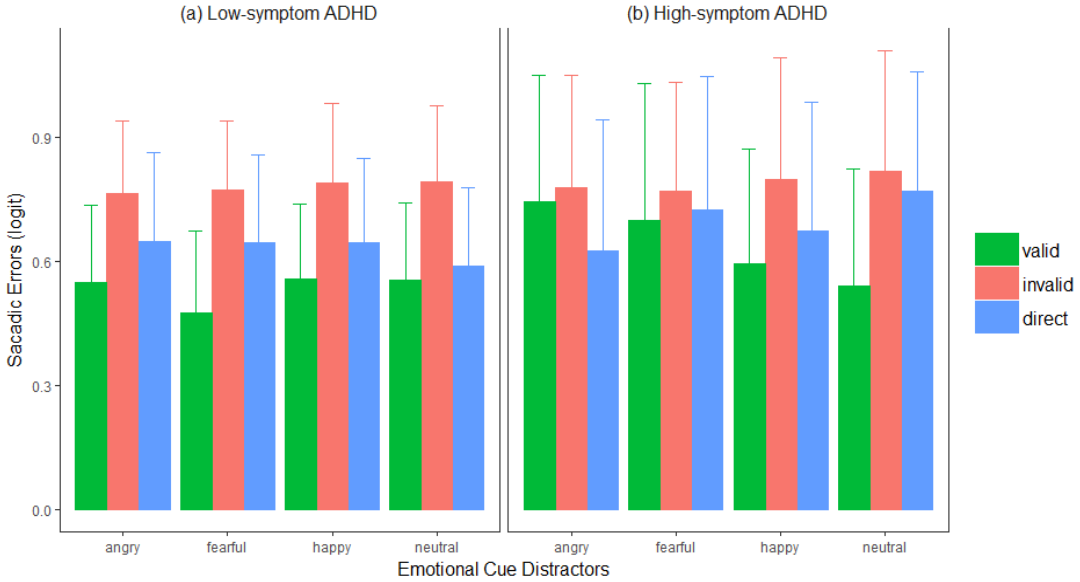

Figure 6.4: GLMMs effects of saccadic errors (shown in logit values) as a function of ADHD symptoms, validity trials and emotional cue distractors. For a better visualisation ADHD symptoms were divided in low-and – high symptom based on the lower and upper quantiles. Error bars represent 95% confidence intervals.

6.3.4.3 **The interaction between ADHD and GAD symptoms.** There was no significant interaction among ADHD, GAD symptoms and emotional faces on the outcome measures. However, GAD and ADHD symptoms interacted significantly with validity trials on saccadic errors, showing that poorer cueing effect associated with elevated ADHD symptoms was improved with elevated symptoms of both ADHD and GAD. Specifically, elevated symptoms of ADHD were associated with reduced saccadic errors for invalid compared to valid (β = .19, SE = .09, z = 2.15, p < .05) and no-cue (β = .20, SE = .07, z = 2.72, p < .01) distractors, whereas increase in both ADHD and GAD symptoms was associated with increased saccadic errors for invalid relative to valid and no-cue distractors (see *figure 6.5*).

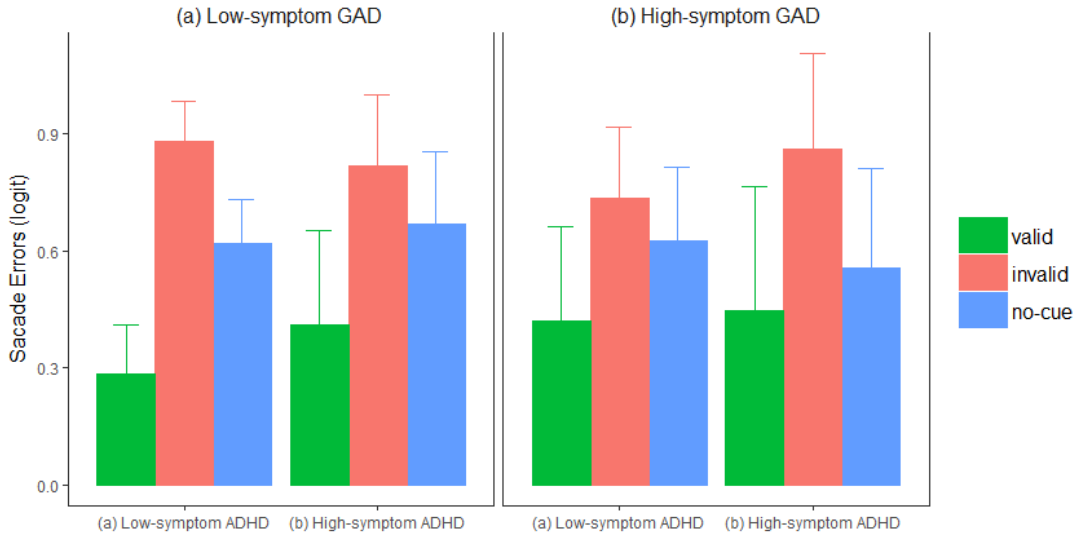

Figure 6.5: GLMMs effects from the three-way interaction among ADHD symptoms, GAD symptoms and validity trials on Saccadic errors (shown in logit values). For a better visualisation ADHD and GAD symptoms were divided in low-and – high symptom based on the lower and upper quantiles. Error bars represent 95% confidence intervals.

6.4 Discussion

This study examined the effects of eye-gaze cues and interference from emotional faces on attentional orienting in children and adolescents with ADHD and GAD. First, we replicated the findings from Chapter 5, showing stronger, more automatic orienting of attention following arrow cues relative to eye-gaze cues. In addition, individuals with increased GAD symptoms showed increased saccadic errors for valid compared to invalid

and no-cue trials, supported a poorer cueing effect. A similar pattern was found for individuals with increased ADHD symptoms (i.e., ADHD symptoms associated with slower saccade latencies for valid compared to invalid trials). Young people with increased GAD symptoms showed faster responding for negative emotional expressions (fearful and angry faces) and neutral faces compared to positive emotional expressions (happy faces). This effect was modulated by gaze cueing, such that young people with increased GAD symptoms showed stronger gaze cueing and attentional facilitation for gaze cues of negative emotional expressions as well as neutral faces relative to happy gazes. Furthermore, young people with increased GAD symptoms followed invalid gaze of angry more than fearful faces, but showed more saccadic errors for direct gaze of fearful relative to angry faces. Attentional orienting in young people with increased ADHD symptoms was associated with better cueing effect following neutral eye-gaze cues relative to happy, angry and fearful eye-gaze cues, thus supporting reduced emotional interference control for ADHD. In addition, increased levels of ADHD were associated with greater disengagement difficulties for direct gaze of angry (vs fearful) faces, and better cueing following eye gazes of angry (vs fearful) faces were associated with stronger cueing effect for individuals with increased ADHD symptoms. Finally, in line with the results from Chapter 5, the interactive effects between ADHD and GAD showed that elevated symptoms of ADHD (with reduced GAD symptoms) were associated with poorer cueing effect, whereas elevated symptoms in both ADHD and GAD were associated with better cueing effect (i.e., more saccadic errors for invalid and direct eye-gaze cues relative to valid-averted gaze cues).

Young people with increased GAD symptoms showed poorer automatic orienting following directional cue distractors compared to those with lower GAD symptoms. This finding may reflect increased distractibility that characterises anxious individuals (e.g. MacNamara & Proudfit, 2014). Previous evidence on reduced attentional orienting and increased distractibility in high anxious individuals is mainly derived from emotional and particularly, threat-related contexts (i.e., presence of fearful faces) (e.g. Mathews et al., 2003; Tipples, 2006). However, the effects we found here were regardless of the affective context of the stimuli. This finding also supports the results we found in Chapter 5 in regards to the greater negative effects of anxiety symptoms in children and adolescents relative to adults. Specifically, we found that increased trait anxiety in young people was

associated with poorer cueing effect, similar to the results found here for young people with increased GAD symptoms. Together these findings suggest that evidence from subclinical levels of anxiety on attentional orienting following directional cues, in younger populations, can be generalised to clinical anxious populations.

Poorer attentional cueing effect following directional cue distractors was also found for young people with increased ADHD symptoms (i.e., ADHD symptoms associated with slower saccade latencies for valid compared to invalid trials). This finding showed greater attentional disengagement from directional cues and thus supports previous accounts on reduced processing efficiency and slower responding in individuals with ADHD (Adams, Milich, & Fillmore, 2010; Andreou et al., 2007; Nigg, Swanson, & Hinshaw, 1997).

Increased symptoms of GAD were associated with faster saccade latencies for angry, fearful and neutral faces, relative to happy faces, indicating that negative and neutral faces were associated with faster disengagement, relative to happy faces. Faster attentional disengagement from threat-related faces (such as fearful and angry faces) is in line with the vigilance-avoidance hypothesis (Mogg, Bradley, Miles, & Dixon, 2004) in which, attentional biases and initial facilitation of threat detection is followed by avoidance (moving attention away from threat) in anxious individuals ,thus reflecting an attempt for anxious individuals to reduce stress and discomfort (Cisler & Koster, 2010; Mogg & Bradley, 2016). In support, a recent study that examined attentional orienting in the presence of centrally presented emotional faces in adults with GAD and showed faster disengagement from and fearful faces relative to happy or neutral faces (Yiend et al., 2015). Earlier evidence showed attentional biases away from angry faces in a dot probe task in adolescents (aged 9-17) diagnosed with GAD, compared to healthy controls (Monk et al., 2006). However, these findings contradict evidence showing increased attentional biases towards (rather than away from) angry faces in adults with GAD (e.g. Mogg, Millar, & Bradley, 2000), and further highlight potential developmental differences in GAD underpinning attentional responses in emotional information. Further evidence has demonstrated that high trait anxiety was associated with slower responding in both angry and happy faces compared to neutral ones (Derakshan & Koster, 2010). In this study (Derakshan & Koster, 2010), participants were required to identify the different target face within a 'crowd' of faces. Adults with high trait anxiety showed slower response processing when an angry face appeared in a happy crowd

and vice versa than when a neutral face was either a target or a crowd. However, whether the slower responding was driven by happy, angry or both faces, was unclear. In addition, a previous study employed a visual search paradigm and showed that adults high in trait anxiety showed slower responses for happy relative to angry faces, when the emotional valence of the stimuli was task irrelevant (Dodd, Vogt, Turkileri, & Notebaert, 2017).

In addition, young people with increased GAD showed better cueing effect and attentional facilitation for averted eye-gaze cues of negative and neutral faces compared to happy faces. Previous studies showed that threat-related facial expressions (i.e., fearful faces) elicits stronger eye-gaze cueing effect in anxious individuals compared to that of happy facial expressions (Putman, Hermans, & van Honk, 2006; Tipples, 2006), which supports the current findings. A number of studies have shown that anxious individuals often interpret neutral or ambiguous stimuli as threatening (Mathews & MacLeod, 2005; Mogg & Bradley, 2016). This 'interpretation bias' may explain the similar pattern of results including the stronger cueing effect (i.e., fewer errors for valid vs invalid and direct-gaze cues) found in both negative and neutral eye-gaze cues relative to the happy gaze cues, in the current study. Our results from subclinical (trait) anxiety in children and adults also showed that averted gaze of angry faces were associated with stronger cueing effects compared to other facial emotional expressions (see Chapter 4).

Young people with high GAD symptoms showed differential effects of processing angry and fearful faces. GAD symptoms were associated with higher emotional interference and increased attentional costs for following eye-gaze cues of angry relative to fearful faces (due to more saccadic errors found for invalid averted gaze of angry faces than fearful faces). Our results from Chapter 5 showed that high levels of trait anxiety were associated with better cueing effect for eye-gaze cues of angry faces (i.e., faster saccade latencies for valid and slower for invalid cues) compared to fearful faces. Even though, we did not replicate this finding, we showed that young people with elevated GAD symptoms followed angry gaze cues more than fearful ones, which reflected increased attentional costs. As discussed in Chapter 5, these findings, however, contradict evidence suggesting stronger cueing effect for fearful than angry faces (Fox et al., 2007). The differences between our findings and the results by Fox et al. (2007) could be attributed to a number of methodological issues. For example, in the study by Fox et al. (2007), direct and averted gaze cues were separately analysed, and thus a direct comparison between the two cue

conditions as well as potential interactive effects were not directly examined. In addition, in the study by Fox et al. (2007) averted gaze cues were collapsed and analysed across 300ms and 700ms SOAs (stimulus onset asynchronies), during which cueing effect may have elicited different effect. Evidence shows that stronger cueing effect for central cues is elicited within 300ms (Frischen et al., 2007), and that reflexive cueing effects decline at longer SOAs (*see* also Friesen & Kingstone, 1998). In the current study, we also examined attentional orienting effects based on saccadic performance instead of manual RTs, that allow a more accurate measure of temporal attentional effects for target detection and we considered interactions between validity cues from emotional expressions across averted and direct gazes within the same analysis at SOA of 300ms.

Contrary to the effects of anxiety, young people with ADHD symptoms were also associated with poorer interference control and greater disengagement difficulties for direct angry faces compared to fearful ones, with averted eye-gaze of angry faces associated with better cueing effect than those of fearful faces. Evidence on emotion recognition deficits in ADHD consistently reported for negative emotional faces (Williams et al., 2008); fearful (e.g. Aspan et al., 2014; Miller, Hanford, Fassbender, Duke, & Schweitzer, 2011) and angry (e.g. Köchel, Schäfer, & Schienle, 2012; Kochel, Leutgeb, & Schienle, 2013; Pelc, Kornreich, Foisy, & Dan, 2006) facial expressions. Our results show that angry direct faces were linked to higher interference and attentional disruption than direct fearful faces but eye-gaze cues were associated with less automatic orienting than angry eye-gaze cues. These findings have implications about social interaction and communication as well as peer relationships for young people with ADHD.

Furthermore, young people with increased ADHD symptoms showed an overall poorer eye-gaze cueing effect following emotional facial expressions (happy, angry and fearful), relative to neutral faces. This finding indicates that young people with high ADHD symptoms show greater disruption in attentional processing of social cues (i.e., eye-gaze) of emotional facial expressions (both positive and negative) compared neutral eye-gaze cues. In line with our predictions, individuals with ADHD show increased emotional interference and disrupted attentional orienting processes in the presence of emotional-loaded compared to non-emotional stimuli. Increased emotional interference and disruption in cognitive performance (i.e., working memory) was previously demonstrated in

children (Villemonteix et al., 2017) and adults (Marx et al., 2011) with ADHD, suggesting that emotionally loaded stimuli disrupt cognitive processes in ADHD.

Finally, the interactive effects between symptoms of ADHD and GAD with validity trials showed that individuals with increased ADHD and GAD symptoms made more saccadic errors for invalid cues compared to those with increased ADHD only or GAD only. This finding indicates that increased in ADHD and GAD together lead to typical cueing effect (such as that observed when both symptom levels were low). One study that examined attention network functioning (i.e., executive attention, alerting and orienting) in children with ADHD and anxiety, showed that even though children with anxiety disorders did not show evidence of disrupted attentional interference from valid or invalid cues, children with subclinical level of anxiety showed poorer interference control (Mogg et al., 2015). In the same study, and contrary to the current findings (showing reduced validity effect on saccade latency for children with increased ADHD symptoms), children with ADHD also showed poorer interference control from spatial cues; effects that remained significant after controlling for anxiety symptoms. However, these results were based on reaction time responses between invalid and valid cues and therefore may not directly examined the same processes regarding interference control, as the current study. Nevertheless, the interactive effects between ADHD and anxiety on attentional orienting in a similar paradigm was not previously examined but our results highlight distinct attentional processes that characterise young people with increased ADHD and anxiety.

In summary, the current study provides evidence on how symptoms of ADHD and GAD interact to affect attentional orienting in the presence of social cue distractors. The interactive effects between ADHD and GAD symptoms showed that high symptoms levels in both conditions is associated with higher influence of the spatial cues (both arrows and eye-gaze) regardless of the emotional valence of the stimuli. Furthermore, symptoms of ADHD and GAD separately have differential effects on attentional orienting performance in the presence of eye-gaze cues of emotional facial expressions. Evidence of ADHD symptoms may derive from reduced emotional sensitivity whereas evidence of anxiety may underlie increased sensitivity and hyper arousal towards specific emotional stimuli (i.e., threat-related stimuli) over others.

Overall, the current paradigm has not been widely examined using central

emotionally loaded stimuli with eye-gaze manipulations in the context of ADHD and/or GAD. This study should stimulate more research in the area as it has implications on social cognition and interaction in these populations. Future studies should consider the effect of task relevant over irrelevant stimuli as well as attentional processes that require responses towards or from emotional stimuli, and disentangle attentional engagement and disengagement processes.

Chapter 7 General Discussion

The aim of this thesis was to examine the synergistic effects between the symptoms of ADHD and anxiety on cognitive control and emotional processing. This programme of work examined saccadic eye-movements on two attentional paradigms that measure sustained attention, inhibitory control and attentional orienting processes using emotional and non-emotional stimuli. We considered cognitive and behavioural mechanisms in a healthy sample of children/adolescents and adults with subclinical symptoms of ADHD and anxiety. In addition, we extended findings from subclinical ADHD and anxiety, in larger sample of children and adolescents that consisted of a mixed clinical and subclinical sample and considered symptoms of ADHD and GAD on the same attentional mechanisms. This chapter provides a summary of the key empirical findings emerged from the studies of the thesis. In addition, it presents an integrative analysis with previous research to highlight how the findings fit with and extend current research. Following this, research and clinical implications of the findings are discussed. Finally, the strengths and limitations of the studies considered in this thesis are outlined, along with considerations for future research.

7.1 Summary of key findings

ADHD and anxiety are often comorbid conditions in child and adolescent and adult populations (Biederman, 2005; Jarrett & Ollendick, 2008). Difficulties with executive control and emotion processing are two core features associated with both ADHD and anxiety. Despite the high comorbidity rates, very few studies have aimed to understand the cognitive mechanisms underpinning the co-occurring symptoms of ADHD and anxiety.

7.1.1 Age-related effects on Attentional Processes related to ADHD and Anxiety symptoms

Considering the differences in task performance between children/ adolescents and adults with ADHD, our results from the Go/No-Go task, showed a trend towards greater disruption of attentional processing in adults compared to children with elevated symptoms of ADHD. This trend was modulated in the presence of emotional stimuli, showing slower responses for angry faces, relative to non-face stimuli in adults with

elevated symptoms of ADHD, compared to young people. We further replicated these findings and showed that ADHD symptoms had a greater negative impact (i.e., less accurate performance) on attentional orienting processes in adults compared to children, as indicated by increased attentional costs. This finding may be attributed to higher symptoms of inattention that might characterise adults relative to young people with ADHD. In support, previous evidence showed that symptoms of hyperactivity and impulsivity decline with age, whereas symptoms of inattention remain persistent over time (e.g. Biederman, 2000). In contrast, the effects of anxiety symptoms were associated with better attentional orienting processes (i.e., attentional facilitation in response to directional cues) for adults relative to children. However, age-related effects in individuals with elevated anxiety levels were not found in the Go/No-Go task. Previous studies showed that young people high in trait anxiety were affected by greater emotional interference that impaired cognitive control processes (i.e., working memory) compared to adults with high trait anxiety (Ladouceur et al., 2009). Although there is limited research in the development of attentional processes in high anxious individuals in the absence of emotional information, our findings suggest that there are developmental differences associated with interference control and attentional orienting processes in anxious individuals.

7.1.2 Effects of ADHD symptoms

Individuals with ADHD showed increased impairment in IC, reduced sustained attention and poorer attentional orienting processes, specifically when processing of angry faces was required and when responding to the eye-gaze cues of angry faces, relative to other facial emotional expressions and neutral faces. This finding fits with previous empirical studies showing IC deficits specific for angry, relative to happy and neutral faces in children (Kochel et al., 2013) and adults with ADHD (Köchel et al., 2012), suggesting that individuals with increased symptoms of ADHD show attentional control difficulties that are specific to the emotional valence of the stimuli used. Together, these findings support previous accounts of emotion dysregulation as a core deficits and a potentially diagnostic feature in ADHD (Shaw et al., 2014). In addition, individuals with elevated symptoms ADHD were characterised by reduced ability to control emotional interference to effectively use social cues such as eye-gaze. This finding extends previous research to demonstrate that cognitive control processes in ADHD, are further disrupted in the presence of emotionally-

loaded stimuli (Marx, Höpcke, Berger, Wandschneider, & Herpertz, 2013; Villemonteix et al., 2017).

From the results of Chapter 4, the effects of ADHD symptoms on performance in the Go/No-Go task showed reduced sustained attention with fewer attentional lapses, regardless of the emotional valence of the stimuli, suggesting a more general attentional deficit that characterises young people with ADHD. Even though the age related findings in Chapter 3 did not reach statistical significance, it may be possible that disrupted attentional processing seen in negative emotional contexts (i.e. angry faces) is driven by ADHD symptoms in the adult population. These findings also, support previous accounts on cognitive heterogeneity in ADHD, where individuals may not be characterised by a common single cognitive deficit, but instead some individuals show persistent deficits in specific cognitive domains while some others do not (Nigg, Willcutt, Doyle, & Sonuga-Barke, 2005; Salum et al., 2014; Sonuga-Barke, 2002, 2005). For example, we found that subclinical levels of ADHD on disrupted attentional processing was specific to the emotional content being processed (Chapter 4), however, we also showed that our mixed clinical and subclinical sample showed more attentional lapses, thus reduced sustained attention, regardless of the emotional content of the stimuli (Chapter 4)

7.1.3 Effects of Anxiety Symptoms

Increased subclinical levels of anxiety were associated with more efficient processing for angry relative to happy faces (Chapter 3). However, in the absence of the social component (eye-gaze cues), subclinical levels of anxiety were associated with greater emotional interference that led to poorer performance in the presence of angry relative to other facial emotions (Chapter 5). However, this finding was not evident in young people with elevated GAD symptoms. Rather, young people with GAD symptoms showed overall faster responding in the presence of negative emotional expressions (fearful and angry faces) compared to positive emotional expressions (happy faces). Recent studies have demonstrated faster attentional disengagement in response to centrally presented angry faces relative to other emotional expressions in adults with GAD (but not elevated trait anxiety), using similar paradigms (Yiend et al., 2015). This, further highlights that there might be differential processes linked to the attentional biases towards threat-related stimuli between clinical and subclinical levels of anxiety. However, in the study by Yiend et

al. (2015), the presence of eye-gaze cues on emotional faces did not modulate attentional orienting effect.

In addition, results from Chapter 5 showed that trait anxiety was associated with better attentional orienting processes following eye-gaze cues of angry relative to other facial emotions. Similarly, GAD symptoms were associated with attentional facilitation for negative emotional expressions relative to positive ones when following eye gaze cues (Chapter 6). Furthermore, young people with elevated GAD symptoms followed eye-gaze cues of angry faces more than those of fearful faces; an effect that reflected increased attentional costs in the context of the task (Chapter 6). Previous empirical studies on attentional biases to threat–related stimuli in anxious individuals, have also found facilitated attentional orienting towards threatening stimuli, especially angry and fearful faces, compared to happy or neutral faces (Fox, 2002; Koster, Verschuere, Crombez, & Van Damme, 2005), as well as attentional avoidance (i.e. of negative scenes; Koster, Crombez, Verschuere, Van Damme, & Wiersema, 2006; Mogg, Bradley, Miles, & Dixon, 2004). It has been argued that anxiety is associated with hypervigilance towards threat detection in high trait anxiety (Cisler & Koster, 2010), that might subsequently lead to attentional avoidance over time from these stimuli, in an attempt to reduce stress levels. Our findings on attentional processes in anxiety, contradict previous accounts showing that anxious individuals are characterised by disengagement difficulties from threating stimuli (review by Dudeney, Sharpe, & Hunt, 2015; Koster, Crombez, Verschuere, & De Houwer, 2004; Richards, Benson, & Hadwin, 2012). These mixed findings may be attributed to the variation in different methodological manipulations (i.e., task relevant and irrelevant stimuli, peripheral or centrally presented targets), including the wide range of paradigms used in anxiety literature as well as the nature and anxiety symptoms being measured.

7.1.4 The interactive effects between ADHD and Anxiety symptoms

Across the two paradigms, we showed that the increased anxiety symptoms, when ADHD symptom were high, was associated with a compensatory role. More specifically, elevated symptoms of both anxiety and ADHD were associated with more efficient attentional disengagement in response to negative stimuli (Chapter 3 and 4), improved sustained attention, regardless of the emotional content of the task (Chapter 4), and improved attentional orienting processes (Chapter 5 and 6). These findings suggest that

anxiety levels in ADHD may have a 'protective' role on the disrupted emotional processing found in ADHD. Previous studies showed that young people with comorbid ADHD and anxiety are characterised by higher physical symptoms of anxiety relative to young people with ADHD-only, based on parent-reports (Jarrett et al., 2012). In addition, previous evidence have shown that anxiety counteracted impairments in emotion recognition in children with comorbid externalising disorders, such as CD (Short et al., 2016). Elevated levels of anxiety in ADHD might be associated with optimal levels of arousal that lead to improved attentional performance (Arnsten, 2009). Attenuation in PFC function (Rubia et al., 1999) and reduced prefrontal connectivity (Casey et al., 2007; Sowell et al., 2003) has been implicated in individuals with ADHD, which further derives from weaker noradrenaline production leading to impairments with sustained attention (Bellgrove et al., 2006). Therefore, the increased anxiety levels in ADHD might be associated with moderate levels of catecholamine (i.e., noradrenaline and dopamine) release that in turn improve PFC function (i.e., attentional processes) (Arnsten, 2009). Overall, the synergistic effects between ADHD and anxiety provide evidence towards a potentially distinct cognitive phenotype.

Our findings provide evidence for earlier theoretical models suggesting that the presence of anxiety would attenuate the severity and impairment of ADHD, such that inhibition and fear of negative evaluation that characterises anxiety counteracts externalising behavioural symptoms such as aggression or impulsivity (Gray 1987; Quay 1988)(Quay, 1997). Support for this 'attenuation hypothesis', is mainly derived from studies on anxiety and childhood conduct problems (i.e., ODD and CD) (e.g. Mason et al., 2004; O'Brien & Frick, 1996; Walker et al., 1991). However, empirical evidence between anxiety and ADHD are less consistent (Becker, Luebbe, Stoppelbein, Greening, & Fite, 2012). For example, previous work showed that that individuals with comorbid anxiety and externalising condition (i.e., CD, ODD and ADHD) are less likely to have a comorbid substance use disorder than those with either externalising-only or anxiety-only (Hofmann, Richey, Kashdan, & McKnight, 2009). In addition, further longitudinal evidence showed that self-reported shyness in childhood inhibits violence later in life (Mason et al., 2004). Consistently, our results showed that the presence of behavioural over control that characterises anxiety inhibits disrupted cognitive control processes and attentional biases in ADHD.

7.2 Implications

The results of this thesis provide information about the cognitive phenotype of ADHD and anxiety and their comorbidity. This information has important implications about the clinical profile of comorbidity in ADHD and anxiety and existing as well as future therapeutic interventions. For example, the disrupted attentional processing in threat contexts and specifically ineffective use of social cues found in ADHD, provide further evidence towards impaired social cognition (Uekermann et al., 2010), poor social skills, susceptibility to anger, irritability and intolerance for distress that characterise individuals with ADHD (review by Faraone et al., 2018). These factors, may further contribute towards lower quality of life and impaired functioning and adjustment in social (such as school, work) and family environments (Agarwal, Goldenberg, Perry, & IsHak, 2012; Classi, Milton, Ward, Sarsour, & Johnston, 2012; Danckaerts et al., 2010). These characteristics draw the importance of developing training programs for young people, parents and teachers that focus on emotion regulation strategies. For example, mindfulness-based interventions have received empirical support on improving attentional control (see review by Keng, Smoski, & Robins, 2011) and emotion regulation (see review by Chambers, Gullone, & Allen, 2009). More specifically, research on mindfulness-based practices has provided evidence for treatment efficacy for both young people and adults with ADHD (e.g. van de Weijer-Bergsma, Formsma, de Bruin, & Bögels, 2012; Zylowska et al., 2008) and anxiety (e.g. Koszycki, Benger, Shlik, & Bradwejn, 2007; Semple, Lee, Rosa, & Miller, 2010). Future studies, should also consider examining the mediating effect of executive control and emotional processing on the effectiveness of these interventional in regards to symptom reduction across these conditions.

In addition, emerging evidence on attentional trainings and especially those focusing on bias modifications (ABM; Attention Bias Modification), aim to reduce clinical symptoms (i.e., of anxiety) by reducing negative attentional biases through attention training that involves processes such as orienting attention away from threat or towards non-threat stimuli (e.g. Mogg & Bradley, 2016, 2018). This interventional approach has received preliminary evidence and mainly adapted for anxiety disorders that are related to these attentional biases, but our findings suggest that this approach could also be considered for ADHD, that is found to be associated with attentional –biases related in threat contexts. Specifically, the interactions between motivational-driven and goal-

directed influences on cognitive control that underlie both ADHD and anxiety along with the variable manifestations of attentional biases (orienting towards and away from threat; threat-distractor interference) provide essential information for future effective interventions.

More specifically, the results of the current programme of research showed that individuals with high levels of anxiety are characterised by attentional biases away from threatening information. In this case, bias modification trainings that focus on enhancing threat distractor inhibition and positive –search training can improve top-down cognitive control and thus reduce the influence of bottom-up/ threat- salience evaluation system. The positive search training involves a visual search attention training for which individuals are required to look for 'pleasant' and 'calm' target pictorial stimuli that were presented among unpleasant background images and has been previously shown to be efficacious for individuals with anxiety (Waters et al., 2015, 2016). The positive-search training has been proposed to be a promising approach that can be adapted to individuals characterised pre-existing attentional biases either towards or away from threatening information (Karin Mogg & Bradley, 2016)

Furthermore, our results indicated that disrupted attentional processes related to emotional content and particularly negative stimuli in ADHD, were moderated by elevated levels of anxiety. This finding highlights the need for clinicians to consider internalising comorbid conditions in diagnostic criteria used for externalising conditions (i.e., ADHD) and vice versa.

7.3 Strengths and Limitations

The empirical studies included in this thesis had a number of methodological advantages over previous studies conducted in this area of research. First, we considered emotion and cognition interaction in co-existing symptoms of ADHD and anxiety. To our knowledge, very few studies have examined executive control process in emotional contexts that related to comorbidity between ADHD and anxiety. In addition, beyond the cognitive profile of ADHD and anxiety, we further examined differences in two age groups (adults vs. children and adolescents) in relation to ADHD and anxiety, and provided evidence from potential developmental differences. Again, the evidence that cognitive and

emotional processes in ADHD and anxiety symptoms across different developmental stages is limited. Further, we adapted dimensional measures of ADHD and anxiety, based on accounts of previous taxonomic studies arguing that psychiatric disorders and psychopathology more broadly should be examined dimensionally rather than categorically (Hyman, 2010; Shear et al., 2007).

In addition, the empirical evidence provided in this thesis are derived from eye-movement measurements that were adapted in two widely used experimental paradigms that measure attentional processes. Eye-movements provide effective measures of on-line cognitive processing and are more sensitive in identifying underpinning neurocognitive mechanisms that characterise psychopathology (Bittencourt et al., 2013; Hutton, 2008) and development (Luna et al., 2008). Furthermore, the statistical analyses were conducted using LMMs (linear mixed effect models) that provide a number of advantages, including no data loss due to aggregation that is used in other statistical analyses (i.e., ANOVA), better consideration of the influence of individual characteristics (i.e., participants included as a random factor), as well as better statistical power (Baayen, Davidson, & Bates, 2008).

Regardless of the substantial strengths of the present studies, a number of limitations should also be considered. For the studies conducted in Chapters 3 and 5, the ADHD symptoms were obtained using different informants between the two age groups, i.e. children's ADHD symptoms were based on parent-reports and adults' ADHD symptoms were based on self-report measures. It is possible that parents judge symptoms in offspring differently based for example on a specific (e.g. family) setting. For better reliability among measures, future research should aim to use the same informant across measures of individual characteristics. In addition, in order to account for discrepancies across different informants on child symptomatology, future research should aim to obtain information based on multiple informants (i.e. children, parents and teachers).

For the studies in Chapters 3 and 5, we utilised a normative, non-clinical population with measures of ADHD and anxiety within typical range and thus below clinical thresholds. It is therefore important to consider this when interpreting conclusions regarding the potential neuropsychological mechanisms underpinning the interaction and comorbidity in ADHD and anxiety. Future research aims to replicate these findings should use a wider spectrum of ADHD and anxiety levels that include individuals who report symptoms above clinical cut-offs.

Furthermore, our sample size from Chapters 3 and 4 included a relatively wide age range (8-15 years) from both children and adolescents. Children and adolescents may be characterised by different regulatory processes related to cognitive control and emotional processing (e.g. Hare et al., 2008). However, the relatively small sample size of children and adolescents did not allow a comparison of potential developmental differences between these groups.

The measures of cognitive ability (estimated IQ) that were examined for the young people (children and adolescents) in Chapters 4 and 6 were not obtained for the adult sample used in Chapters 3 and 5, which may have affected the consistency of the results. However, this constitutes a minimal concern in regards to altering the results of the study, as the estimated IQ did not have an effect on the outcome measures used for either the Go/No-Go task or the Spatial Cueing Task when examined in the younger populations. In support, previous studies also showed that inhibitory control deficits in children with ADHD did not associated with IQ (Bitsakou et al., 2008; Scheres et al., 2004).

Considering the fact that the number of participants falling in the clinical diagnostic groups of ADHD and/or anxiety were unequal in size and relatively small, we used the DISC symptom count adapting a dimensional examination of symptom across the whole sample of young people used in Chapters 4 and 6. The symptom count was derived from the DISC that is an extensive, structured diagnostic interview, which provides indication for diagnosis integrates together the level of impairment and the duration of symptoms across each condition. Therefore, the symptom count might not give a direct indication of the severity of each condition.

Finally, in order to maximise recruitment strategies and increase our sample size, and thus power of the current findings, we did not exclude all potential comorbid conditions from our sample used in Chapter 4 and 6. Specifically, we allowed the presence of depression for participants met diagnostic criteria for anxiety and respectively, the potential comorbidity of ODD for children and adolescents who met diagnostic criteria for ADHD. Therefore, the findings derived across ADHD and anxiety in children and adolescents may not be directly generalizable to other findings linked to non-comorbid anxiety and/or ADHD. However, considering that both disorders are highly comorbid with other, internalizing and externalizing disorders (Johnston & Mash, 2001; Maughan et al., 2004;

Newcorn et al., 2001), 'pure' ADHD and 'pure' anxiety may be the exception rather than the rule.

7.4 Future Research

This thesis extended our understanding on the interactive effects between symptoms of anxiety and ADHD in children/adolescents and adults about attentional control and processing emotional information. The evidence derived from the current thesis are based on cross-sectional data that allowed the investigation of the neurocognitive profile underlie ADHD and anxiety both separately and synergistically. However, the direction of the causal links between the two disorders should be a focus for future longitudinal research that will inform preventative and interventional strategies that will help reduce impairment and enhance daily living in social and family contexts for individuals with ADHD and anxiety.

Taken together, the findings in this thesis have important implications, especially in terms of intervention approaches aiming to emotion regulation and cognitive performance in individuals with ADHD and/or anxiety. Our findings highlight the attentional control difficulties in conjunction with emotion regulation challenges that characterise individuals with ADHD. Effective interventions should target attentional training as well as improvement of social interactions and peer relationships in individuals with ADHD. Psychological therapies can help individuals with ADHD to better recognise emotions accurately, but also to cope with intense negative emotional reactions and improve general emotion regulation strategies.

Future studies can further examine whether ADHD and anxiety presentations can account for differential cognitive process in emotional contexts. For example, different anxiety disorders are characterised by fearful states (such as specific phobias, social anxiety disorder) and others characterised by "worry" states (i.e., generalised anxiety disorder) which might interact differently in the context of elevated ADHD to influence attention in the presence of threatening or other emotional contexts. Apart from pathological anxiety, the current findings focused on trait anxiety could be extended on state anxiety (i.e. situational anticipation of threat) to examine whether a different modulation of attentional processes exist in this context. A previous study for example, showed that trait anxiety was associated with reduced executive control whereas state anxiety was associated with over

functioning of alerting and orienting attention networks; supporting a double dissociation between trait and state anxiety on attentional performance (Pacheco-Unguetti et al., 2010).

In addition, concerning the underlying neuropsychological mechanisms that characterise ADHD and anxiety comorbidity, future research should further consider potential influence of specific emotion regulation strategies when investigating attentional biases. For example, cognitive reappraisal refers to re-evaluation of emotional stimuli or situations in an attempt to reduce its emotional impact, and expressive suppressions refers to the suppression of expressed emotions (Gross, 2015; Gross & John, 2003). These strategies may directly mediate the attentional biases characterised comorbidity in ADHD and anxiety.

Furthermore, future studies that consider cognitive attentional biases using socially relevant stimuli and particularly facial emotional expressions, would benefit from using facial expressions that very in intensity and dynamically manipulated rather than using static morphed expressions (e.g. Martin-Key, Graf, Adams, & Fairchild, 2018). Beyond facial emotional expressions, stimuli that vary in intensity (highly or less aversive) should provide further information about attentional biases and interactions with cognitive control related to psychopathology.

7.5 Conclusion

The current programme of research examined the effects of symptoms of ADHD and anxiety and their interaction in attentional processes among children/adolescents and adult populations. Increased symptoms of ADHD were associated with impaired inhibitory control and disrupted processing, in the context of threat (such as angry faces), as well as reduced sustained attention. Individuals with ADHD showed difficulties following social cues such as eye-gazes, especially when those gazes were from negative emotional expressions (such as angry and fearful faces) relative to other emotional expressions. Anxiety symptoms were associated with faster processing of negative facial expressions and improved attention following social cues of negative relative to other facial expressions. Anxiety was also linked to better attentional orienting following social cues of angry faces relative to fearful faces. The interactions between anxiety and ADHD showed

that elevated anxiety symptoms were associated with attenuation of disrupted attentional processes found in ADHD including faster processing of negative emotional expressions relative to positive ones, improved sustained attention and better attentional orienting in response to social cues. These findings improve our understanding on the social and cognitive characteristics across these conditions separately as well as synergistically and particularly how individuals with ADHD and/or anxiety can interpret, process and respond to social cues and emotional information in the environment. This area of research should stimulate future research to further investigate the interaction between cognition and emotion across a wider spectrum of ADHD and anxiety symptoms and clinical samples. This research has implications on potential interventional approaches used for these conditions, targeting attentional training, social skills and peer relationships.

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Appendices

Appendix A1: Invitation Letters for Parents

Study title: ***Emotional Differences between Children with attention-hyperactivity problems and children with anxiety problems***

Athina Manoli

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Dear Parent/Guardian,

We are writing to invite you and your child to take part in a research study taking place at the University of Southampton.

We are currently recruiting participants for a study that is aiming to investigate the cognitive and emotional factors that differentiate children that have been diagnosed with attention deficit/hyperactivity disorder (ADHD) and anxiety from children with ADHD only, children with anxiety disorder(s) only and children with neither disorder. To achieve this we will

employ eye - tracking equipment (eye-movement measurements) that is used to provide a measure of attentional and behavioural control.

If your child falls into <u>ALL</u> of the following inclusion criteria then he/she is able to take part in the study if both you and your child are happy to take part.

Children will be eligible for inclusion into the study if they:

- Are aged between 8 and 15 years old.
- Have anxiety and worry problems and/ or have been previously diagnosed with anxiety disorder(s).
- Have hyperactivity-impulsivity and/ or inattention problems and/ or have been previously diagnosed with ADHD
- Have no other mental health disorder (including Conduct Disorder)
- Have no severe learning difficulties or special educational needs.
- Are able to speak and understand English and their parent is also able to speak and understand English.
- Give written assent to participate and have a parent or legal guardian to provide written consent to participate.

<u>What does this research study involve?</u>

Initially, we have to ask you some general/demographic questions about you and your child to see if it is possible for you to take part. We will then phone you to arrange a convenient time for your and your child to visit the Psychology Academic Unit at the University of Southampton. If your child is medicated and it is safe to do so, please ensure he/she refrains from taking any medication 48 hours prior to testing.

A typical visit to the University

When you arrive at the University, we explain the study to you. You and your child will be asked to sign forms to say that you are still happy to take part. You will be told that the tasks you are asked to do take around two and a half hours.

Your child will then be asked to complete two computer tasks and we will measure their eye movements as they complete the tasks. Before we start, we make sure your child is in a comfortable position and understands what the equipment measures and what they will be asked to do. The tasks involve identifying targets on a computer screen and ignoring distractors (e.g., arrows or emotional faces) or using these different stimuli to decide where they will look or how they will respond. Each task takes about 30-40 minutes to complete. Your child will be given the opportunity to take breaks while they are doing each task, as well as between tasks. After completing the computer tasks your child will be asked to complete a few questionnaires. These ask your child to report how they feel and behave and they will take around 45 minutes to complete. After that, we will ask your child to spend around 20 minutes two complete two short thinking games. While your child is doing the computer and questionnaire tasks, we will ask you to do a short interview and complete two questionnaires. These will include questions about your child's behaviour, emotions, academic and social performance. They will take about 2 hours to complete.

Once you and your child have both finished , we will explain more about what you were asked to do and why and you will be given a related statement will be provided with a written debriefing statement. The whole testing session should take no longer than 3 hours.

If you and your child are interested in taking part, please read the Information Sheet that has been sent to you along with this Invitation Letter and fill in the **reply slip, demographics form** and send them back to us using the FREEPOST envelope provided.

If you prefer, you are also welcome to email (am32g13@soton.ac.uk) or phone us on 02380596652.

Appendix A2: Demographics form for Young People

UNIVERSITY OF Southampton

DEMOGRAPHICS FORM

(Version 1; 04/06/2015)

Study title: ***Emotional Differences between Children with attention-hyperactivity problems and children with anxiety problems***

Researcher name: Athina Manoli

Study ID: 15220

Thank you for expressing an interest in our research. Please complete this demographics form and post it back to us (along with the reply slip) in the FREEPOST envelope provided (no stamp is needed).

If you prefer, you may also email this information to Athina at: study19026@gmail.com

To be completed by a parent or carer (see next page)

Name of parent or carer																			
Young Person's Name																			
Young Person's Gender (✓)	**Male**				**Female**														
Young Person's Race (✓)	**White**			**Black**				***Asian***			***Other (specify)***								
Young Person's D.O.B (dd/mm/yyyy)			**/**			**/**					**Age (yrs)**								
Home Address & Postcode																			
Tel. Home																			
Mobile																			
Email																			

Has the young person been diagnosed with any mental health disorder? **ADHD-Attention Deficit/Hyperactivity Disorder** **Anxiety Disorder (Specific Phobia, Social Phobia, Separation Anxiety Disorder, Panic Disorder, Generalised Anxiety Disorder)** **Depression** **Oppositional Defiant Disorder (ODD)** **Conduct Disorder (CD)**	**YES** ***(please specify)***		**NO**	

Does the young person take any medication at the moment?	**YES** ***(please specify)***		**NO**	

Does the young person has any severe learning difficulties or special educational needs?	**YES** *(please specify)*		**NO**	
Has the young person been diagnosed autism or any other paediatric developmental disorder (such as Down syndrome?)	**YES** *(please specify)*		**NO**	

Has the young person taken part in more than three studies at the University of Southampton in the past year?	**YES**		**NO**	

Is the parent/carer able to speak and understand English?	**YES**		**NO**	
Is the young person able to speak and understand English?	**YES**		**NO**	

Appendix A3i: Information Sheet for Parents

UNIVERSITY OF Southampton

INFORMATION FOR PARENTS

(Version1; 13/04/16)

Study title: ***Emotional Differences between Children with attention-hyperactivity problems and children with anxiety problems***

Researcher name: Athina Manoli

ERGO ID 19026

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.

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part and remember that your participation is voluntary.

My name is Athina Manoli and I am a PhD student at the University of Southampton. I would like to invite you and your child to take part in my research study that is being done as part of my degree. Before you decide whether to take part, I would like to explain why the research is being done and what it would involve for you and your child. I will go through this information sheet with you and answer any questions you may have.

What is the purpose of the research study?

Attention Deficit and Hyperactivity disorder (ADHD) is one of the most common childhood disorders. Often children and adolescents who have a diagnosis of ADHD also report feelings of worry and anxiety. The aim of this study is to understand why and how some young people experience both ADHD and anxiety. We want to consider attention and emotion in children and adolescents who have a diagnosis of ADHD or anxiety compared with those who are diagnosed with one disorder. The study will measure how young people move their eyes when completing tasks that require them to attend to different parts of the screen to achieve the task goals. Understanding attention will help us to think through causes of disorders in children and adolescents, as well as to develop effective treatments.

Why has your child been chosen to take part?

Your child has been invited to take part since we are recruiting children aged between 8-15 years throughout schools in the Hampshire area. We require both your and your child's agreement to take part to the study. We do require assent from your child to participate (i.e. he/she should be willing to take part) and we require from you to agree if he/she should take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form. Even after agreeing to take part, you are still free to withdraw at any time without giving a reason.

If your child is currently taking psychoactive medication, you will be asked not to administer the medication 48 hours before testing-(Please note that this is a standard procedure followed by many research studies that working with children and adolescents who have a diagnosis of ADHD and anxiety, therefore it is unlikely that any repercussions will occur). If you are happy to do so and take part then you will be asked to sign a consent form. Even after agreeing to take part you are still free to withdraw at any time without giving a reason.

What does this research study involve?

Initially, we will ask you some general/demographic questions about you and your child to see if it is possible for you to take part. We will then phone you to discuss any questions or concerns that you night have. We will also ask you to give us a verbal consent if you agree

not to give any psychoactive medication to your child 48 hours prior to the research. After your verbal consent, we will arrange a convenient time for you and your child to visit the Psychology Academic Unit at the University of Southampton. If your child is medicated and it is safe to do so, please ensure he/she refrains from taking any medication 48 hours prior to testing.

A typical visit to the University

When you arrive at the University, we will explain the study to you. You and your child will be asked to sign forms to say that you are still happy to take part. You will be told that the tasks you are asked to do take around three hours.

Your child will then be asked to complete two computer tasks and we will measure their eye movements as they complete the tasks. Before we start, we make sure your child is in a comfortable position and understands what the equipment measures and what they will be asked to do. The tasks involve identifying targets on a computer screen and ignoring distractors (e.g., arrows or emotional faces) or using these different stimuli to decide where they will look or how they will respond. Each task takes about 30 minutes to complete. Your child will be given the opportunity to take breaks while they are doing each task, as well as between tasks. After completing the computer tasks your child will be asked to complete a number of questionnaires. These ask your child to report how they feel and behave and they will take around 25 minutes to complete. While your child is doing the computer and questionnaire tasks, we will ask you to answer a number of questions about your child's behaviour, emotions, academic and social performance. They will take about 2 hours to complete. After finishing the computer tasks and completing the questionnaires, we will ask from your child to complete two short thinking tasks.

Once you and your child have both finished, we will explain more about what you were asked to do and why, and you will be provided with a written debriefing statement. In order to thank you for taking part your child will receive £15 for his or her help, you will receive £10 for participation and time, and your travel expenses will be reimbursed as well. The whole testing session should take no longer than 3 hours.

What are the possible disadvantages and risks for taking part?

If you taking psychoactive medication 48 hours prior to the study this might cause some changes in child's behaviour such as increased impulsiveness and difficulty to concentrate. It is up to you to decide if you will take your child off medication and you are free to restart medication any time if you feel that this is best for your child. In addition, the tasks and measures we will ask you to do will take time and effort. During the session your child may experience some discomfort and boredom due to the length of the computer tasks and because he/she will be asked to keep still so we can record eye movements clearly. However, we always aim to support your child through the tasks to make the experience as enjoyable as possible for them. In addition, we will allow them to take frequent breaks where we will provide snacks and refreshments.

What are the possible benefits for taking part?

By taking part in the study both you and your child will help us understand better the factors that might place children at risk for developing a disorder. The information we collect will be important in understanding causes of different disorders and how we can start to treat them.

Will information collected during the study be kept confidential?

All data is anonymized and confidential. Your child's identity will be protected by changing his/her name into a subject code during analysis. Any information and research study documentation taken for this research will remain confidential and will be available only to the principal investigator and members of the research team directly involved in the study. However, we will tell you if your child reports very high levels of anxiety on the questionnaire measures. In addition, if you need further support or advice in this circumstance, you will be informed (as a parent/guardian) and if you require further support or advice we will provide you with a person you can contact for further advice. All your data and information will be held in confidence, which means that it will only be shared with those who have a need or a right to know.

What happens if I no longer want my child to participate?

Even if you and your child decide to take part you both are still free to withdraw from the study at any time without having to give a reason.

What will happen to the results of the research study?

When the study has been completed, data will be analyzed and the findings will be written up for publication in peer-reviewed scientific journals and may be presented at scientific conferences. You and your child would not be identified in any way. If you would like to know the results we can provide you with a summary report, or a copy of the final paper.

Who has reviewed the study?

The University of Southampton Research Ethics Committee and the South Central Berkshire – B Research Ethics Committee have both reviewed and approved the study.

Who can I contact for further information?

If you have a concern or complaint regarding any aspect of this study you can contact the Research Governance at the University, Phone number: 02380 595058, Email address: rgoinfo@soton.ac.uk

For further queries, please contact me or my supervisor via email:

Athina Manoli (email: am32g13@soton.ac.uk) or Dr Julie Hadwin (email: jah7@soton.ac.uk)

Appendix A3ii: Information Sheet for Young People

UNIVERSITY OF Southampton

INFORMATION FOR PARTICIPANTS

(Version 1; 13/04/16)

Study title: ***Emotional Differences between Children with attention-hyperactivity problems and children with anxiety problems***

Researcher name: Athina Manoli

ERGO ID 19026

My name is Athina Manoli and I am a student at the University of Southampton. I would like to invite you to take part in my research study that is being done as part of my degree. Before you decide whether to take part, I would like to explain why the research is being done and what it would involve for you. I will go through this information sheet with you and answer any questions you may have.

What is this research study about?

In this study we want to find differences between children who have difficulty paying attention and might be overactive most of the time, children who worry, children who have attention-over activity and/or worry problems and children who have none of those problems. We will achieve this by measuring eye-movements because they can give us a lot of information about people's attention and behaviour.

Why have I been asked to take part?

You are invited to take part since we are recruiting children 8-15 years old, who have attention and/or hyperactivity as well as anxiety and worry difficulties. It is up to both you

and your parent/carer to decide whether or not you take part. If you decide to take part, you will be given this sheet to keep and be asked to sign a form. Even after saying you want to take part you are still free to stop at any time without giving a reason.

Did anyone else check the study is OK to do?

Before any research is allowed to happen, it has to be checked by a group of people called a Research Ethics Committee. They make sure that the research is fair. The project has been checked by the University of Southampton Research Ethics Committee and the South Central Berkshire B Research Ethics Committee.

Do I have to take part?

No, it is up to you. Before you make this decision, you can ask the researcher to answer any questions that you might have. If you think that you might want to take part you can fill out a form that you will be given by the researcher after reading all the information. If you agree to take part, you are still free to stop at any time, without giving a reason.

What will happen to me if I take part?

If you decide to take part, we will contact your parent/carer to arrange a convenient time for both of you to come at The University of Southampton to do the experiment. Before the study, I will show you the room and the equipment that we will use for the experiment so you can understand everything before we begin. We will ask you to do a few tasks on the computer, complete some questionnaires about how you feel and complete two thinking games. There will not be any right or wrong answers to those questions and you will also have as many breaks as you like during the session and between the tasks. At the end of the study, you will receive £15 for your time and effort.

Will anybody know my scores?

Nobody except me and the research team will know your answers to the questions. Your name will be changed into a number/code for the analyses of the results so nobody will know your name and your answers. Only if your parent/carer asks for your scores we tell him/her.

What are the benefits of taking part?

By taking part in the study both you and your parent/carer will help us to understand better some of the factors that differentiate children with attention difficulties, children with worry problems, children with both attention and worry problems and children with none of the above problems.

What if there's a problem or something goes wrong?

It is very unlikely that you will have any problems while you are doing this study. If you are worried about anything you and your parent/carer can stop any time you wish so. If you feel you have been treated badly during this study you can contact the **Research Governance** Office at the University of Southampton (phone number: 02380 595058, Email address: rgoinfo@soton.ac.uk)

What happens if I want to find out more?

You can ask me any questions you have now or you can contact me later (Athina Manoli, telephone number: 02380596652 or send me email on am32g13@soton.ac.uk and ask me anything you like. You can also contact my supervisor (Julie Hadwin, University of Southampton, telephone number: 02380592590, email: jah7@soton.ac.uk)

Appendix A4: Assent Form (Young People)

UNIVERSITY OF Southampton

ASSENT FORM (Version 1; 04/06/15)

Project title: ***Emotional Differences between Children with attention-hyperactivity problems and children with anxiety problems***

Researcher: Athina Manoli

Study ID: 15220

Please circle yes or no if you agree with the statement(s):

Has somebody explained this project to you?	Yes/no
Do you understand what this project is about?	Yes/no
Have you asked all the questions you want?	Yes/no
Have you had your questions answered in a way you understand?	Yes/no
Do you understand it's OK to stop taking part at any time?	Yes/no
Are you happy to take part?	Yes/no

If any of the answers are "no" or you don't want to take part, please don't sign your name.

If you do want to take part, you can write your name below:

Your name: _____

Signature: _____

Date: _____

The researcher who explained this to you needs to sign:

Signed: _____

Date: _____

Appendix A5: Consent Form (Parent)

UNIVERSITY OF Southampton

CONSENT FORM FOR PARENTS

(Version 2; 03/09/15)

Study title: Emotional Differences between Children with attention-hyperactivity problems and children with anxiety problems

Researcher name: Athina Manoli

Study ID: 15220

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

I have read and understood the information sheet (Version 2; 03/09/15) and have had the opportunity to ask questions about the study ☐

I agree to take part to take part in this research project and agree for my data to be used for the purpose of this study ☐

I agree for my child to take part in this research project and for the data collected to be used for the purpose of this study ☐

I understand my participation and the participation of my child is voluntary and that both my child and myself may withdraw from the study at any time without our rights being affected ☐

I agree for my and my child's data to be looked by regulatory authorities ☐

I agree for my details to be kept within the Developmental Brain Behaviour Laboratory, and I am willing to be contacted about - **Yes / No**

Name of parent/carer (print name)……

Signature of parent/carer……..

Signature of Researcher…….

Date…….

Appendix A6i: Debriefing Statement for Parents

UNIVERSITY OF Southampton

Parent's Debriefing Statement

(Version 2, 03/09/2015)

Study Title: ***Emotional Differences between Children with attention-hyperactivity problems and children with anxiety problems***

Thank you for taking part in this experiment!

Study Background:

Attention Deficit and Hyperactivity disorder (ADHD) is one of the most common childhood disorders. Often children and adolescents who have a diagnosis of ADHD also report feelings of worry and anxiety. The aim of this study is to understand how some young people experience both ADHD and anxiety. We want to consider attention and emotion in children and adolescents who have a diagnosis of ADHD or anxiety compared with those who are diagnosed with one disorder.

Eye-movements:

Eye movements are argued to provide an on-line measure of cognitive processes as reflected in saccades (rapid eye-movements) and fixations (retention of the visual gaze on a single location). The study measured how these groups of young people (ADHD, Anxiety, comorbid ADHD/Anxiety, typically developing) move their eyes when completing tasks that require them to attend to different aspects of a computer based task to achieve its goals. Understanding attention will help us to think through causes of disorders in children and adolescents as well as to develop effective treatments.

Once again, let us remind you that the results of this study will not include any personal details such as your child's name and that all the details will be number coded. If you have any further questions about the study, please contact me, Athina Manoli, am32g13@soton.ac.uk

If you have a concern or complaint regarding any aspect of this study you can contact the Research Governance at the University, Phone number: 02380 595058, Email address: rgoinfo@soton.ac.uk

If you or your child feel any distress due to the questionnaires you completed or at any other point during the study you can contact Dr Samuele Cortese, Honorary Consultant in Child and Adolescent Psychiatry, Solent NHS Trust, Phone number: 02380296230 or 02380296232, Email address: Samuele.Cortese@soton.ac.uk

Thank you again for your participation!

Signature: _____ Date: _____

Name: _____

Appendix A6ii: Debriefing Statement for Young People

UNIVERSITY OF Southampton

Debriefing Statement for Participants

(Version 1,04/06/2015)

Study Title: ***Emotional Differences between Children with attention-hyperactivity problems and children with anxiety problems***

Thank you for taking part in this experiment!

We would like to tell you why we asked you to do the computer tasks and answer the questions.

Some children and young people have attention and concentration difficulties. Some children have worry problems. There are also children that have both attention and worry difficulties. The computer tasks you have completed and by measuring your eye-movements you helped us to understand the characteristics of attention in these children and find out what are the differences and the similarities between them. The tasks and eye-movements helped as also to understand the differences and similarities in the way these children and young people can understand emotions such as happiness, anger, fearfulness.

Once again, let us remind you that the results of this study will not include any personal details such as your name and that your details will be number coded. If you have any further questions about the study, please contact me, Athina Manoli, am32g13@soton.ac.uk

If you have any questions or feel worried about anything we asked you to do please let me know so we can talk about it. You can also talk to someone you know, like your parent or guardian or a teacher from your school.

You can also talk to people from outside the school by ringing the Child line. People on Child line will talk to you about any worries you might have but they will not tell anyone what you said to them. You can speak to someone on Childline by calling 0800 1111. There are other ways of contacting childline. You can find out more information online at: http://www.childline.org.uk/

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 Research and Graduate Office at the University of Southampton (02380 595058, rgoinfo@soton.ac.uk) who will be happy to help or discuss your concerns.

Appendix B1: Adult Participants – Demographics Form

UNIVERSITY OF Southampton

DEMOGRAPHICS FORM

(Version 1; 17/11/2016)

Study title: ***Attentional control under emotionally-loaded tasks: An eye-tracking study***

Researcher name: Athina Manoli

ERGO ID 24457

Thank you for expressing an interest in our research. Please complete this demographics form before proceeding with the experimental tasks

Name																				
Gender (✓)	**Male**			**Female**																
Race (✓)	**White**			**Black**				***Asian***				***Other (specify)***								
D.O.B (dd/mm/yyyy)			**/**			**/**						**Age (yrs)**								
Home Address & Postcode																				
Tel. Home																				
Mobile																				
Email																				

Have you ever been diagnosed with any of the following mental health disorders? **ADHD-Attention Deficit/Hyperactivity Disorder** **Anxiety Disorder (**Specific Phobia, Social Phobia, Separation Anxiety Disorder, Panic Disorder, Generalised Anxiety Disorder) **Depression** **Oppositional Defiant Disorder (ODD)** **Conduct Disorder (CD)**	**YES** ***(please specify)***		**NO**	

Do you take any medication at present?	**YES** ***(please specify)***		**NO**	

Do you have any severe learning difficulties or special educational needs?	**YES** ***(please specify)***		**NO**	

Have you ever been diagnosed with autism or any other developmental disorder (such as Down syndrome?)	**YES** ***(please specify)***		**NO**	

Are you able to speak and understand English?	**YES**		**NO**	

Appendix B2: Adult Participants – Information Sheet

UNIVERSITY OF Southampton

INFORMATION FOR PARTICIPANTS

(Version1; 17/11/16)

Study Title: ***Attentional Control under Emotionally-loaded tasks: An eye-tracking study***

Researcher name: Athina Manoli

ERGO ID 24457

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.

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part and remember that your participation is voluntary.

My name is Athina Manoli and I am a PhD student at the University of Southampton. I would like to invite you to take part in my research study that is being done as part of my degree. Before you decide whether to take part, I would like to explain why the research is being done and what it would involve for you. I will go through this information sheet with you and answer any questions you may have.

What is the purpose of the research study?

The aim of the study is to examine oculomotor control in simple computer tasks using emotional and non-emotional stimuli. The study will measure eye-movements in young adults to understand how attentional control can be modulated in the presence of emotional stimuli. Understanding attention in adults will help to compare performance in similar tasks in children and adolescents to identify attentional and emotional processing mechanisms across development.

Why have I been chosen?

You have been invited to participate since you have enquired about our study and you meet the age criteria.

What does this research study involve?

Initially, we will explain what the study involves and ask you to sign a consent form to say that you are happy to take part. We will ask then ask you to complete a short demographics form and we will carry out a short screening interview asking you about your psychiatric history. After that, you will be asked to complete simple computer tasks during which we will measure your eye-movements. You will also be asked to complete a number of questionnaires.

Eye tracking:

To track your eye movements, you will be seated in front of a computer screen. At the beginning of the experiment you will be adjusted into a comfortable height position in the chair and the chin rest will be positioned in front of you at an appropriate height. You will be asked to place your chin on the chin rest while eye tracker is tracking your eyes. You will be asked to remain as still as possible to minimise head movements which can affect the quality of the eye tracking data.

You will be asked to complete two computer tasks that are divided in 6 blocks in total. Each block takes approximately 10-15 minutes to complete. The tasks involve identifying and discriminating targets on a computer screen while ignoring distractors (*e.g.* arrows and emotional faces), moving your eyes in response to some targets and withholding your eye-movements in response to others (*e.g.* coloured squares and emotional faces). You will be

given the opportunity to take frequent breaks between the tasks. After completing the computer tasks you will be asked to complete the questionnaires that include questions about your feelings, emotions and behaviours and they will take around 15 minutes to complete.

Once you finished, we will explain more about the study, and you will be provided with a written debriefing statement. In order to thank you for taking part you will receive £12 (£6 per hour) or 24 credits for 2 hours (12 credits per hour) for your participation. This is the standard set by the University of Southampton Psychology Ethics Committee.

Finally, the whole testing session should take no longer than 2 hours.

What are the possible disadvantages and risks for taking part?

The disadvantage in taking part is the time and effort the study will take. Participants who meet any of the exclusion criteria should not take part in the study. These include diagnosis of various psychiatric disorders such as anxiety disorders depression and schizophrenia. During the session, you may experience some discomfort and boredom due to the length of the computer tasks and because you will be asked to keep still so we can record eye movements clearly. However, we will encourage you to take frequent breaks at any point you feel so during the session.

What are the possible benefits for taking part?

By taking part in the study, you help us understand attentional mechanisms in emotionally loaded tasks that underlie healthy adults and further compare those mechanisms in development and psychopathology more broadly. Participants who complete the study will receive a payment of £12 or 24 credits (for Undergraduate students) for their time and effort.

Will information collected during the study be kept confidential?

All data is anonymized and confidential. Your identity will be protected by changing your name into a subject code during analysis. Any information and research study documentation taken for this research will remain confidential and will be available only to the principal investigator and members of the research team directly involved in the study.

What happens if I no longer want to participate?

Even if you decide to take part, you are still free to withdraw from the study at any time without having to give a reason.

What will happen to the results of the research study?

When the study has been completed, data will be analyzed and the findings will be written up for publication in peer-reviewed scientific journals and may be presented at scientific conferences. You would not be identified in any way. If you would like to know the results we can provide you with a summary report, or a copy of the final paper.

Who has reviewed the study?

The University of Southampton Research Ethics Committee has reviewed and approved the study.

Who can I contact for further information?

If you have a concern or complaint regarding any aspect of this study you can contact the Research Governance at the University, Phone number: 02380 595058, Email address: rgoinfo@soton.ac.uk

For further queries, please contact me or my supervisor via email:

Athina Manoli (email: am32g13@soton.ac.uk) or Dr Julie Hadwin (email: jah7@soton.ac.uk)

Appendix B3: Adult Participants – Consent Form

UNIVERSITY OF Southampton

CONSENT FORM

(Version 1; 17/11/2016)

Study title: ***Attentional control under emotionally-loaded tasks: An eye-tracking study***

Researcher name: Athina Manoli

ERGO ID 24457

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

I have read and understood the information sheet

(Version 1; 17/11/2016) and have had the opportunity to ask questions about the study ☐

I agree to take part 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 from the study at any time without my rights being affected ☐

I agree for my data to be looked by regulatory authorities ☐

I agree for my details to be kept within the Developmental Brain Behaviour Laboratory, and I am willing to be contacted about - **Yes / No**

Name of participant (print name)……

Signature of participant……..

Date……..

Name of research investigator……..

Signature of Researcher…….

Date……..

Appendix B4: Adult Participants – Debriefing Statement

UNIVERSITY OF Southampton

Debriefing Statement

(Version 1, 17/11/2016)

Study Title: ***Attentional Control under Emotionally-loaded tasks: An eye-tracking study***

ERGO ID 24457

Thank you for taking part in this experiment!

Study Background:

Cognition and emotion interact to determine ongoing behaviours in humans. In this study, we investigated the interaction between cognition and emotion during inhibitory control and attentional orienting using the go/No-Go task and the spatial cueing task, respectively. Previous research has found that the presence of emotion can either enhance or impair performance based on emotional potency of the stimuli involved. In addition, previous studies have shown that attentional control in the presence of emotional faces changes across different age groups. The aim of this study is to understand the impact of emotional stimuli on attentional processing in young adults and further explore how this differs from our previous studies with children and adolescents.

Eye-movements:

Eye movements are argued to provide an on-line measure of cognitive processes as reflected in saccades (rapid eye-movements) and fixations (retention of the visual gaze on a single

location). Studies have shown that saccadic eye-movements provide reliable and valuable information about attentional and executive control processes. The current study measured number of saccades towards targets and saccade latency (time elapsed from the presentation of the target until the initiation of the first correct eye-movement to the target) during the computer tasks.

Once again, let us remind you that the results of this study will not include any personal details such as your name and that all the details will be number coded. If you have any further questions about the study, please contact me, Athina Manoli, am32g13@soton.ac.uk

If you have a concern or complaint regarding any aspect of this study you can contact the Research Governance at the University, Phone number: 02380 595058, Email address: rgoinfo@soton.ac.uk

If you feel any distress due to the questionnaires you completed or at any other point during the study you can contact the University Counselling Service (http://www.southampton.ac.uk/edusupport/counselling/), Nightline, on 023 8059 5236 (free from halls on (78)25236) or visit http://nline.susu.org/

Thank you again for your participation!

Signature: _____ Date: _____

Name: _____

Appendix C: Mini- International Neuropsychiatric Interview (MINI)

NEUROPSYCHIATRIC INTERVIEW
Based on screening questions in the MINI-plus
(D. Sheehan, J. Janavs, R. Baker, K. Harnett-Sheehan, E. Knapp, M. Sheehan, University of South Florida, Tampa, USA
and Y. Lecrubier, E. Weiller, T. Hergueta, P. Amorim, L. I. Bonora, J. P. Lépine
Hôpital de la Salpétrière - Paris)

Date (dd/Mon/yy): |_|_|_|_|_|_|_|_|

Instructions:
1. When "YES" investigator and study physician have to discuss the subject before inclusion
2. In the gray fields all items have to be answered "YES".

Depression	NO	YES
Have you been consistently depressed or down, most of the day, nearly every day, for the past two weeks?	☐	☐
In the past two weeks, have you been less interested in most things or less able to enjoy the things you used to enjoy most of the time?	☐	☐
Have you felt sad, low or depressed most of the time for the last two years?	☐	☐
Did you ever make a suicide attempt?	☐	☐

Mania	NO	YES
Have you ever had a period of time when you were feeling 'up' or 'high' or so full of energy or full of yourself that you got into trouble, or that other people thought you were not your usual self? (Do not consider times when you were intoxicated on drugs or alcohol.)	☐	☐
Are you currently feeling 'up' or 'high' or full of energy? IF PATIENT IS PUZZLED OR UNCLEAR ABOUT WHAT YOU MEAN BY 'UP' OR 'HIGH', CLARIFY AS FOLLOWS: By 'up' or 'high' I mean: having elated mood; increased energy; needing less sleep; having rapid thoughts; being full of ideas; having an increase in productivity, motivation, creativity, or impulsive behavior.	☐	☐
Have you **ever** been persistently irritable, for several days, so that you had arguments or verbal or physical fights, or shouted at people outside your family? Have you or others noticed that you have been more irritable or over reacted, compared to other people, even in situations that you felt were justified?	☐	☐
Are you currently feeling persistently irritable?	☐	☐

NEUROPSYCHIATRIC INTERVIEW *continued*

Anxiety	NO	YES
Have you, on more than one occasion, had spells or attacks when you **suddenly** felt anxious, frightened, uncomfortable or uneasy, even in situations where most people would not feel that way?	☐	☐
Did the spells peak within 10 minutes?	☐	☐
Do you feel anxious or uneasy in places or situations where you might have a panic attack or the panic-like symptoms we just spoke about, or where help might not be available or escape might be difficult: like being in a crowd, standing in a line (queue), when you are alone away from home or alone at home, or when crossing a bridge, traveling in a bus, train or car?	☐	☐
In the past month, were you fearful or embarrassed being watched, being the focus of attention, or fearful of being humiliated? This includes things like speaking in public, eating in public or with others, writing while someone watches, or being in social situations.	☐	☐
Have you worried excessively or been anxious about several things over the past 6 months?	☐	☐
Are these worries present most days?	☐	☐

Obsessive compulsive disorder	NO	YES
In the past month, have you been bothered by recurrent thoughts, impulses, or images that were unwanted, distasteful, inappropriate, intrusive, or distressing? (For example, the idea that you were dirty, contaminated or had germs, or fear of contaminating others, or fear of harming someone even though you didn't want to, or fearing you would act on some impulse, or fear or superstitions that you would be responsible for things going wrong, or obsessions with sexual thoughts, images or impulses, or hoarding, collecting, or religious obsessions.) (DO NOT INCLUDE SIMPLY EXCESSIVE WORRIES ABOUT REAL LIFE PROBLEMS. DO NOT INCLUDE OBSESSIONS DIRECTLY RELATED TO EATING DISORDERS, SEXUAL DEVIATIONS, PATHOLOGICAL GAMBLING, OR ALCOHOL OR DRUG ABUSE BECAUSE THE PATIENT MAY DERIVE PLEASURE FROM THE ACTIVITY AND MAY WANT TO RESIST IT ONLY BECAUSE OF ITS NEGATIVE CONSEQUENCES.)	☐	☐

NEUROPSYCHIATRIC INTERVIEW *continued*

PTSD	NO	YES
Have you ever experienced or witnessed or had to deal with an extremely traumatic event that included actual or threatened death or serious injury to you or someone else? EXAMPLES OF TRAUMATIC EVENTS INCLUDE: SERIOUS ACCIDENTS, SEXUAL OR PHYSICAL ASSAULT, A TERRORIST ATTACK, BEING HELD HOSTAGE, KIDNAPPING, FIRE, DISCOVERING A BODY, SUDDEN DEATH OF SOMEONE CLOSE TO YOU, WAR, OR NATURAL DISASTER.	☐	☐
Did you respond with intense fear, helplessness or horror?	☐	☐
During the past month, have you re-experienced the event in a distressing way (such as, dreams, intense recollections, flashbacks or physical reactions)?	☐	☐

Addiction	NO	YES
In the past 12 months, have you had 3 or more alcoholic drinks within a 3 hour period on 3 or more occasions?	☐	☐
Have you ever got into trouble by the use of alcohol and/or have you ever been tackled by someone about your drinking behavior?	☐	☐
In the past 12 months, did you take any of these drugs more than once, to get high, to feel better, or to change your mood?	☐	☐
Cross <u>each</u> drug taken:		
Stimulants: ☐ amfetamine, ☐ 'speed', ☐ crystal meth, ☐ Dexedrine, ☐ Ritalin, ☐ diet pills, ☐ 'Rush'.		
Cocaine: ☐ snorting, ☐ IV, ☐ freebase, ☐ crack, ☐ speedball.		
Narcotics: ☐ heroin, ☐ morphine, ☐ opium, ☐ Dilaudid ☐ Demerol ☐ methadone, ☐ codeïne, ☐ Percodan, ☐ Darvon.		
Hallucinogens: ☐ LSD (acid), ☐ mescaline, ☐ PCP ('angel dust'), ☐ 'mushrooms', ☐ XTC, ☐ MDA, ☐ MDMA, ☐ peyote, ☐ psilocybin, ☐ STP		
Inhalants: ☐ glue, ☐ ethylchloride, ☐ laughing gas, ☐ amyl- of butyl nitraat ('poppers').		
Marijuana: ☐ hashish (hasj), ☐ THC, ☐ weed, ☐ "pot", ☐ "grass", ☐ "reefer".		
Tranquillizers: ☐ Quaalude ☐ Secondal ('reds'), ☐ Valium, ☐ Xanax, ☐ Librium, ☐ Ativan, ☐ Dalmane, ☐ Halcion, ☐ barbiturates ☐ Miltown.		
Miscellaneous: ☐ steroids, ☐ nonprescription sleep or diet pills, ☐ GHB ☐ Any others?		

NEUROPSYCHIATRIC INTERVIEW *continued*

Do the participant have a family history of panic disorder/panic attacks. (✓)	**YES**		**NO**	
Has the interview revealed anything abnormal? (✓)	**YES**		**NO**	

If YES, *Please specify below*

Comments	

Appendix D1: ADHD- Current Symptom Scale ('Self')

Initials/ID #:_____
Date:_____

Current Symptoms Scale – Self

(Barkley & Murphy, 2006)

Please rate yourself by indicating the frequency next to each item that best describes your behaviour *during the last 6 months.*

	Never or Rarely	Sometimes	Often	Very Often
1. Fail to give close attention to details or make careless mistakes in my work				
2. Fidget with hands or feet or squirm in seat				
3. Have difficulty sustaining my attention in tasks or fun activities				
4. Leave my seat in situations in which seating is expected				
5. Don't listen when spoken to directly				
6. Feel restless				
7. Don't follow through on instructions and fail to finish work				
8. Have difficulty engaging in leisure activities or doing fun things quietly				
9. Have difficulty organising tasks and activities				
10. Feel "on the go" or "driven by a motor"				
11. Avoids, dislike, or am reluctant to engage in work that requires sustained mental effort				
12. Talk excessively.				
13. Lose things necessary for tasks or activities				
14. Blurts out answers before questions have been completed				
15. Am easily distracted				
16. Have difficulty awaiting turn				
17. Am forgetful in daily activities				
18. Interrupt or intrude on others				

Score:_____

Appendix D2: ADHD- Current Symptom Scale ('Other')

Initials/ID #:_____

Date:_____

Current Symptoms Scale – Other

(Barkley & Murphy, 2006)

Please rate the person who gave you this form by indicating the frequency next to each item that best describes this person's behaviour *during the last 6 months.*

	Never or Rarely	Sometimes	Often	Very Often
1. Fails to give close attention to details or makes careless mistakes in his/her work				
2. Fidgets with hands or feet or squirms in seat				
3. Has difficulty sustaining his/her attention in tasks or fun activities				
4. Leaves his/her seat in situations in which seating is expected				
5. Doesn't listen when spoken to directly				
6. Seems restless				
7. Doesn't follow through on instructions or fails to finish work				
8. Has difficulty engaging in leisure activities or doing fun things quietly				
9. Has difficulty organising tasks and activities				
10. Seems to be "on the go" or "driven by a motor"				
11. Avoids, dislikes, or is reluctant to engage in work that requires sustained mental effort				
12. Talks excessively.				
13. Loses things necessary for tasks or activities				
14. Blurts out answers before questions have been completed				
15. Is easily distracted				
16. Has difficulty awaiting turn				
17. Is forgetful in daily activities				
18. Interrupts or intrudes on others				

Score:_____