

Visual Social-emotional Attention in ADHD
Including the Impact of Autism

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ABSTRACT

ADHD is a common neurodevelopmental condition with poor long-term outcomes. The core problem that this project sought to address is a common clinical issue encountered in children with ADHD presenting to services with impairing social cognitive difficulties, including poor emotion recognition. The aim was to understand if emotion recognition difficulties were a primary consequence of abnormal patterns of visual attention in ADHD or alternatively social processing difficulties typically found in autism. Findings from two novel independent study samples demonstrated that visual attention to faces in children with ADHD (ADHD and ASD+ADHD) differed from children without ADHD (ASD and typically developing controls) using a 2x2 factorial approach. Specifically, children with ADHD (ADHD and ASD+ADHD) showed an atypical 'hyper-extensive' scanning of emotional faces compared to those without ADHD (ASD and typically developing controls). In contrast, Children with ASD (ASD and ASD+ADHD) were slower to orient to faces in ADOS (Autism Diagnostic Observation Schedule) pictures compared to those without ASD (ADHD and typically developing controls). Findings were in keeping with different visual attention profiles in ADHD compared to ASD with overlapping features in the comorbid group, indicating true comorbidity. Differentiation of visual social-emotional attention was also found at the group level using machine learning and discriminant function analysis, and the highest classification rate of 88% was found for the ADHD group. The findings of this research have implications for the diagnosis and the management of ADHD and associated social-emotional impairments.

DEDICATION

This Thesis is dedicated to my sons, Milan and Jai.

ACKNOWLEDGEMENTS

I am most fortunate to have had the clinical academic training that I have received. I would like to thank Prof Chris Hollis for his excellent clinical academic teaching and for his faith in my abilities during the difficult phases of this project. I would like to thank Dr Maddie Groom for her tremendous all-round supervision throughout this project. I am grateful to Dr Elizabeth Liddle for her support and advice during the beginning of the data analysis of the project. I would also like to thank Iti Arora and Alessio Bellato for providing peer support during the later stages of the PhD and my clinical colleagues who have supported my academic pursuit. I would like to thank all the participants that made the time and effort to take part in the studies. I would like to acknowledge the Waterloo Foundation and the Baily Thomas Charitable Fund for funding the studies. I am grateful to the Royal College of Psychiatrists Academic Faculty for awarding me the Gosling Fellowship, which contributed to funding my PhD. I would also like to express my gratitude to my family including my husband Manas for his remarkable support and encouragement. A special thanks also goes to my mother Neena who has not only been a role model for me but also helped to raise my sons Milan and Jai while I pursued this work.

STATEMENT OF WORK

This PhD was completed on a part-time basis and I have had much support along the journey. I had the opportunity of an NIHR funded academic clinical fellowship to conceptualise the proposal for this Thesis which allowed me to pick the subject that motivated me to complete the work. During my clinical lectureship in child psychiatry at the University of Nottingham, I was a named investigator on the first study in this Thesis and, was part of the recruitment and testing team with Marina Simeou and Dr Maddie Groom. I had help on the programming of the tasks from Maria Simeou; programming scripts for the dynamic eye gaze from Dr Elizabeth Liddle; and machine learning from Drs Shashank Jaiswal and Michelle Valstar for the first study in Chapter 2. I conducted all the analysis for the first study in Chapter 3. I was part of the clinical testing team for the second study sample. I took the lead on the clinical research diagnoses for both studies and Prof Chris Hollis was also part of the clinical consensus team with me. My colleagues Iti Arora and Alessio Bellato completed the recruitment and the eye tracking testing for the second study, and I was a locality clinical site co-ordinator and advised on clinical recruitment in my capacity as consultant child psychiatrist. I conducted all the analysis for the second study and wrote up this Thesis. I have presented work from Chapters 1–6 at local, national and international conferences including the Centre for ADHD and Neurodevelopmental Disorders across the Lifespan (CANDAL) at the University of Nottingham, Child Psychiatry Research Society, Junior-European Network for Hyperkinetic Disorders (J-EUNETHYDIS) and the Royal College of Psychiatrists International Congress.

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ABBREVIATIONS AND GLOSSARY

ADHD: ***Attention Deficit Hyperactivity Disorder***

ADOS: ***Autism Diagnostic Observation Schedule***

ASD: ***Autism Spectrum Disorder***

CAMHS: ***Child and Adolescent Mental Health Services***

CBRS: ***Conners' Behaviour Rating Scale***

CD: ***Conduct Disorder***

CNV: ***Copy Number Variant***

DAWBA: ***Development and Well-Being Assessment***

DFA: ***Discriminant Function Analysis***

DSM-IV: ***Diagnostic and Statistical Manual of Mental Disorders—4th Edition***

DSM-5: ***Diagnostic and Statistical Manual of Mental Disorders—5th Edition***

DT: ***Dwell Time-*** *an eye tracking measure indicating the amount of time spent viewing a specified area. Calculated as the sum of the duration of all the fixations falling in the specified area of interest of the stimulus.*

Emotion Recognition- *the ability to decipher an emotional state for example happiness.*

Empathy- *the ability to put yourself in someone else's shoes and to really feel and experience their emotional state as your own, not just to be able to recognise it.*

Eye tracking- *measurement of eye movement dynamics during visual stimulus presentation using infrared eye tracker technology.*

Fixation- *a set of eye locations within a defined area for a selected amount of time which represents the stationary period between eye movements indicating attention during visual stimulus presentation.*

FC: ***Fixation Count-*** *an eye tracking measure indicating exploration and processing of information in a specified area, calculated as the total number of fixations falling in the specified area of interest of the stimulus.*

FFT: ***First Fixation Time-*** *an eye tracking measure indicating speed of orienting to a specified area.*

FSPL: ***Fixation Scanpath Length-*** *a spatial eye tracking measure indicating breadth of attention, calculated as the sum of the distances from fixation to fixation per trial.*

FSIQ: ***Full Scale Intelligence Quotient***

GP: ***General Practitioner***

GWAMA: ***Genome Wide Association Meta-analyses***

GWAS: ***Genome Wide Association Studies***

HI: ***Hyperactive Impulsive***

IA: ***Inattentive***

Interest area - *a specified area of interest on the visual stimulus for example the mouth region of a face stimulus.*

IAPS: ***International Affective Picture System***

ICD-10: ***International Classification of Diseases—10th Revision***

IQ: ***Intelligence Quotient***

LEA: ***Left Eye Area-*** *a specified area of interest on the face stimulus. The left eye area of the face stimulus corresponds to the eye region in the left hemi field of the face stimulus from the viewer's perspective.*

LI: ***Laterality Index-*** *an eye tracking measure indicating hemispheric lateralisation of fixation direction during face processing. A negative index equals more leftward fixations associated with typical right hemisphere lateralisation in face processing.*

MA: ***Mouth Area-*** *a specified area of interest on the face stimulus which corresponds to the mouth region of the face.*

MFD: ***Mean Fixation Duration-*** *a temporal eye tracking measure indicating processing rate, calculated as the average fixation duration per trial.*

MLBF: ***Mean Length Between Fixations-*** *a spatial eye tracking measure indicating breadth of attention, calculated as the average distance between fixations per trial***.**

ODD: ***Oppositional Defiant Disorder***

PDD: ***Pervasive Developmental Disorders***

RC: ***Run Count-*** *an eye tracking measure that indicates exploration and processing between specified areas of the stimulus.*

REA: ***Right Eye Area-*** *a specified area of interest on the face stimulus. The right eye area of the face stimulus corresponds to the eye region in the right hemi field of the face stimulus from the viewer's perspective.*

Scanpath- *execution of a particular sequence of eye movements when a visual stimulus is processed.*

SCQ: ***Social Communication Questionnaire***

SD: ***Standard Deviation***

SDLBF: ***Standard Deviation Length Between Fixations-*** *a spatial eye tracking measure indicating variation in breadth of attention, calculated as the standard deviation of the distance between fixations.*

Social-emotional stimuli- *include stimuli with social and emotional content for example an image of a face depicting happiness.*

Social Cognition- *allows individuals to make sense of their own and another's feelings, thoughts, beliefs and desires and to interact with other people in a reciprocal social world.*

SPSS: ***Statistical Package for Social Sciences***

SSRI: ***Selective Serotonin Reuptake Inhibitor***

ToM: ***Theory of Mind-*** *is the ability to decipher mental states so that an individual can interpret what another person could be thinking or feeling.*

TFD: ***Total Fixation Duration-*** *a temporal eye tracking measure indicating processing rate, calculated as the sum of the fixation duration per trial.*

TFN: ***Total Fixation Number-*** *a temporal eye tracking measure indicating processing rate, calculated as the sum of the number of fixations per trial.*

VSA: ***Visual Social-emotional Attention-*** *refers to visual attention to social-emotional stimuli measured using eye tracking technology.*

WASI: ***Wechsler Abbreviated Scale of Intelligence-*** *used to measure the full scale intelligence quotient*

1 INTRODUCTION AND LITERATURE REVIEW

1.1 OVERVIEW

1.1.1 SYNOPSIS OF THE PROBLEM AND CLINICAL RELEVANCE

The core problem that this project seeks to address is a common clinical issue encountered in children, young people and families with Attention Deficit Hyperactivity Disorder (ADHD). Children with ADHD presenting to clinical services have observed impairing social cognitive difficulties including poor emotion recognition. As detailed in Case 1 (see Case vignettes; Appendix I.), the first case example with ADHD presented with poor concentration, disruption in class, difficulties with lining up in queues and turn taking, butting into conversations and getting easily frustrated if he lost in sports games. He also had significant social-emotional difficulties including getting into arguments with peers, misinterpreting social situations and found it difficult to express his emotions. It is not clear if social cognitive difficulties including poor emotion recognition that present in children with ADHD are a primary consequence of ADHD or secondary to a co-occurring disorder such as autism. As detailed in Cases 1 and 3 (see Appendix I.), both cases presenting to clinical services with ADHD also had social cognitive difficulties. Case 3 for example also met criteria for an independent diagnosis of ASD, including difficulties with spontaneous emotion recognition and empathy on the Autism Diagnostic Observation Schedule (ADOS).

In the ideal clinical situation, individuals presenting with ADHD would benefit from an efficient and accurate assessment of social-emotional difficulties from the outset so that their treatment plan can address these needs. However, the reality is quite different and, typically after diagnosis and prescription of ADHD medication, children and young people with ADHD continue to suffer from significant social-emotional difficulties (see Case 3; Appendix I.). Social-emotional difficulties in ADHD have been assumed to be a consequence of core ADHD symptoms such as inattention, poor listening skills, difficulties waiting turn and social impulsivity. However, the fact that social-emotional problems clinically observed to persist in many individuals treated with stimulant medication that are so effective at improving core ADHD symptoms, suggests that other mechanisms could be leading to social cognitive difficulties in ADHD. As the comorbidity between ADHD and Autism Spectrum Disorder (ASD) is increasingly recognised, this could be one possible explanation for the social cognitive difficulties in ADHD. There is, however, still uncertainty if all social cognitive difficulties are due to an independent autism diagnosis, diagnostically subthreshold autism symptoms or a severe and broader ADHD phenotype. This can present as a significant clinical challenge as detailed in Case 3 (see Appendix I.).

In clinical practice, children with ADHD can be assessed for an independent diagnosis of autism using gold standard interviews and observations schedules. However, these were designed to be used in community populations to distinguish autism from typically developing children. There can be overlap between the questions asked in clinical interviews for

autism and symptoms of ADHD. For example, the Autism Diagnostic Observation Schedule (ADOS) used in the assessment of autism has tasks designed to identify emotion recognition and to test for social saliency and pick up on others' emotions. As children with ADHD may have independent difficulties in this area, the scores could be artificially raised leading to a false positive diagnosis of ASD on this instrument. Thus, current interviews and assessment tools for autism when used in children with ADHD, require the clinician to have appropriate extensive training. Additionally, the final diagnosis relies on clinical judgement and can be prone to subjectivity.

A consequence is that children with ADHD who have significant social-emotional difficulties which cause impairment and are often missed at the outset, leading to an unmet need. This can lead to extensive morbidity for the individual and poor socio-economic outcomes for society. Individuals with ADHD who are referred for further investigation of social-emotional problems, suspected to be of an autistic nature, have further healthcare costs and extensive waits, as assessment of autism in ADHD is a highly specialist area of clinical expertise.

In order to address the above problem, this Thesis attempts to bridge the gaps through this innovative research project investigating visual social-emotional attention using eye tracking in children with ADHD, ASD, and comorbid ASD+ADHD, as well as typically developing control children. For the purpose of this Thesis, Visual Social-emotional Attention (VSA) refers to visual attention to social-emotional stimuli (for example, faces depicting emotion) measured using eye tracking technology. Visual social-

emotional attention is synonymous with visual social attention, a term used to address visual attention to social stimuli in autism (Guillon, Hadjikhani, Baduel, and Rogé 2014). Visual social-emotional attention is the preferred term for this Thesis, serving as a reminder that both social and emotional processing are inextricably linked and particularly important when studying ADHD (Dickstein and Castellanos 2012).

1.1.2 Main proposal and argument of the Thesis

The proposal of this Thesis is that the study of visual social-emotional attention (VSA) in ADHD will uncover important insights into social-emotional difficulties including emotion recognition. It is suggested that visual social-emotional attention will also help to clarify comorbidity between ADHD and ASD. In particular, it is argued that children with ADHD will have a primary problem with visual social-emotional attention, which could explain emotion recognition difficulties previously described in this population; and this would differentiate from visual social-emotional attention difficulties in ASD. It is proposed that some visual social-emotional attention measures could differentiate ADHD from ASD while other measures which overlap between them, potentially explain comorbidity between the disorders.

Through two novel empirical studies, this Thesis propelled the argument by showing how visual social-emotional attention in ADHD can:

1) improve understanding of emotion recognition deficits and social processing in ADHD;

2) identify important similarities and differences compared with ASD and ASD+ADHD, shedding insights into diagnostic specificity and comorbidity;
3) offer some potential as a diagnostic aid characterising ADHD, ASD and ASD+ADHD groups.

1.1.3 THESIS STRUCTURE SUMMARY

Chapter 1 includes a general overview of ADHD including the prevalence of comorbidity with ASD and putative models of the comorbidity between them. Social cognitive deficits in ADHD are reviewed and visual social-emotional attention findings in ADHD, ASD and controls from the eye tracking literature are compared. Chapter 2 describes the methods used for the first empirical study investigating visual social-emotional attention to emotional faces in children with ADHD, ASD, ASD+ADHD and typical controls. Chapter 2 also presents the findings from qualitative analysis of the eye-tracking data from this first study as well as the findings from a machine learning approach that was designed to validate the qualitative findings in a data-driven way.

Chapter 3 describes and presents the results of analysis of quantitative visual social-emotional attention measures using eye tracking from the first study, including fixation latencies to emotional faces in an emotion recognition task. Chapter 4 describes the methods and results of the second study which recruited a new sample of children with ADHD, ASD and ASD+ADHD, as well as typically developing controls. Chapter 4 presents

the results of group comparisons on measures of visual social-emotional attention to ADOS images. Chapter 5 presents findings from the second sample of children during free viewing of emotionally neutral faces, to provide a neutral emotion control comparison with the emotional faces in the emotion recognition task from the first study.

Chapter 6 presents the results from Discriminant Function Analysis including prediction of diagnoses from visual social-emotional attention measures that yielded significant group differences in the preceding chapters. Chapter 7 summarises the results from the previous chapters and gives a discussion of the main findings including clinical relevance and future research avenues. Chapter 7 also evaluates visual social-emotional attention using eye tracking as a potential diagnostic aid in neurodevelopmental assessment. Final conclusions are drawn regarding the study of visual social-emotional attention using eye tracking as a potential solution to the problem of social-emotional difficulties in ADHD and the impact of autism.

1.2 ATTENTION DEFICIT HYPERACTIVITY DISORDER, A GENERAL OVERVIEW

1.2.1 DIAGNOSIS AND EPIDEMIOLOGY

Attention Deficit Hyperactivity Disorder (ADHD) is a common heterogeneous neuro-developmental disorder characterised by developmentally inappropriate levels of hyperactivity, impulsivity and inattention (American Psychiatric Association 2013) (Figure 1.1). According to the Diagnostic Statistical Manual, Fifth Edition (DSM-5), in order to meet criteria for a diagnosis of ADHD, six or more symptoms of inattention or six or more symptoms of hyperactivity/ impulsivity need to be present for at least six months (American Psychiatric Association 2013). In addition to this, the symptoms need to be pervasive, impair functioning in at least one context and be out of keeping with the developmental level of the child. In DSM-5, there are 3 presentations of ADHD. Predominantly inattentive presentation (for which only criteria for inattentive symptoms are met); predominantly hyperactive/impulsive presentation (for which only criteria for hyperactive/impulsive symptoms are met); and Combined presentation (for which criteria for both inattentive symptoms and hyperactive/impulsive symptoms are met; Figure 1.1) (American Psychiatric Association 2013).

In the International Classification of Diseases 10th revision (ICD-10) (World Health Organisation 1994), the disorder is known as Hyperkinetic Disorder (HKD) and although the clinical construct is similar to ADHD the diagnostic criteria are more stringent such that six or more symptoms of inattention and six or more symptoms of hyperactivity/impulsivity need to be

met in two or more settings. Hyperkinetic Disorder in ICD-10 is most similar to DSM-5 ADHD combined presentation (Figure 1.1). ICD-10 and the Diagnostic Statistical Manual, Fourth Edition (DSM-IV) stipulated that ADHD should not meet the criteria for pervasive developmental disorder, now more widely termed Autism Spectrum Disorder (ASD) (World Health Organisation 1994; American Psychiatric Association 2000). However, DSM-5 now allows for the combined diagnoses of both ADHD and ASD (American Psychiatric Association 2013). In addition to ASD, ADHD is also frequently associated with other Axis I childhood psychiatric disorders such as Oppositional Defiant Disorder (ODD), Conduct Disorder (CD) and other developmental disorders such as Tourette's syndrome in addition to mood and anxiety disorders (Taurines et al. 2010; Pliszka 2009, 2000; Kadesjö et al. 2003).

ADHD combined presentation has been shown to be the most severe of the ADHD presentations in DSM, with poorer levels of functioning at home and at school. Children with ADHD combined presentation are also more likely to have a disruptive disorder such as ODD compared with ADHD hyperactive/impulsive and inattentive presentations although, children with inattentive subtype are more likely to need extra help at school (Faraone et al. 1998). Children with ADHD have more emotional dysregulation and social dysfunction, leading to poorer prognosis (Nijmeijer et al. 2008; Greene et al. 1996; Gillberg 2014). However, it remains unclear if social deficits are secondary to additional diagnoses including ASD or core to the primary ADHD deficits.

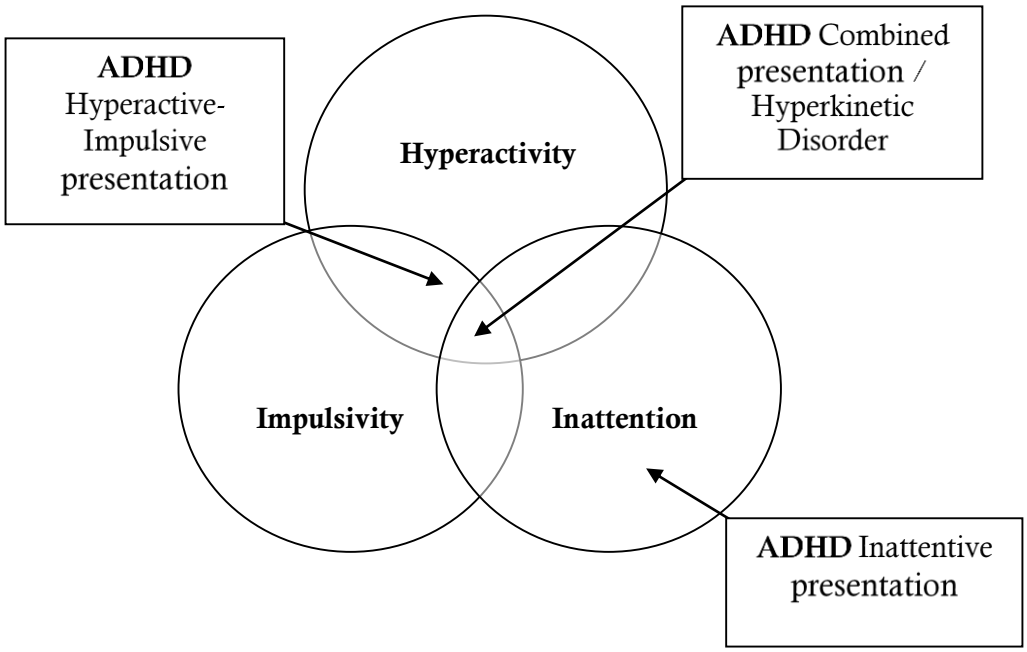


Figure 1. 1: Symptoms and presentations of ADHD

Circles denote symptom domains. Overlapping parts of the Venn diagram denote overlapping symptom domains (NB these do not reflect prevalence of presentations e.g. combined is more common that hyperactive-impulsive presentation). Arrows indicate overlapping symptom domains for the ADHD presentations in the respective attached textbox

ADHD is a highly prevalent disorder affecting 3–9% of the childhood population (NICE 2018; Willcutt 2012; Polanczyk et al. 2007; McArdle, Prosser, and Kolvin 2004). The condition is more common in boys than girls with a ratio of 4:1 in the British Mental Health Survey (Ford, Goodman, and Meltzer 2003). ADHD is a persistent condition with approximate prevalence rates of 4% in adults with 0.6–1.2% meeting diagnostic criteria for ADHD at 25 years and 2–4% in partial remission (Biederman et al. 2006; NICE 2008). ADHD is associated with high levels of financial burden on the community and stress within families with adverse outcomes at school

and at work (Biederman et al. 2006). As well as functional impairments at home and at school, ADHD is associated with poor self-esteem, substance misuse, self-harm, delinquency and social and relationship difficulties with peers and adults (Steinhausen 2009).

1.2.2 CAUSAL FACTORS

As described above, diagnosis of ADHD is currently based on the classification of behavioural symptoms according to the ICD-10 and DSM-5. There is a vast amount of literature reporting the causal factors of ADHD; although, none so far have proved to be diagnostic (American Psychiatric Association 2013). Nevertheless, the goal is that one-day diagnosis will be linked more closely to causal factors and that diagnostic tests will be available to aid diagnosis. In this section the well-studied causal factors will be reviewed including the genetics, and neural basis of ADHD in order to put the work in this Thesis in context.

ADHD is a highly heritable condition with an estimated heritability rate between 60–90% (Brikell, Kuja-Halkola, and Larsson 2015; Jansen et al. 2019; Nikolas and Burt 2010; Thapar 2018). A recent Genome Wide Association Meta-analysis (GWAMA) of ADHD and controls identified variants surpassing genome-wide significance in 12 independent loci; some related to neural mechanisms including synapse formation and action (Demontis et al. 2019). As Genome Wide Association Studies (GWAS) identify common DNA variants, some of the heritability of ADHD could be due to single nucleotide polymorphisms, suggesting ADHD could be an extreme form of trait symptoms (Demontis et al. 2019).

ADHD is a heterogeneous condition and environmental factors have also been implicated in its aetiology. Foetal exposure to alcohol, exposure to certain toxins, maternal smoking, pregnancy and birth complications, prematurity, head injury and psychosocial adversity such as low social status, maternal psychopathology and systemic factors including family dysfunction are all associated with ADHD (Max et al. 2005; Banerjee, Middleton, and Faraone 2007; Johnson et al. 2010b). As most of these factors occur very early in life it is likely that the presence of these factors increases the risk of ADHD (which is a developmental condition) in genetically predisposed individuals. The interplay between genes and environment have also been associated with the development of ADHD symptomatology through gene-environment interactions and also influence the response to stimulant and non-stimulant medication in ADHD (Palladino et al. 2019; Assary et al. 2018; Grizenko et al. 2012).

At a neuro-chemical level, the dopamine deficit theory and role of dopamine receptors have been implicated in ADHD. Dopamine levels are affected by levels of cell firing with release of dopamine, uptake of dopamine by the dopamine transporter and the metabolism of transmitter enzymes; abnormalities in any of these can lead to dopamine dysfunction (Swanson et al. 2007). The main mechanism of stimulant medication such as methylphenidate and dexamphetamine used in ADHD to help with the core symptoms is to increase synaptic levels of dopamine (Biederman 2005). Early candidate gene studied in ADHD included the dopamine transporter gene (*DAT1*) and the dopamine receptor type 4 gene (*DRD4*), based on the dopamine hypothesis of ADHD (Swanson et al. 2007). In addition to *DAT1*

and *DRD4*, the D5 dopamine receptor gene (*DRD5*), dopamine transporter gene *(SLC6A3),* serotonin transporter gene *(5HTT)* and the serotonin IB receptor gene *(HTRIB)* have also been shown to be significantly associated with ADHD across multiple studies (Faraone and Larsson 2019; Gizer, Ficks, and Waldman 2009; Li et al. 2014).

In addition to dopamine, norepinephrine which is also a catecholamine has also been implicated in ADHD and is increased by stimulant and non-stimulant medication in ADHD (Faraone 2018). Neurotransmitter transporters, adrenergic receptor genes *(ADRA2A, ADRA2C)* and cholinergic receptor gene *(CHRNA4)* have also been frequently associated with ADHD (Li et al. 2014). Furthermore, glutamate, an excitatory neurotransmitter is associated with hyperactive/impulsive symptoms and, GABA an inhibitory neurotransmitter is associated with inattentive symptoms; suggestive of excitatory and inhibitory neurotransmission imbalances in the pathogenesis of ADHD (Naaijen et al. 2017).

Neuroimaging studies have shown an overall reduction in brain volumes and cortical and subcortical alterations including the prefrontal cortex basal ganglia in ADHD (Greven et al. 2015; Shaw and Rabin 2009). Recent studies have also shown bilateral reductions in the amygdala, accumbens and hippocampus in addition to differences in growth rate of the white matter in the cerebellum and have implicated subcortical brain maturation and structural connection atypicalities in ADHD (Hoogman et al. 2017; Shaw et al. 2018). These findings suggest atypical neural connectivity and dysfunction in neural networks including the default mode network and motivation and reward systems are aberrant in ADHD (Fair et al. 2010; Sripada et al.

2014; Rubia et al. 2009). The threshold for deactivating the default mode network is increased in ADHD, however both motivation and methylphenidate have been shown to reduce the threshold to deactivate the default mode network which is required for focussed task-related attention (Liddle et al. 2011).

Dysfunction in brain networks leads to a broad range of cognitive impairments across a range of cognitive functions. ADHD is known to be associated with lower IQ levels and children with ADHD have IQ's as much as 7 points lower than controls (Jepsen, Fagerlund, and Mortensen 2009). In addition to lower than average IQ, executive functioning is also commonly impaired on neuropsychological testing in children with ADHD. Executive functions are higher mental functions used to govern behaviour including planning to maintain a later goal (Willcutt, Doyle, et al. 2005). The most common executive deficits found in ADHD are impairments in response inhibition, working memory and planning and this is independent of IQ (Willcutt, Pennington, et al. 2005).

To date, the search for a single brain or cognitive endophenotype for ADHD has not been successful and it is increasingly recognised that there are likely multiple pathways from the underlying neurobiology to the emergent phenotype of ADHD (Sonuga-Barke 2005; Sonuga-Barke and Coghill 2014). Social cognition including emotion recognition in ADHD has not been included in multi-pathway models of ADHD which focus on deficits in inhibitory control and reward circuits (Sonuga-Barke and Coghill 2014). While social cognitive deficits are viewed core to ASD, which is often

comorbid with ADHD, the exact basis of this co-occurrence is unclear. Elucidating the basis of comorbidity between disorders may improve insight between causal factors and diagnoses (see below); adding to the multi-pathway models of ADHD.

1.3 COMORBIDITY IN ADHD AND ASD

In this section, comorbidity is defined and linked to the literature on comorbidity in ADHD and ASD. Current areas of uncertainty including that of true comorbidity on a dimensional level and how this relates to this project was also highlighted.

1.3.1 COMORBIDITY

Comorbidity occurs when two or more disorders occur together more often than predicted by chance alone and is commonly found among disorders in child psychiatry (Caron and Rutter 1991). Several factors relate to high rates of comorbidity found in childhood psychiatric disorders, although none account for it completely (Rutter and Taylor 2002). Of these factors, the first factor that can contribute to high rates of comorbidity is referral bias, a phenomenon also known as Berkson's bias (Rutter and Taylor 2002; Berkson 1946). The second factor that can contribute to high rates of comorbidity in child psychiatry is that the symptoms are a 'phenocopy' of the comorbid disorder in question, such that the symptoms that are present seem to be like symptoms that manifest in other disorders but are really symptoms of the first (only) disorder. These first two factors are not 'true' comorbidity, but rather give spurious rates of comorbidity. The third factor that can contribute to high rates of comorbidity is that children with one disorder may be more likely to underachieve at school and develop a secondary emotional disorder, for example. The fourth factor that can contribute to high rates of comorbidity includes comorbid disorders that are different manifestations of the same underlying cause, for example same genetic and or environmental

cause. The fifth factor causing high rates of comorbidity in childhood psychiatric disorders is when the two disorders occurring together are due to a syndrome or distinct condition, for example manic episodes in combination with depressive disorder would be diagnosed as Bipolar disorder (Rutter and Taylor 2002). Another example of the fifth factor causing high rates of comorbidity due to a distinct condition could be 'Deficits in Attention, Motor control and Perception' otherwise known as DAMP. Although not officially part of ICD-10 or DSM-5, the term DAMP is commonly used in some parts of Europe to describe the combination of ADHD with Developmental Coordination Disorder (DCD) and perceptual deficits (Gillberg 2003). Although autism symptoms are often part of DAMP, the absence of a diagnosis of ASD does not preclude the child from having the condition (Gillberg 2003). Based on longitudinal studies, children with DAMP have more severe long term impairments in adolescence and adulthood than those without DAMP, despite the clinical symptoms of ADHD and DCD being less severe in early adulthood than childhood (Hellgren et al. 1994; Gillberg 2003; Rasmussen and Gillberg 2000). These findings suggest that having DAMP could be associated with more long term impairment than ADHD and/or DCD symptoms in adulthood would predict, providing some evidence of DAMP being a distinct condition.

Of the factors described above contributing to high rates of comorbidity in child psychiatric disorders, factors three through to five are likely to represent true forms of comorbidity (i.e. when two distinct disorders are actually present in the same individual). True comorbidity among disorders

raises important research questions, including revealing important information about shared aetiology, risk factors for the disorders and treatments (Neale and Kendler 1995). Neale and Kendler (1995) proposed several multifactorial models of comorbidity. In relation to this Thesis, two models may have particular relevance; these include the extreme multiformity model and the correlated liabilities model. Extreme multiformity includes cases where disorder A (above certain thresholds) generates symptoms of disorder B and, correlated liabilities, includes comorbidity of disorder A and disorder B when risk factors for disorder A and B are above threshold for the disorders (Neale and Kendler 1995).

1.3.2 ASD

As stated above, DSM-5 now allows for the combined diagnoses of ADHD and ASD (American Psychiatric Association 2013). Autism Spectrum Disorder (ASD) is a complex neuro-developmental syndrome consisting of deficits in: social reciprocity; communication; and unusual restricted, repetitive and stereotyped behaviours (World Health Organisation 1994). ASD is an 'umbrella-term' which incorporates the more severe 'classic' autism, first described by Kanner, at one end of the spectrum and 'high functioning autism' and Asperger's syndrome at the other end of the spectrum. In ICD-10, this group of disorders is named Pervasive Developmental Disorders (PDD) and is characterised by qualitative abnormalities in reciprocal social interactions and in patterns of communication and by a restricted, stereotyped, repetitive repertoire of interests and activities. According to ICD-10, these qualitative abnormalities are a pervasive feature of an individual's functioning in all situations. Asperger's syndrome is

characterised by the same type of qualitative abnormalities of social interaction as autism (restricted, stereotyped repetitive behaviours) but differs from autism as there is no general delay in language or cognitive impairment. As stipulated above, in Asperger's syndrome there is no delay in language acquisition. However, there are still communication difficulties in terms of higher-order communication, for example taking the meaning of things literally and difficulty in understanding jokes.

The subclassification and terminology in ICD-10 and DSM-IV were very similar. However, in DSM-5 the term PDD has been replaced by ASD and the 5 sub-diagnoses including Asperger's syndrome in DSM-IV have been removed with all diagnoses meeting criteria for ASD subsumed under the ASD diagnostic category (American Psychiatric Association 2013). The triad of deficits in DSM-IV have been compressed to a dyad of deficits in DSM-5 to include social communication deficits and restricted repetitive patterns of behaviour. Changes in the subtext in DSM-5 include deficits in social-emotional reciprocity in the social communication domain and reactivity to sensory input in the restricted and repetitive patterns of behaviour domain. The age of onset was also changed from age 3 in DSM-IV to early developmental period in DSM-5 (American Psychiatric Association 2000, 2013). DSM-5 also contains additional clauses regarding symptoms masked by learned strategies and, symptoms not being fully manifest until the social demands exceed limited capacities to allow for individuals to be identified across the whole autism spectrum, including females and adults (American Psychiatric Association 2013). Specifiers in-

cluding the presence or absence of additional intellectual impairment, language impairment, an associated medical, genetic or another neurodevelopmental condition are also included in DSM-5 (American Psychiatric Association 2013).

The current childhood prevalence of ASD is estimated to be approximately 1% and, has increased in part due to better identification of the disorder and also due to its classification into a broader autism phenotype to include the whole autism spectrum and milder forms of the disorder (Lord et al. 2000; Happe and Frith 2020; Christensen et al. 2016; Elsabbagh et al. 2012). Like ADHD, ASD is a highly heritable condition which is more common in boys (Fombonne 2009). As well as genetic factors, environmental factors including paternal age (Lundstrom et al. 2010), maternal infection during pregnancy (Patterson 2011), prematurity and low birth weight (Johnson et al. 2010a) have been implicated in ASD, indicating an epigenetic pathway of aetiology in this complex neurodevelopmental disorder.

When comparing executive function deficits between ASD and ADHD, findings have been mixed. Geurts et al. (2004) found more pronounced deficits in ASD than ADHD, with more difficulties in planning and cognitive flexibility than ADHD. In contrast, Lukito et al. (2017) found specificity for executive function deficits with ADHD symptoms and ToM deficits with ASD symptoms. Craig et al. (2016), reviewed 26 studies and concluded more deficits in response inhibition in ADHD, more deficits in planning in ASD whilst, other aspects of executive function such as

working memory and fluency were common to both disorders. Heterogeneity in studies on executive function deficits may in part be related to study design including testing and sample characteristics (Craig et al. 2016).

The concept of weak central coherence (attention to detail and local processing rather than global concepts and processing) has also been documented as a cognitive deficit in ASD (Happe and Frith 2006), although, this model of core deficit in ASD has been questioned by others (Chevallier et al. 2012; Fitzpatrick et al. 2018).

1.3.3 Comorbidity between ADHD and ASD

Many research studies have documented coexistence of ASD and ADHD diagnoses and as a result this comorbidity is widely accepted by clinicians. In a recent community-based twin study, a substantial proportion of children with ADHD (32% of males and 75% of females) scored within the clinical range for ASD and, children with severe forms of ADHD were found to have clinically significant symptoms in all three autism symptom domains on the Social Responsiveness Scale (SRS) (Reiersen et al. 2007). In addition, children with ASD have higher than expected rates of ADHD diagnosis for example, in a population derived cohort of children with ASD, 28% were found to have a comorbid diagnosis of ADHD (Simonoff et al. 2008). A recent meta-analysis including studies across development in those with ASD, reported a prevalence of 22% for a comorbid diagnosis of ADHD from population studies and, a prevalence of 34% for a comorbid diagnosis of ADHD from clinic based samples (Lai et al. 2019).

Studies have shown shared aetiology between ADHD and ASD indicating true comorbidity (Banaschewski, Poustka, and Holtmann 2011; Berenguer-Forner et al. 2015; Johnson et al. 2010b; Ayaz et al. 2015). This includes genetic overlap between rare Copy Number Variant (CNV) regions in ADHD and ASD (Martin et al. 2014) and more common loci from GWAMA (Grove et al. 2019). It has also been reported that rare protein-truncating variants (e.g. nonsense, frameshift and essential splice site mutations) have been indistinguishable in ADHD and ASD suggesting shared genetic overlap of the disorders (Satterstrom et al. 2018; Thapar 2018).

However, recent polygenic risk scores (PRS) for ADHD have been associated with ADHD and ASD+ADHD but not ASD, suggesting that the genetic relationship between ASD and ADHD is more complex (Jansen et al. 2019). It has also been proposed that common genetic variants may predict opposing cognitive outcome; with lower function in ADHD versus higher ability and educational attainment in ASD (Thapar 2018; Weiner et al. 2017).

In addition, although rare CNV deletions and duplications are associated with an increased risk for both ASD and ADHD, the patterns of association vary. For example, on 16p11.2 rare CNV deletions were more strongly associated with ASD and 16p11.2 duplications had higher odds of ADHD (Niarchou et al. 2019). Study findings for both CNV deletions and duplication on 22q 11.2 have shown raised risk for ASD and ADHD. However, deletions were associated with higher risk of ADHD and duplications with higher risk of ASD (Lin et al. 2017). These CNV findings lead to the

possibility that imprinted genes on certain risk chromosomes could be related to the expression of either ASD or ADHD in certain individuals. Overall, the genetic findings suggest each individual will have their own genetic fingerprint with common and or rare variants which could lead to expression of ASD, ADHD or ASD+ADHD. This would subsequently be coupled with environmental risks that further delineate the phenotypic profile expressed through gene environment interactions.

The recent genetic findings can also be linked with comorbidity literature on ADHD and ASD. A comprehensive literature review concluded that the majority of evidence on comorbidity between ASD and ADHD supports comorbidity as a third distinct category of ASD+ADHD (Berenguer-Forner et al. 2015). However, latent class analysis in a large sample indicated that the relationship may be more complicated as ASD always occurs with some symptoms of ADHD, falling into two subgroups of comorbidity; primarily ADHD with some ASD, termed ADHD(+ASD) and primarily ASD with some ADHD, termed ASD(+ADHD) (van der Meer et al. 2012). It remains unclear if the presence of comorbid symptoms as described by van der Meer et al. 2012, is due to 'double counting' of overlapping symptoms or 'true' comorbidity. In favour of 'true comorbidity' was that both the ASD(+ADHD) and the ADHD(+ASD) subgroups had some shared visuospatial and verbal working memory deficits compared with the typically developing control group. A potential suggestion against the 'true comorbidity hypothesis was the authors' conclusions for different treatment approaches for ASD(+ADHD) versus ADHD(+ASD), due to distinct cog-

nitive processing profiles. Specifically, a 'detail focused' cognitive style indicative of enhanced local processing was found in the ASD(+ADHD) subgroup compared with the ADHD(+ASD) subgroup (van der Meer et al. 2012).

To complicate matters further, both dimensional and categorical classification in child psychiatry is being advocated, for example allowing a dimension of ADHD symptoms and a categorical diagnosis of ADHD, respectively (Happe, Ronald, and Plomin 2006; Neale and Kendler 1995). Thus, children with a categorical diagnosis of ADHD, for example, may have symptoms of poor social cognition and this could represent i) associated 'ASD-like' symptoms related to primary ADHD (i.e. a 'phenocopy' of ASD symptoms), ii) co-existing ASD symptoms (i.e. a broader ASD dimensional phenotype) or iii) a co-morbid ASD diagnosis (on a categorical level).

Children with comorbid neurodevelopmental disorders are often excluded from research studies and clinical trials in order for the 'pure form' of the disorder to be studied. In addition, studies may not comment on comorbidity making it difficult to interpret findings. In those with a categorical diagnosis of ADHD, even when a categorical diagnosis of ASD had been excluded, it has been found that a substantial proportion of children have more 'ASD-like' symptoms in the social/communication domain but not the repetitive and stereotyped behaviour domains of the Social Communication Questionnaire (SCQ) (Kochhar et al. 2011). In a larger study, when children were assessed primarily for ADHD, a subsample of these children have been shown to have 'ASD-like' symptoms in all domains on the Social Responsiveness Scale (Reiersen et al. 2007). When a child is seen in clinic,

for either ASD or ADHD, it is prudent to screen for other neurodevelopmental disorders. However, different screening tools and scales for ASD may give varying results. It may also be difficult to interpret the results as true comorbid ASD symptoms and 'ASD-like' social cognitive symptoms secondary to ADHD may be very difficult to distinguish. Indeed, rating scales are unlikely to be sufficiently sensitive to the potentially different basis of social cognitive deficits in these populations. Similarly, inattention core to ADHD and social inattention core to ASD are hard to disentangle from questionnaires (Rommelse et al. 2010). Furthermore, current diagnostic methods for ASD are based on semi-structured interviews and observation schedules (the gold standard for diagnosing ASD). However, their use in comorbid psychiatric populations is more complex. Although aids in diagnosis of ADHD are emerging, for example the Qb test (Hall et al. 2014; Hollis et al. 2018) a technique to aid interpretation and classification of social deficits in neurodevelopmental disorders are also warranted in clinical practice. By correctly categorising the social cognitive deficits, it is anticipated this will help to guide treatments and prognosis from the onset of the diagnosis.

In summary, although there are many potential causal overlaps including genetic findings between ADHD and ASD suggestive of true comorbidity, there are also findings that indicate dissociation. It is unlikely that all children with ADHD presenting to services with social emotional impairments will meet criteria for an independent diagnosis of ASD however, although many present with severe impairment including social-emotional difficulties (see Case 3, Appendix I.). Although diagnosis of core deficits in

ADHD is well established, assessment of social difficulties is less so and tends to be viewed through the lens of ASD. Furthermore, as the official introduction of comorbid diagnosis of ADHD and ASD is relatively recent, simultaneous diagnostic assessment of both conditions is in its infancy. Diagnostic assessment and study of social cognition in ASD is very well established. Studying social cognition based on insights from ASD may help to provide a basis for improving diagnosis of social-emotional deficits in ADHD.

1.4 SOCIAL COGNITION IN ADHD

In this section, the literature on social cognition deficits in ADHD was reviewed; focussing in particular on emotion recognition. The literature on social cognition deficits in ASD was referred to where it was relevant to improving understanding of social cognition in ADHD. Social cognition allows individuals to make sense of their own and another's feelings, thoughts, beliefs and desires and to interact with other people in a reciprocal social world (Sharp, Fonagy, and Goodyer 2008). It includes several constructs including emotion recognition, Theory of Mind (ToM), empathy and emotional understanding (Sharp, Fonagy, and Goodyer 2008). This is not an exhaustive list and these constructs are invariably interrelated and evolve and mature during development.

1.4.1 EMOTION RECOGNITION

Emotion recognition is the ability to accurately identify an emotional state for example happiness. Emotion recognition is one component of social

cognition which, may facilitate higher level social cognitions discussed in the next section. The face is one of the most important visual stimuli and the eye region even more so in regards to identifying the emotions of another (Itier and Batty 2009). Deficits in recognising and identifying emotional facial expressions and understanding contextual meaning have been reported in ADHD (Dickstein and Castellanos 2012). Emotion recognition deficits have been reported globally (Da Fonseca et al. 2009; Kats-Gold, Besser, and Priel 2007; Seymour et al. 2013), to negative emotions (Singh et al. 1998; Pelc et al. 2006; Aspan et al. 2014) and to positive emotions (Sinzig, Morsch, and Lehmkuhl 2008). A summary of recent review studies on social cognition deficits including emotion recognition in ADHD are shown in Table 1.1

Table 1. 1: Summary of review articles on social cognitive deficits in ADHD

Review paper	Social cognitive domain	Disorder (s)	Findings
Uekermann et al. (2010)	Several social domains including emotion recognition	ADHD	Review of the literature shows ADHD is associated with social cognition impairments involving facial emotion and prosody perception.
Collin et al. (2013)	Facial emotion recognition	Child psychiatric disorders	Systematic review. Findings suggest abnormalities in facial emotion recognition in a wide range of child psychiatric disorders including ADHD (14 studies), conduct disorder (9 studies), mood disorders (18 studies), anxiety disorder (16 studies) and Schizophrenia (2 studies).
Graziano et al. (2016)	Emotional dysregulation, including emotion recognition and understanding	ADHD	Meta-analysis of 77 studies found a moderate weighted effect size (d=0.64) for emotion recognition/understanding deficits in ADHD. Co-occurring conduct problems or cognitive function did not moderate the link between ADHD and emotion recognition/understanding deficits.
Bora et al. (2016)	Several social domains including emotion recognition and ToM	ADHD versus ASD	Meta-analysis of 44 studies comparing ADHD with healthy controls and 17 studies comparing ADHD with ASD. Facial and vocal emotion recognition (d=0.40–0.44) and ToM (d=0.43) abilities were significantly impaired in ADHD. The most robust facial emotion recognition deficits were evident in anger and fear. Deficits in social cognition, especially ToM, were significantly more pronounced in ASD compared with ADHD.
Rodrigo-Ruiz et al. (2017) *(only abstract available)*	Facial emotion recognition	ADHD	Systematic review showing that most studies (n=28) confirm those with ADHD have facial emotion recognition deficits with poorer accuracy compared to controls. Those with ADHD tend to have a greater difficulty in recognising negative emotions (especially anger, fear and disgust).
Borhani et al. (2018)	Facial emotion recognition	ADHD	Systematic review found 26 studies with some inconsistent findings across the studies noted. Fear was the most poorly processed emotion. Facial emotion recognition deficits did not abate with development.
Romani et al. (2018)	Face processing and facial affect recognition	ADHD	Systematic review found 25 out of 34 studies showed facial emotion recognition deficits in ADHD. Emotion deficits for happy, angry and disgust were commonly listed. Authors concluded that few studies delineate between ADHD and ASD and so it is difficult to interpret results. Also, there were few studies on face processing and memory in ADHD.

As shown in Table 1.1, review articles that also report meta-analysis findings show moderate effect sizes (d=0.4–0.64) for emotion recognition deficits in ADHD compared with typically developing controls (Graziano and Garcia 2016; Bora and Pantelis 2016) which is in line with meta-analysis findings for emotion recognition deficits in ASD compared with typically developing controls (d=0.4) (Uljarevic and Hamilton 2013).

Rodrigo-Ruiz et al. (2017) and Romani et al. (2018) found recognition deficits for negative and positive emotions in ADHD, whereas recognition deficits for fear were most commonly found in the review by Borhani et al. (2018). Fear has also been shown to be misinterpreted in ASD (Uljarevic and Hamilton 2013) and this has been linked to avoidance of the eyes (Cuve, Gao, and Fuse 2018).

As reported by Collin et al. (2013), emotion recognition deficits occur in a number of child psychiatric disorders including ADHD and CD. It can be hypothesised that conduct problems could account for the raised level of emotion recognition deficits in ADHD (Santosh and Mijovic 2004). However, Graziano and Garcia (2016) showed that co-occurring conduct problems did not moderate the link between ADHD and emotion recognition suggesting that the emotion recognition difficulties in ADHD are due to other mechanisms.

In summary, there is consistent evidence of emotion processing deficits in ADHD. As emotion processing is not considered a core feature of the disorder in ICD-10 or DSM-5, it is important to clarify if the emotion recognition deficits in ADHD are due to an underlying comorbid disorder

such as ASD. Understanding the cause of the emotion recognition difficulties will help with the development of an effective treatment plan for children and families with ADHD.

The mechanisms and neurobiology of emotion recognition deficits in ADHD have been proposed. As emotion recognition deficits have been associated with errors on the continuous performance test (Shin et al. 2008) and go/no-go tasks (Sinzig, Morsch, and Lehmkuhl 2008), these problems in social interaction in ADHD are often attributed to attentional difficulties rather than core social impairments (Uekermann et al. 2010). However, there is also evidence that core ADHD symptoms do not explain the emotion processing deficits completely. For instance, Yuill and Lyon (2007) found that children with ADHD performed more poorly on emotion recognition tasks than purely cognitive tasks and that when inhibitory deficits were controlled for, performance in cognitive tasks improved but emotion recognition was still impaired. Studies measuring electrophysiological correlates of emotion processing, show that these may be altered in ADHD when viewing emotions. (Ibanez et al. 2011; Tye et al. 2014). Ibanez et al. (2011) suggested that atypical emotion processing could be related to reward processing in ADHD

As discussed in Section 1.1.1, methylphenidate is the most commonly used medication for ADHD and significantly improves core symptoms of the disorder (Cortese et al. 2018). If as postulated above, emotion recognition deficits in ADHD are due to core deficits, methylphenidate should be equally effective in attenuating emotion recognition deficits as core symptoms in ADHD. Of the studies that have investigated this, the

majority show only partial improvement in emotion deficits (Williams et al. 2008; Beyer von Morgenstern, Becker, and Sinzig 2014; Conzelmann et al. 2016). Williams et al. (2008) showed that despite normalisation of neural activity with methylphenidate, residual emotion deficits and negative mood persisted in ADHD suggesting that comorbidity could continue to cause emotion recognition deficits in those treated with methylphenidate. Beyer von Morgenstern et al. (2014) found improvement in happiness recognition but other emotion deficits remained significant. The authors suggest that emotion recognition deficits may persist despite treatment with methylphenidate because methylphenidate may not be potent enough to affect all the areas of the brain associated with emotion perception.

The amygdala is proposed to be the 'emotion recognition centre' of the brain as bilateral damage to the amygdala has been shown to lead to inability to detect emotions (Adolphs et al. 1996; Adolphs 2001). The orbitofrontal cortex is also important in the top-down regulation of emotion recognition (Kringelbach 2014). Functional imaging studies in ADHD have shown atypicalities in the limbic system, including hyperactivation of the amygdala to neutral faces when rating subjective fear (Brotman et al. 2010). Orbitofrontal dysfunction has also been reported and may be associated with social cognition deficits in ADHD suggesting that there may be top-down regulatory impairments as well as specific limbic dysfunction in ADHD (Brotman et al. 2010; Soliva et al. 2009; Rommelse et al. 2011).

1.4.2 THEORY OF MIND AND EMPATHY

Theory of Mind (ToM)

ToM is perhaps the most well-known construct as it is believed to explain the social deficits in ASD (Baron-Cohen, Leslie, and Frith 1985). ToM is the ability to decipher mental states so that an individual can interpret what another person could be thinking or feeling. First-order ToM is understanding what a person may be thinking or feeling whereas, second-order ToM is understanding what a person's thoughts are relating to another person's feelings and thoughts.

The literature shows mixed results regarding ToM in ADHD with some studies reporting deficits in ToM (Buitelaar et al. 1999; Nyden, Hjelmquist, and Gillberg 2000; Caillies et al. 2014) and others showing normal abilities in ToM (Sharp, Fonagy, and Goodyer 2008; Charman, Carroll, and Sturge 2001). Differences may be due to individuals with ADHD exhibiting subtler deficits and could depend on first-order ToM versus second-order ToM testing (Uekermann et al. 2010; Caillies et al. 2014). A recent meta-analysis by Bora and Pantelis (2006) showed that ToM deficits were more common in ASD than ADHD. Nevertheless, the effect size for ToM deficits were still moderate in ADHD (d=0.43) compared to typically developing controls and, comparable in magnitude to emotion recognition deficits in ADHD compared to typically developing controls (Bora and Pantelis 2016) (Table 1.1).

It has be argued that emotion recognition is a precursor to ToM, as emotion needs to be recognised in order to understand what someone is

thinking and feeling (Sommer et al. 2008). Furthermore, by being able to read the expressions of others we are able to learn from their experiences (Kringelbach 2014). In children with ADHD, parents retrospectively report significantly less imitation at age 4–5 years than children without psychiatric problems (Kochhar et al. 2011) and, as stated above, emotion recognition is impaired in ADHD. Taken together this would suggest that precursors of ToM may be aberrant in ADHD, although even these precursors may be driven by basic level processes including poor visual attentional during development (D'Souza and Karmiloff-Smith 2017) . Furthermore, social cognitive abilities including theory or mind and emotion recognition have been linked to visuospatial abilities in ASD and ADHD (Buitelaar et al. 1999), suggesting visual attention measured by eye tracking could help extend the study of social cognition including emotion recognition.

Empathy

Empathy is the ability to put yourself in someone else's shoes and to really feel and experience their emotional state as your own, not just to be able to recognise it. In order to have empathy one must have intact emotion recognition and theory of mind (Baron-Cohen 2009). Thus, deficits in empathy could be due to deficits in poor emotion recognition and/or deficits in ToM and/or inability to feel another's emotional state. Poor emotion recognition and ToM could thus be considered necessary precursors to having intact empathy. There is less literature on empathy compared to other social cognition deficits in ADHD (Uekermann et al. 2010). However, understanding of its precursors including emotion recognition deficits will be the first step to elucidating deficits of empathy in ADHD.

1.4.3 SUMMARY

In summary, there is a reasonable body of evidence to suggest that social cognition is impaired in ADHD. Emotion recognition is the most well studied social cognitive construct in those with ADHD, with effect sizes for emotion recognition deficits comparable to those with ASD (d=0.4). It remains unclear whether social cognitive deficits in ADHD are secondary to core ADHD symptoms or due to co-occurring ASD symptoms. As emotion recognition could be a necessary precursor to other social cognition deficits in ADHD, elucidating the relationship of emotion recognition deficits between ADHD, ASD and comorbid ADHD+ASD could be an important step to improving understanding of social cognition in ADHD. In addition, emotion recognition is a basic process compared to ToM and empathy which are more complex higher-order social cognitive processes. However, it is likely that emotion recognition as a basic cognition is dependent on attentional processes which can be measured.

1.5 VISUAL ATTENTION

In this section, a brief summary of attention and the use of eye tracking to measure visual attention is given and then a case made for the use of eye tracking as a potential method for studying visual social-emotional attention (VSA) in ADHD.

Attention is defined as the preferential processing of some items to the detriment of others (Findlay and Gilchrist 2003). In 1990, Posner and Peterson proposed three attentional networks: alerting, orienting and exec-

utive control, each with their own brain network and underlying neurobiology (Petersen and Posner 2012). The alerting network is linked with vigilance and associated with both tonic and phasic components. Tonic alertness had been associated with the right cerebral hemisphere. The alerting network is associated with norepinephrine which is released from the locus coeruleus with nodes in the frontal cortex and parietal areas relating to the dorsal visual pathway (Petersen and Posner 2012). Orienting is defined as the shifting of attention to select information in the environment (Desimone and Duncan 1995; Amso and Scerif 2015). The orienting network comprises the premotor cortex including the frontal eye fields with connections to the parietal cortex and dorsal visual pathway (Posner 2016). The ventral visual pathway is also involved in orientating of attention via the temporo-parietal junction. Acetylcholine is the neurotransmitter associated with orienting which is thought to be more bottom-up than the executive network which is related to top-down functions of attention. Top-down effects of the executive network include sustained attention and switching of attention. The executive network includes cingulo-opercular and frontoparietal regions of the brain (Petersen and Posner 2012).

Eyes can be described as a window to the mind and eye tracking can allow inferences to be made about where one is attending (Karatekin 2007). Indeed, Findlay and Gilchrist (2003) ague that vision is not a passive process but rather an active one made up of gaze shifts. Both overt attention (associated with an eye or head movement) and covert attention (not associated with an eye or head movement) can be employed in visual attention including visual orienting and scene perception (Amso and Scerif 2015; Findlay

and Gilchrist 2003). Eye movements are generated by the extra ocular muscles of the eye to form saccades and the cerebellum is involved in the control of eye movements (Robinson and Fuchs 2001). Once a saccade has been made, a location is fixated and an image is generated onto the fovea of the eye where vision is most acute due to the predominance of cone cells. This process of saccades (ballistic eye movements) and fixations (stationary periods between saccades indicating where one is attending) can be captured and measured using eye tracking (Findlay and Gilchrist 2003). Eye tracking measures eye movement dynamics during visual stimulus presentation using infrared eye tracker technology described in Chapter 2.

Although eye tracking is not a direct measure of visual attention, it is suggested that saccades and attention occur in parallel to each other (Deubel 2003) and thus, it could be feasible for eye tracking to be used as a marker to capture visual attention during facial emotion processing as an aid to characterise social cognitive deficits in neurodevelopmental disorders. Furthermore, eye tracking is a relatively non-invasive technique of measuring eye movements accurately and precisely and as technology advances, more portable eye tracking methods are possible making eye tracking an attractive technique to use for children.

One of the primary measures obtained from eye-tracking is the scanpath. A scanpath is the execution of a particular sequence of eye movements when a visual stimulus is processed (Noton and Stark 1971c, 1971b; Findlay and Gilchrist 2003). In particular, adults typically view a face stimulus in a holistic way, configuring a scanpath over the eyes and mouth in

an inverted triangle (Noton and Stark 1971a). Scanpaths can however differ depending on stimulus complexity and the instructions given to participants when viewing a stimulus (Findlay and Gilchrist 2003; Karatekin and Asarnow 1999).

Now, a case will be made for using eye tracking to investigate visual social-emotional attention in ADHD, in particular whether eye-tracking could help determine how emotion recognition is impaired in children with ADHD and if this impairment is qualitatively and quantitatively equivalent to that found previously in ASD. In the previous section, there was most evidence for aberrant emotion recognition in ADHD and emotion recognition deficits have been proposed as endophenotypes in ASD+ADHD as emotion recognition is more heritable than ToM which is also related to language ability (Rommelse et al. 2011). Sinzig et al. found that children with ADHD and ASD+ADHD had more emotion deficits than controls and they discussed that eye tracking while processing emotions would help elucidate these findings (Sinzig, Morsch, and Lehmkuhl 2008). Poor eye contact compared to controls has been found in a sample of ADHD without a comorbid diagnosis of ASD (Kochhar et al. 2011) and eye tracking studies show abnormal eye tracking indices in ADHD (Karatekin 2007; Rommelse, Van der Stigchel, and Sergeant 2008). In particular, children with ADHD have reduced ability to inhibit a saccade to the disallowed location on antisaccade tasks, reduced maintenance of fixation and sustained attention indicated by intrusive saccades and, variable and latent prosaccades towards a visual stimulus (Rommelse, Van der Stigchel, and Sergeant 2008; Karatekin 2007). These findings are thought to be due to a

reduction in the ability to supress unwanted saccades and a primary failure in visual fixation; since basic eye movement control may be deviant, dysfunctions of frontal eye fields and the cerebellum may be implicated in ADHD (Gould et al. 2001; Rommelse, Van der Stigchel, and Sergeant 2008). Effects with methylphenidate have variable results and a review by Karatekin (2007) points out that the majority of studies included participants of different ADHD subtypes and comorbid conditions and these were not always reported or analysed.

Those with ASD have some difficulty with antisaccades and smooth pursuit movement when visually tracking a moving stimulus on a horizontal path, however prosaccade tasks suggest difficulty in disengaging fixation (Rommelse, Van der Stigchel, and Sergeant 2008). Thus, although eye tracking indices are deviant in both ADHD and ASD, findings suggest children with ADHD have difficulty maintaining fixation, whereas children with ASD have difficulty disengaging fixation to non-social stimuli. Thus, visual attention to social-emotional stimuli could help to understand the basis of social-emotional deficits such as emotion recognition in ADHD and, whether these are similar or different from those in ASD.

1.5.1 Visual Social-emotional Attention in ADHD: a review of eye tracking studies

A summary of studies that have investigated visual social emotional attention in children and adolescents with ADHD are summarised in Table 1.2. All the studies used social emotional stimuli during eye tracking meeting the definition of visual social-emotional attention (VSA) in this Thesis. Six studies used emotional and/or neutral faces as stimuli (Marsh 2008; Muszkat et

al. 2015; Tsang 2016; Airdrie et al. 2018; Serrano, Owens, and Hallowell 2018; Gliga et al. 2018), four studies used pictures containing people/social scenes (Karatekin and Asarnow 1999; Pishyareh et al. 2012; Pishyareh et al. 2015; Frost-Karlsson et al. 2019) and two studies used a video containing people as stimuli (Tseng et al. 2013; Au - Tsang and Au - Chu 2018) . The studies also used a combination of different visual attention measures including fixation indices to the whole stimulus and fixation duration to interest areas within the stimuli as summarised in Table 1.2.

Of the 12 studies included in Table 1.2, nine included children with ADHD and two included children with ASD+ADHD (n=3). Of the 12 studies, only two studies compared ASD with ADHD and three studies compared ASD+ADHD with ASD. None of the 12 studies compared ADHD with ASD+ADHD, ASD and typically developing controls.

As shown in Table 1.2, three out of four studies that measured visual attention to emotional or neutral faces found atypical visual attention in children with ADHD compared to typically developing children. Marsh (2008) used a combination of eye tracking measures to quantify visual attention, including fixation latencies relating to temporal and spatial measures to the whole face stimulus and, fixation duration to interest areas of the face (see Table 1.2). Marsh (2008) found increased variability in the distance between fixations and reduced fixation duration to whole face stimuli compared to typically developing children but, not to fixation latencies relating to interest areas eyes, mouth and nose. Muszkat et al. (2015) and Serrano et al. (2018) found reduced fixation duration to eyes and mouth of faces in children with ADHD compared to typically developing children however this finding was

not replicated by Airdrie et al. (2018) who only presented findings of fixation duration to eyes but not to the mouth. Overall findings from these studies suggest that visual social-emotional attention to faces is atypical in ADHD compared to controls when a combination of fixation latencies to the whole face stimulus and to interest areas e.g. eyes and mouth are measured.

Serrano et al. (2018) and Marsh (2008) also studied the association of emotion recognition accuracy and visual social-emotional attention but there are mixed findings. Serrano et al. (2018) found a significant association between increased fixation duration to interest areas (eyes and mouth) and emotion accuracy ($r= 0.32$; $p<0.05$). Serrano et al. (2018) also found a trend between fixation duration to interest areas (eyes and mouth) and teacher rated inattentive symptoms ($r=-0.28$; $p<0.10$). Marsh (2008) found no association with emotion recognition and atypical visual attention. As Marsh (2008) only used happy, sad and neutral faces rather than all six basic emotions as stimuli, a lack of association could be due to reduced stimulus range. Due to the small number of studies and mixed findings, further clarification regarding the association between emotion recognition and visual social-emotional attention in ADHD is required.

Karatekin et al. (1999) and Pishyareh et al. (2015) found reduced fixation duration to pleasant and neutral pictures containing people during free viewing tasks in children with ADHD compared with controls. Pishyareh et al. (2015) found reduced fixation latencies to pleasant versus unpleasant pictures, suggesting that emotional valence of the picture affects visual attention in children with ADHD. Serrano et al. (2018) found highest effect sizes for

reduced visual attention to angry (d=-0.73) and scared faces (d=-0.50) in social scenes and, happy (d=-0.42) and angry (d=-0.38) face stimuli in children with ADHD. These findings suggest that atypical visual attention could be emotion specific in ADHD however, due to the difference in methodologies and small number of studies firm conclusions are difficult to make.

As described above, only two studies have compared visual social emotional attention in ADHD with ASD. Muszkat et al. (2015) found increased fixation duration to the mouth in neutral faces in children with ADHD compared with ASD. Frost-Karlsson et al. (2019) found that time of first fixation to people in social scenes was slower in children with ASD compared with ADHD however, fixation duration was not different between the groups. These two studies suggest that visual social-emotional attention could differ between ADHD and ASD however, supplementary measures to fixation duration such as first fixation time could possibly improve differentiation amongst the groups when viewing social scenes.

Of the three studies that compared ASD+ADHD with ASD, significant differences were not found using fixation duration to eyes and mouth in static faces (Tsang et al 2016). Differences amongst a child with ASD compared with ASD+ADHD were found qualitatively on the image of the case study scanpaths provided by Au-Tsang et al. (2018). Gliga et al. (2018) found differences between high risk infants for ASD versus ASD+ADHD using fixation re-entry counts to interest areas such as faces and non-social objects. No studies comparing visual social-emotional attention in ADHD and ASD+ADHD were found. However, based on the findings in ASD and ASD+ADHD, visual social-emotional attention in comorbidity is likely to

require measurement of additional fixation indices to fixation duration in order to elucidate any underlying differences amongst the groups.

In summary, studies investigating visual social-emotional attention in children with ADHD suggest that visual attention could be atypical compared with typically developing children. A combination of fixation indices to face stimuli and fixation duration to interest areas eyes and mouth showed significant differences amongst the studies using face stimuli. Emotion specific findings and correlation between visual attention and emotion recognition was only tested in two studies and both had differing results suggesting that further clarification is needed. One study differentiating visual social emotional attention in children with ADHD from ASD used additional fixation measures to fixation duration including first fixation time to neutral social scenes. Only three visual social emotional attention studies using eye tracking comparing ASD and ASD+ADHD were found, one of which included single case studies in children and, another was in high risk infants. No studies comparing ADHD with ASD+ADHD were found suggesting that further studies are needed to clarify visual social-emotional attention in ADHD compared with ASD and ASD+ADHD.

Table 1. 2: Summary of studies investigating Visual Social-emotional Attention in ADHD

Study	Groups (size; age range)	Task	Visual attention measures	Findings for ADHD
Karatekin (1999)	ADHD (n=30; age 9–19 years) Youth-onset schizophrenia (n=13; age 9–19 years) Controls (n=24; age 10–17 years)	Viewing static thematic pictures (n=6) from children's books.	1) Total fixation duration 2) Distance between fixations	ADHD group had shorter fixations compared to control children
Marsh (2008)	ADHD (n=42; age 12–18 years) First Episode Schizophrenia (n=20; age 13–25 years) Controls (n=37; age 12–25 years)	Implicit and explicit emotion processing of static neutral, sad and happy faces (1 trial of 3 stimuli) versus Rey geometric figure in both conditions.	**Temporal** 1) Median fixation duration 2)Total fixation duration 3) Total fixation number **Spatial** 1) Median distance between fixations 2) Individual SD of distance between fixations 3) Raw scanpath length 4) Fixation scanpath length **Fixation duration to interest areas** (eyes, mouth, nose) compared to non-features	Implicit task: ADHD had > SD of distance between fixation to neutral face compared to controls. ADHD showed extended (longer) scanpaths to faces and greater dispersal of fixations to Rey figure compared to First Episode Schizophrenia. Explicit task: ADHD < median and total fixation duration to sad faces compared to control group.
Pishyareh et al. (2012)	ADHD (n=30; age 6–11 years) Controls (n=30; age 6–11 years)	Free viewing of static paired emotional and neutral scenes from International Affective Picture System (IAPS).	1)Duration of first gaze 2) Duration and number of first fixation.	Duration of first gaze was shorter for pleasant pictures and longer for unpleasant pictures in the ADHD group.
Muszkat et al. (2015)	ADHD (n=15; mean age 9.4 years, SD 2.3)	Free viewing of static social stimuli neutral female, male	Total fixation duration and number of fixations to interest area (eyes and mouth).	ADHD > fixation duration to the mouth compared to other groups.

	ASD (n=15; mean age 11.6 years, SD 2.7); Controls (n=15; mean age 9.5 years, SD 3.8)	and dog faces. Control stimuli (cloud and plant).		Both ADHD and ASD groups < fixation duration to the eyes compared to controls.
Tseng et al. (2013)	ADHD (n=21; mean age 11.19 years, SD 8.3) Foetal Alcohol Syndrome (n=14; mean age 12.31 years, 2.1) Controls (n=18; mean age 10.67, years, SD 1.2)	Free viewing of a video (20 minutes containing several clips including people)	**Oculomotor based features** 1)distribution of saccade amplitudes 2)fixation duration **Saliency based features** (predicted from computational model of visual salience) **Group based features** (gaze allocations based on normative group of young controls)	Saliency based features categorised ADHD compared to controls. A combination of oculomotor, saliency and group based features categorised ADHD compared to Foetal Alcohol Syndrome.
Pishyareh et al. (2015)	ADHD (n=30; age 6–11 years) Controls (n=30; age 6–11 years)	Free viewing of paired emotional and neutral scenes from IAPS	Total fixation duration, fixation count.	ADHD < fixation duration and number of fixations to pleasant versus unpleasant pictures
Tsang et al. (2016)	No ADHD group ASD (n= 11) ASD+ADHD (n=15) Controls (n=13) (age 7–12 years)	Emotion identity, orientating and intensity rating on static emotional faces (negative, positive, complex, angry, fear, disgust, surprise)	Total fixation duration in and out of interest area (eyes and mouth), number of fixation gazes in and out of interest area. Scanpath plots downloaded.	ASD < controls for fixation duration in interest areas. No significant results for ASD+ADHD group which had results between ASD and controls groups. One scanpath plot for ASD versus control showed differing scanpath with inverted triangular scanning of eyes and mouth in control group only. Did not report on scanpath plot for ASD+ASD group.

Au-Tsang et al. (2018)	No ADHD group ASD (n=1) ASD+ADHD (n=1) Control (n=1) (age 7–9 years)	Free viewing of social video.	First fixation duration, total fixation duration and fixation count.	Child with ASD+ADHD < fixation duration and counts and extensive (longer) scanpath than other groups.
Airdrie et al. (2018)	ADHD (n=36) ADHD + Conduct Disorder (CD) (n=27) Controls (n=41) (age 11–18 years)	Static facial emotion recognition task (happy, sad, angry, scared, neutral faces), 60 trials.	Fixation duration to the eyes, time to first fixation to the eyes.	ADHD+CD < fixation duration to eyes than ADHD and controls for all emotions. ADHD+CD > time to first fixation to eyes of neutral faces compared to ADHD & controls.
Serrano et al. *(2018)*	ADHD (n= 19; mean age 9.16 years, SD 0.9) Controls (n=26; mean age 9.77 years, SD 0.95)	Static facial emotion recognition task (happy, sad, angry, scared, disgust, surprise and neutral faces) and emotion situation task	Proportion of total fixation duration on all interest areas (eyes and mouth)	ADHD < proportion of fixation duration to interest area for all 6 basic facial emotions and most of the emotion situations.
Gliga et al. (2018)	No ADHD group High risk for ASD (n= 26) High risk for ASD + ADHD (n=20) Low-risk infants (n=50)	Array of social (faces) and non-social stimuli (car, bird, phone and degraded face).	Fixation duration to interest area (stimulus). Time to first fixation to the interest area and fixation re-entry counts to the specified interest area	High risk for ASD > fixation re-entry counts to previously visited interest areas compared to high risk for ASD+ADHD and low risk groups.
Frost-Karlsson et al. (2019)	ASD (n=23) Non-ASD (includes ADHD +/- dyslexia; n= 13) No typically developing control group (age 12.9–20 years)	Free viewing of neutral social scenes.	Fixation duration to social areas (people). First Fixation time to social areas. Pupil size to social areas.	No difference in fixation duration but slower first fixation time to social areas in ASD group. No difference in pupil size in ASD but increase in pupil size to social versus non-social areas in non-ASD group.

1.5.2 VISUAL SOCIAL-EMOTIONAL ATTENTION IN ASD COMPARED TO TYPICALLY DEVELOPING CONTROLS AND ADHD

Although the primary focus of this Thesis is on visual social-emotional attention (VSA) in ADHD, comparison with findings from ASD eye tracking literature will help to draw distinctions and similarities between the two conditions. Studies investigating social cognition using eye tracking in ASD have shown varied results. However, overall studies have found that ASD participants fixate less on the eyes and more on the mouth when doing facial emotion recognition tasks compared to controls (Karatekin 2007; Spezio et al. 2007). ASD participants have been found to have more analytical rather than holistic processing compared to controls (van der Geest et al. 2002; Guillon et al. 2015) and scanpaths also are different in ASD with lack of triangulation between both eyes and mouth compared to controls (Pelphrey et al. 2002).

Compared to the ADHD literature described in Section 1.5.1, there is extensive literature on visual social-emotional attention using eye tracking across development in ASD. Much of this literature has also been reviewed recently by several independent groups (Frazier et al. 2017; Black et al. 2017; Chita-Tegmark 2016; Guillon, Hadjikhani, Baduel, and Rogé 2014; Falck-Ytter, Bölte, and Gredebäck 2013).

The ASD reviews cited above show that eye gaze to the mouth can be inconstant across ASD studies. The majority of studies in the ASD literature however, do not take co-existing ADHD symptoms into account. As

stated in the previous section, Muszkat et al. (2015) (see Table 1.2) found that children with ADHD fixated more on the mouth and less on the eyes whereas the children with ASD looked less at the eyes only when looking at neutral faces. Also, Children with ADHD in Muszkat et al. (2015) had a higher IQ than the children with ASD so this could have confounded the findings. Furthermore, it has previously been proposed that children with high functioning ASD look more to the mouth (Klin et al. 2002) and less to the eyes unless there is language impairment (Norbury et al. 2009). This pattern of social versus communication and eye and mouth looking was corroborated by Falck-Ytter et al. (2010) who found social impairments on the ADI-R and SCQ were positively correlated with fixation to the mouth and negatively correlated with fixation to the eyes, whereas communication impairments had the opposite effect on mouth and eye looking. This highlights the importance of exploring the ASD symptom dimension profile in children as this can have an impact on face processing.

It has been known for some time that adults typically view a face in a holistic way, configuring a scanpath over the eyes and mouth in an inverted triangle (Noton and Stark 1971a). Although face processing typically develops into early adulthood (Haist and Anzures 2017), developing children as young as 4 years old have been shown to process faces holistically, showing a preference for upright rather than inverted faces (Pellicano and Rhodes 2003). Atypical scanpaths have been documented in ASD (Heaton and Freeth 2016; Liberati et al. 2017) and it has been postulated that this is due to disruption of the amygdala (Frazier et al. 2017; Weston 2018). Liberati et al. (2017) found a reduced scanpath length in ASD.

Scanpath length could therefore be a dissociable eye tracking parameter among ASD and ADHD, as more extensive scanpath lengths have been seen in adolescents with ADHD viewing neutral faces (Marsh 2008) (see Table 1.2).

In summary overlapping and dissociable findings in visual social-emotional attention between those with ASD and those with ADHD from eye tracking studies in the literature include:

1) Fixation duration to the eyes and mouth of the face have shown to be reduced in those with ASD and also reduced, albeit to a lesser extent in those with ADHD compared with typically developing control children.
2) Latency to first fixation to social stimuli is increased in those with ASD compared to those with ADHD and typically developing controls.
3) Fixation scanpath length has been shown to be reduced in those with ASD compared to typically developing controls, suggesting a restricted scanpath in those with ASD. Conversely extensive scanpaths to social stimuli have been found in those with ADHD compared to typically developing controls.

In ASD, other studies using data driven approaches, are taking advantage of machine learning and nodal networks to explore configurational processing of the facial features. Gullion et al. (2015) found that looking at right eye in the right hemi field versus the left eye in the left hemi field of the face stimulus from the viewers perspective in ASD compared with

controls differed using nodal networks and, others (Amestoy et al. 2015) found that these changes differed in ASD children versus adults. Machine learning as a methodology is also being utilised to explore eye tracking as a potential screening tool for ASD (Wang et al. 2015). Making use of these data driven approached could also be helpful in distinguishing ASD from those with ADHD for the purposes of this thesis.

1.6 SUMMARY OF THE LITERATURE AND GAPS IN CURRENT EVIDENCE BASE

In summary, there is a reasonable body of evidence in the literature that demonstrates that children and adolescents with ADHD have difficulties with social cognition. From the social cognition literature described in section 1.4.1, there are a greater number of studies examining emotion recognition deficits in ADHD with effect sizes comparable to emotion recognition deficits in ASD. It is unclear if emotion recognition deficits are due to ADHD core symptoms or secondary to ASD which is commonly co-occurring in ADHD. ASD is defined by significant social communication deficits and visual social emotional attention has been shown to be atypical in the literature described, albeit with some mixed findings. Eye tracking measures, indexing visual social-emotional attention classically include fixation duration to interest areas such as emotional faces in the ASD studies.

Compared to the ASD literature, which is well established, there are few studies investigating visual attention to social-emotional stimuli in ADHD. Emotion processing is associated with the amygdala and, control

of eye movements has been associated with the cerebellum. The amygdala and the cerebellum have been reported as atypical in ADHD, providing a neural basis for studying emotion recognition using eye tracking in ADHD. As summarised in Table 1.2, studies investigating visual social emotional attention in children with ADHD suggest that visual attention could be atypical compared with typically developing children. Due to the small number of studies (n=2) and mixed findings, the association between atypical visual attention and emotion recognition deficits requires further clarification.

Direct comparison between visual social emotional attention in ADHD versus ASD was limited due to the number of combined studies (n=2) however, differences emerged when studies used a combination of social-emotional stimuli and fixation latencies. This could be because different variables give clues to underlying neuro-circuitry and cognitive processes. As the literature on causal factors shows that several gene-environment interactions, neurotransmitters and neural networks are involved across development in ADHD; comparison with ASD likely increases this interplay. Having different fixation latencies to social- emotional stimuli potentially has more power to draw out any differences in underlying neuro-circuitry between two complex heterogeneous developmental disorders.

Only three visual social emotional attention studies using eye tracking comparing ASD and ASD+ADHD were found which included single case studies in children and another was in high risk infants. No studies comparing visual social emotional attention using eye tracking in ADHD

with ASD+ADHD were found highlighting a gap in the literature. Addressing this gap may reveal important similarities and differences in visual social emotional attention between the disorders. This would allow for improved understanding of visual attention in relation to emotion recognition deficits in ADHD, ASD and ASD+ADHD. This work could have future translational implication including better understanding of visual attention in emotion recognition deficits which could lead to potential new targets for treatment. Improved differentiation between the groups using visual attention to social-emotional stimuli could also allow for visual social-emotional measurement using eye tracking as a diagnostic aid in clinical assessment in future.

The importance of incorporating a developmental framework into interpretation of findings from complex neurodevelopmental disorders was highlighted by Karmiloff-Smith (1998; D'Souza and Karmiloff-Smith 2017). Furthermore, the importance of comorbid symptoms of ASD and ADHD at different time points may also affect the outcome. If co-occurring symptom severity and a complement of eye tracking measures are explored, then it is more likely that subtle differences may start to emerge along the developmental trajectory where compensation is continuously taking place.

1.7 THESIS RESEARCH QUESTIONS AND AIMS

The three main research questions of the Thesis are:

1) Is there an association between emotion recognition deficits in ADHD and visual attention to social-emotional stimuli?
2) Can visual attention to social-emotional stimuli clarify if emotion recognition deficits in ADHD are primary to ADHD or secondary to co-occurring ASD?
3) Does visual attention, indexed by eye tracking differentiate ADHD, ASD and ASD+ADHD on emotion recognition and social processing tasks?

The broad aim of the Thesis was to answer these research questions. This aim was addressed through complementary methodological approaches described in the subsequent chapters. As there are few studies directly comparing visual social-emotional attention in ADHD, ASD and ASD+ADHD, the first method was to observe eye gaze patterns to emotional faces in a subsample of children to characterise visual social-emotional attention within each group. This observational method was used to begin to answer the questions of the thesis including the use of eye tracking to differentiate the groups. The second method was to investigate whether quantitative eye tracking measures to emotional faces in ADHD are associated with emotion recognition deficits on a prompted emotion recognition task, analyse any association of visual attention to emotional faces with clinical symptom severity and, compare visual social-emotional attention

amongst the groups. This second method, seeks to address the questions of the thesis on the association of visual attention to emotional faces on a prompted emotion recognition task; a commonly used task in the study of ASD.

The third method includes the comparison of visual social-emotional attention during free viewing of social scenes used in the ADOS amongst the groups and, analyses any association of visual attention to ADOS images with clinical symptom severity. The third method, seeks to address the questions of the thesis on the association of visual attention to social scenes from the ADOS and spontaneous emotion recognition difficulties on the ADOS; a commonly used clinical tool in the assessment of ASD.

The fourth method includes comparison of visual attention, as a measure of social processing during free viewing of neutral faces amongst the groups and, analyse any association of visual attention to neutral faces with clinical symptom severity. The fourth method, seeks to address the questions of the thesis further on the association of visual attention to neutral faces without emotional content and analyse if visual attention to neutral faces is primarily associated with ADHD or ASD symptom severity.

The final method is to analyse which visual social-emotional attention measures derived from the methodologies two, three and four best classified the groups in order to consider if visual social-emotional attention using eye tracking could show potential as a diagnostic aid in clinical assessment. This final methodology seeks to comprehensively address the final

question of the thesis on the utility of visual social-emotional attention, indexed by quantitative eye tracking measures to differentiate the groups. These methods are addressed in the subsequent chapters with the hypotheses related to each method described within each chapter.

2 METHODS OF STUDY 1: CHARACTERISING VISUAL ATTENTION TO EMOTIONAL FACES IN ADHD AND ASD

2.1 OVERVIEW

The methodology of the first empirical study testing emotion recognition in ADHD is described in this chapter. This chapter also includes the basic method for the eye tracking procedure used in the first study.

At the time of writing this Thesis and as discussed in Chapter 1, there have been few studies directly comparing visual social-emotional attention in ADHD, ASD and ASD+ADHD using eye tracking. This chapter presents the description and characterisation of eye-tracking patterns to emotional faces in a subsample of children with ADHD, ASD, ADHD+ASD and typically developing control children. This chapter describes a novel observational coding framework to consider if certain viewing patterns are qualitatively different among clinical groups. Methods and preliminary machine learning results were presented to validate the observational coding method. In particular, this chapter begins to address the questions of this thesis, by exploring qualitative eye tracking patterns including scanpaths to emotional faces to discover if visual social-emotional attention differs between the groups.

2.2 METHODS

2.2.1 PARTICIPANTS AND ETHICAL APPROVAL

Participants were recruited as part of a larger study funded by The Waterloo Foundation (grant number 981-1335) in the Division of Psychiatry and Applied Psychology at the University of Nottingham. The funded study was called SOCCA (Social Cognition in Children with ADHD) and was an electroencephalography (EEG) study investigating a gaze cue paradigm in children (Groom et al. 2017). A large proportion of the children recruited to the SOCCA study also took part in this eye tracking study, investigating explicit facial emotion recognition in ADHD.

Ethical approval for the study was given by the East Midlands Research Ethics Committee (REC) (12/EM/0111), IRAS project number 99018. After complete description of the study, written informed consent was obtained from parents. All children had an IQ ≥70 and verbal assent was obtained after an age-appropriate description of the study.

A power calculation to estimate the number of participants required in each group was calculated using G*power software (version 3.1.9.2). In the literature, medium effect sizes (Cohen's d=0.4-0.6) have been found in the ADHD group compared to the control group for fixation latencies to negative emotional faces (Marsh 2008; Serrano, Owens, and Hallowell 2018). Similar effect sizes have also been documented in the ASD literature on visual social attention (Cohen's d=0.4-0.5) (Chita-Tegmark 2016). Effect sizes were not presented by Marsh (2008) so, the effect size was derived using G*power based on the mean, standard deviation and group

sample sizes provided by the author. Using G*power, 35-40 participants per group were calculated as required in order to detect a medium effect size, with 80% power and an alpha criterion of 0.05. As there are few studies that compare visual social-emotional attention amongst the clinical groups (ADHD, ASD and ASD+ADHD) it was more difficult to predict what effect size was required for the study to be adequacy powered in order to detect significant differences amongst the clinical groups. A projected total sample size of 140-160 (35-40 participants per group) was therefore based on the control group versus the pure group eye tracking literature and associated power calculation described above.

2.2.1.1 **CLINICAL GROUP**

INCLUSION CRITERIA

Children and adolescents aged 8–15 years with a clinical diagnosis of ADHD, ASD or ASD+ADHD were recruited from Child and Adolescent Mental Health Services (CAMHS) and community paediatric clinics in Nottinghamshire. Some children were also recruited from local autism and ADHD charities. Children from ASD and ADHD support groups were also informed of the study by the support group convenor.

EXCLUSION CRITERIA

Clinicians were asked to refer children without comorbid diagnosis of Tourette's syndrome or learning disability (IQ<70) or epilepsy. Children with visual problems (such as colour blindness) and hearing problems were also excluded.

COMORBIDITIES

Children with comorbid mental health conditions including anxiety disorders, mood disorders and conduct disorders were also included. Children with comorbid specific learning disorders including e.g. dyslexia or developmental coordination disorder were also included.

MEDICATION

Patients taking stimulant medication were asked not to take this medication on the day of the study. Patients taking ADHD non-stimulant medication such as atomoxetine were excluded due to its longer duration of action and those taking dexamphetamine were also excluded due to its low rate of prescribing. Children on medication for sleep such as melatonin or taking Selective Serotonin Reuptake Inhibitors (SSRIs) were also included. Children taking antipsychotics such as risperidone were excluded as this could potentially affect our measures of interest and not be easily withdrawn.

DIAGNOSTIC METHOD FOR GROUP ASSIGNMENT

Diagnoses were confirmed or overturned by PK (an experienced clinical rater) after the Development and Wellbeing Assessment (DAWBA) transcripts (Goodman, Ford, Richards, et al. 2000) and screening questionnaires were completed. Further details how DAWBA diagnoses were operationalised are given in section 2.2.2.3. Where diagnostic decisions were complex, clinical consensus with at least two child and adolescent psychiatrists (PK and CH) took place. This included discussing all the information available (described in Section 2.2.2) making the final diagnoses based on the overall consensus. This methodology has been employed previously by PK and CH (Johnson et al. 2010b, 2010a)

2.2.1.2 CONTROL GROUP

Letters detailing the study were sent to families of children in primary and secondary schools in the Nottinghamshire region. From an initial sample who volunteered to take part, a group of controls matched pairwise for age (± 6 months) were selected. Those with significant ADHD or ASD symptoms on the Conners' parent rating scale (T score > 65) or Social Communication Questionnaire (SCQ; total score > 15) were excluded from the study.

2.2.2 SYMPTOM AND DIAGNOSTIC MEASURES

Children were screened for ASD using the SCQ-lifetime version (Rutter 2003). Children's parents also completed the Social Aptitudes Scale (SAS) as part of the Development and Wellbeing Assessment (DAWBA) (Goodman, Ford, Richards, et al. 2000). In the clinical groups, all scales were rated when the child was off medication and the parent was asked to rate what their child was like when they were off medication in the last six months for all but the SCQ which also requires parents to comment on their child's behaviour when they were aged 4–5 years old.

2.2.2.1 SOCIAL COMMUNICATION QUESTIONNAIRE (SCQ)

The Social Communication Questionnaire (SCQ)-lifetime version, formally known as the Autism Screening Questionnaire, was developed from the Autism Diagnostic Interview revised (ADI-R) (Lord, Rutter, and Le Couteur 1994) and is well validated (Rutter 2003; Charman et al. 2007;

Corsello et al. 2007). It is a 40-item, parent rated questionnaire and comprises 3 subscales: social reciprocal interaction domain, communication domain and, repetitive stereotyped behaviour domain. The SCQ was designed to separate ASD from non-ASD diagnoses at all IQ levels, with a cut-off of 15 or more proving most effective, giving a sensitivity and specificity of 0.85 and 0.75 respectively (Berument et al. 1999).

2.2.2.2 **SOCIAL APTITUDES SCALE (SAS)**

The Social Aptitudes Scale (SAS) is a 10-item scale that forms part of the Development and Wellbeing Assessment (DAWBA) and is a broad measure of complex interactive social skills. Parents are asked to compare their child's behaviour across a range of situations to their peers. Scores can range from 0 to 40 and low scores have been shown to be associated with ASD in community samples (Liddle, Batty, and Goodman 2008). It should be noted that higher rates of difficulties on the SAS than the SCQ have been found in those with ADHD without a comorbid diagnosis of ASD in a clinical sample (Kochhar et al. 2011). Thus, the SAS taps into a broader range of current difficulties in social understanding and behaviour compared with the SCQ which is more closely related to core ASD symptoms in current and early development. A score of 12 or less on the SAS indicates difficulties in social functioning and necessitates that all items of the development Section (ASD diagnostic Section) of the DAWBA are completed.

2.2.2.3 DEVELOPMENT AND WELLBEING ASSESSMENT (DAWBA)

The Development and Wellbeing Assessment (DAWBA) is a structured interview, which can be administered by interviewers to informants or completed directly online by parents, teachers or adolescents (11–17 years old) to generate DSM-IV and ICD-10 diagnoses. In this study, the DAWBA was administered by interviewers (PK and MS) to parents. The DAWBA primarily measures emotional, behavioural and hyperactive disorders, although less common disorders such as eating disorders are also covered. The DAWBA also has a developmental section covering ASD. The developmental section consists of 43 questions. However, the whole Section is only completed if scores on the SAS are 12 or less; if SDQ peer problems is 2 or more points higher than the pro-social score (see below for SDQ); or if the child continues to have problems in any of the 5 parts of question R6. Question R6 asks about concerns in the child's first 3 years of life including speech development; getting on with people; pretend and make-believe play; odd rituals and habits that are hard to interrupt; and the ability to learn new things.

All sections of the DAWBA parent interview generally takes between 1–2 hours to complete and may be shorter where appropriate using 'skip rules' which enable sections to be shortened or skipped completely when screening questions indicate a particular disorder is highly unlikely. Where potential problems are highlighted, open ended questions are asked, which are transcribed verbatim. Data is collected online or subsequently entered into a computer, which generates a predicted diagnosis and forms

the starting point for the diagnostic group assignment and clinical consensus (see above). DAWBA computer predictions are based on information from large studies of representative samples of children and young people from the general population (Goodman, Ford, Richards, et al. 2000). DAWBA computer diagnoses are operationalised based on the level of these predictions and in this study, computer predictions of 50% or more were considered for further rating by PK. The DAWBA computer diagnoses bring together the information from the structured questions based on DSM-IV and ICD-10 criteria and are not definitive but form a starting point for clinical rater(s) to confirm or overturn the diagnosis based on all the information including the open ended comments given by the informants (Goodman, Ford, Simmons, et al. 2000).

2.2.2.4 AUTISM DIAGNOSTIC OBSERVATION SCHEDULE (ADOS)

All clinical participants were invited to attend an Autism Diagnostic Observation Schedule (ADOS) (Lord et al. 1989) as part of the research diagnostic assessment. Due to limitations in time, the ADOS took place on a separate day to the eye tracking testing. Only a subset of the clinical participants (60%) consented to attend the second study day when the ADOS took place. The ADOS is an observational (cross-sectional) assessment of ASD requiring the assessor to have research reliability accreditation (completed by PK) for standardised use in research studies. Module 3 or 4 of the ADOS was used depending on chronological age and verbal fluency of the participant. The assessment takes 45 minutes to complete and the child is observed doing 14 tasks (e.g. description of a picture). The assessment provides scores in the

communication, reciprocal and social interaction and stereotyped behaviours and restricted interests domains. Based on cut-off scores, an ADOS classification of autism or autism spectrum is generated, which is used to help reach a research diagnosis in the clinical consensus.

2.2.2.5 CONNERS' RATING SCALE

Parents also completed the Conners' questionnaire (Long Version) (Conners 1997). The Conners' questionnaire (Long Version) was originally developed to measure medication response. The Conners' questionnaire has 13 subscales. In order to be included in the ADHD group of the study, the T-scores on the Conners' questionnaire had to be more than 1.5 standard deviations above the mean on the attention scale (this equates to T-scores of more than 65).

2.2.2.6 STRENGTH AND DIFFICULTIES QUESTIONNAIRE (SDQ)

Parents completed the Strength and Difficulties Questionnaire (SDQ) (Goodman 2001). The SDQ is a 25 item questionnaire with a 3-point scale (not true, somewhat true and certainly true) to measure emotional and behavioural difficulties in children. Five domains are measured (conduct, emotions, hyperactivity, peer problems and prosocial behaviour), each using 5 questions. With the exception of the prosocial scale, high scores are associated with problem behaviours. A total difficulties score is generated by calculating the sum of all scales (with the exception of the prosocial scale). The SDQ can be used as a general measure of psychopathology, although the

hyperactivity subscale is often used in ADHD assessments. Participants required a hyperactivity score of more than 5 to be included (except on the teacher scale, since this is usually rated when the child is on medication).

2.2.2.7 WECHSLER ABBREVIATED SCALE OF INTELLIGENCE (WASI)

All children completed an abbreviated intelligence test, Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler 1999), which is an abbreviated measure of IQ and takes around 20 minutes to complete. Two sections (vocabulary and block design) enable performance, verbal and full-scale IQ to be generated. Any participants with a full-scale IQ of less than 70 were excluded from the study.

2.2.3 EMOTION RECOGNITION TASK

Children completed a facial emotion recognition task adapted from the Frankfurt test and training of social affect (FEFA) described by Bolte et al. (2002) and used by Sinzig and colleagues (Sinzig, Morsch, and Lehmkuhl 2008). Photographs of 60 faces (in 3 blocks) representing the six basic emotions (happy, sad, anger, disgust, fear and surprise) were presented sequentially in random order on a computer screen. Standardised coloured photographs of adults from different racial origins were used from the NimStim face set (Tottenham et al. 2009) (see Figure 2.1 for details).



Figure 2. 1: Example stimuli used in facial emotion recognition task

During each trial, after fixating on a central fixation cross for 500ms, the emotional face image would appear in the centre of the screen for 4500ms. After this 5000ms time lapse, the 6 emotional word options were presented immediately below the face image and, the participant was requested to match the emotion depicted by the image to one of the 6 emotional word options, using a games controller (Figure 2.2).



Figure 2. 2: Facial emotion recognition condition

After a short break, the children were shown 36 images (in two blocks) of 'eyes only' (taken from the same NimStim face set but images of different people were used compared to the face condition; Figure 2.3).

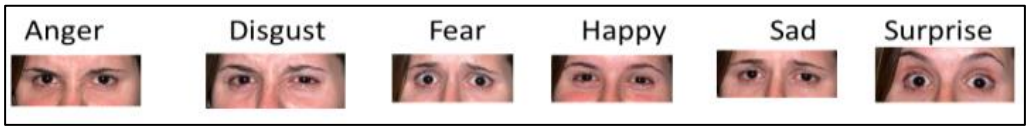


Figure 2. 3: Example stimuli used in the 'eyes only' emotion recognition condition

Again, these images of 'eyes only' depicted the 6 basic emotions and children were required to match these to the corresponding emotion by selecting one from 6 word options presented immediately below the 'eyes only' on each trial, using the games controller. Each 'eyes only' emotion image was presented sequentially in a random order as described for the emotional face images.

2.2.4 EYE TRACKING PROCEDURE

While children completed the emotion recognition tasks, their eye movements were captured using the Cambridge Research Systems (CRS) eye tracker which has a sampling rate of 250Hz, a resolution of 0.05 degrees and an accuracy of 0.125–0.25 degrees (CRS 2006). This is a non-portable set up and the eye tracking apparatus includes a high speed camera and an infrared mirror. The participant rests their chin on a chin rest at a fixed point from the computer screen which displays the visual stimulus (Figure 2.4). The laboratory eye tracking room had no natural light allowing the lighting in the room to be kept constant during the eye tracking procedure.

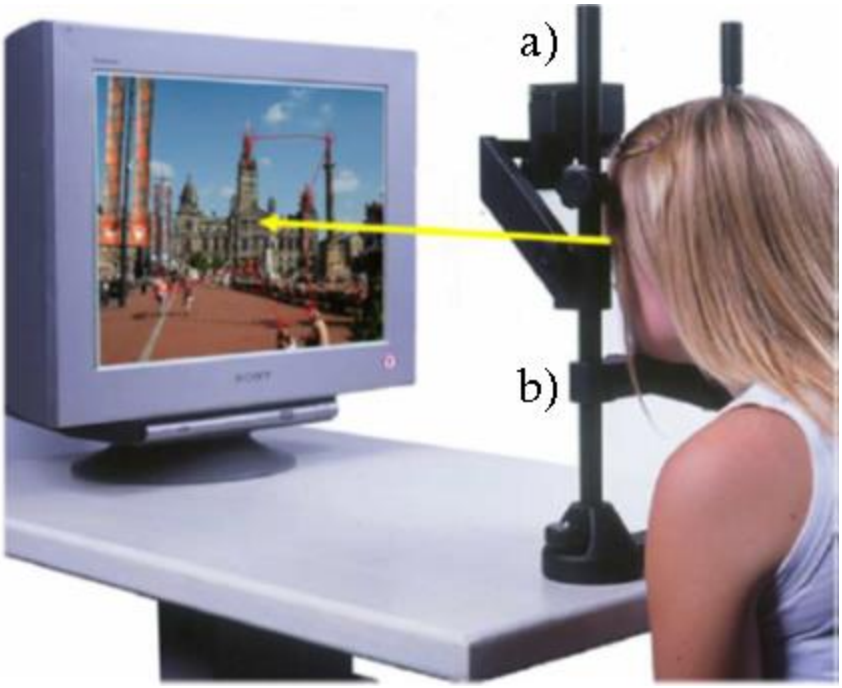


Figure 2. 4: Cambridge Research Systems eye tracker apparatus setup

a) Eye tracker high speed camera and infrared mirror; b) chin rest

The eye tracking took place in the Institute of Mental Health laboratory at the University of Nottingham. The viewing distance was 70 cm from the computer screen displaying the visual stimulus and, the screen size was 38cm wide x 30cm height (resolution 1280x1024 pixels). Prior to the task the children underwent a 20-point calibration on the eye tracker and were given a test run to make sure they understood the task. Prior to each emotional face stimulus appearing on the screen, the children were required to fixate on a central cross for 500ms to make sure their start position was the same at the beginning of stimulus onset. The emotional face stimulus (5cm wide x 6.5cm height) was present on the screen for 4500ms to allow free viewing of the face, after which options appeared at the bottom of the screen for an emotion to be selected. The task was programmed

on MATLAB R2012 (MathWorks, UK). Eye tracker variables for fixation position (x and y co-ordinates and degrees) and pupil size were measured over time. Reaction time, emotion recognition scores for faces and eyes only were recorded on each trial during the eye tracking procedure. Of the 44 participants tested, one participant from the ADHD group was unable to complete the calibration and eye tracking tasks so eye tracking data was not available for this participant.

2.2.5 DATA EXTRACTION

The eye tracking and behavioural variables for each participant were extracted into an excel spreadsheet using MATLAB. A fixation was defined with a minimum duration of 500ms for the purposes of the observation of eye gaze described in this chapter. Firstly, each fixation over the emotional face stimulus was displayed over the whole trial time so that the fixations could be observed over space and this was termed static patterns of eye gaze. The static patterns of eye gaze informed the initial observation on four case studies described below. Secondly, each fixation over the emotional face stimulus was displayed over time so that the fixation sequence pattern over time and space could be observed and this was termed dynamic patterns of eye gaze. Static and dynamic patterns of eye gaze were extracted and displayed on-screen using purpose-built MATLAB scripts. These scripts were designed to display the eye-tracking patterns on each trial, for each participant, so that the eye gaze patterns could be observed and a coding framework established by the experimenter (described in section 2.2.6).

2.2.5.1 **CASE STUDIES**

The first child recruited from each group (typically developing control, ADHD, ASD, ASD+ADHD) was used as a case study to form the initial observation from static eye gaze patterns. Each fixation was represented by a blue circle and was superimposed on the emotional face stimulus to produce a map of the child's eye gaze on the photo of the face as shown in the examples in Figure 2.5a)-d). The static eye gaze patterns were observed separately for each trial (n=60) for the 4 case studies.

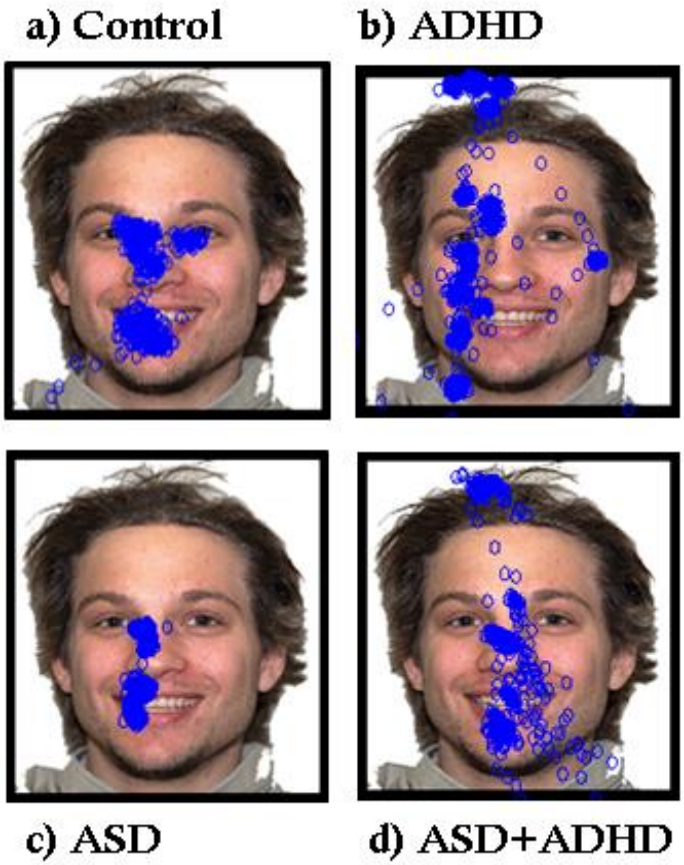


Figure 2. 5a-d): Case examples of static eye gaze patterns in one trial

The left eye refers to the eye in the left hemi space of the face stimulus and, conversely the right eye is the eye in the right hemi space of the stimulus. Blue circles represent a single fixation (minimum duration of 500ms)

On observation, the control participant's static eye gaze patterns to the face stimulus shows that the blue fixation circles appear to coalesce around both eye areas, the mouth and the nose (see Figure 2.5a)) In Figure 2.5b), the participant with ADHD is observed to have blue fixation circles that appear to be more spread out on observation over the photo. The fixation circles are observed to coalesce somewhat on the eye in the left hemispace and the mouth. There are also fixation circles over the person's hair and background behind the face. On observation, the static eye gaze patterns for the participant with ASD shows that the blue fixation circles appear to coalesce around the mouth and the nasal bridge (see Figure 2.5c). In Figure 2.5d), the participant with ASD+ADHD, is observed to have blue fixation circles that appear to coalesce around the mouth and the nasal bridge. The fixation circles also appear to be spread out over the bottom half of the photo.

These observed static patterns of eye gaze fixations shown on the single trial for each case study were observed to be similar over several trials within each of the four case studies. Although these static eye gaze patterns from the four case studies illustrate some potential spatial eye-tracking patterns, they do not provide much information about the sequence or timing of these eye gaze patterns. For this, a dynamic representation is required.

2.2.6 OBSERVATION OF DYNAMIC EYE GAZE AND CODING FRAMEWORK

In order to gain a deeper understanding of the timing and sequence of fixations over the emotional face stimulus amongst the groups (ADHD, ASD, ASD+ADHD and Controls), dynamic eye gaze patterns were observed and a coding framework was developed. This coding framework development included a protocol for predicted diagnostic group allocation. Compared to the static eye gaze patterns from case studies described in the previous section, dynamic eye gaze observation was conducted blind to diagnostic status of the participant. Using excel, a subset of children (n=33) were randomly selected and the observation, coding and initial analysis based on the protocol was completed blind to group allocation.

Observation of dynamic eye gaze was completed using a purpose-built MATLAB script; fixations were plotted in time and space over each emotional face stimulus presented during the emotion recognition task. The MATLAB script provided a slowed down version of the fixation patterns (like a short video) and PK viewed the dynamic eye gaze patterns for the randomly selected subset of participants (total of 1980 trial videos assessed).

During the observation, transcript notes were made on the common themes of eye gaze patterns that emerged for that participant. For example, the sequence of fixations on core facial features such as the eyes and the mouth, the sequence of fixations over other areas of the face stimulus and, how quickly and far apart the fixations appear. These themes were grouped

into models and the most common models during the observation were included in the coding framework. The coding framework was developed based on observations of dynamic eye gaze blind to group allocation, static eye gaze patterns from the four case studies described in the previous section and, the literature of visual social-emotional attention in ASD, ADHD described in Chapter 1. The developed coding framework then acted as an initial protocol for a predicted group allocation.

By the end of the dynamic eye gaze observation for each participant, a proposed group allocation was made in accordance with the observed common themes and models that emerged and, the subsequent coding framework protocol that related to those models. The first stage of the group predictions was based on proposed control versus clinical status. For example, if the fixations were over core features (eyes and mouth) of the face, this would indicate a potential typically developing control based on the coding framework. If however, the fixations were more widely spread and appeared quite fast over non-core features of the face, a potential clinical case status was predicted based on the coding framework. If a clinical status was predicted, a second stage of predictions was made proposing the specific clinical group status (ADHD, ASD or ASD+ADHD) based on the coding framework. Details of the coding framework are provided in the results (section 2.3.1). The appendix provides transcripts from four of the participants to give further examples of the observation and coding framework procedure for the control and the clinical groups (A.II). One child from the ADHD group had to be excluded from this analysis as fixation

was poor and time spent on the screen was too low for the variables in the protocol to be reliably generated.

In order to assess the prediction of proposed group allocation from the developed coding framework, chi squared was calculated based on this predicted group versus the actual group status. Statistical analyses were conducted using SPSS Version 22 (IBM©).The first chi squared analysis was based on clinical versus control group status from the initial coding framework protocol. Those cases that were misclassified were re-examined by checking their detailed notes from the transcripts during the blinded observation (examples provided in the appendix A.II). The protocol was then revised un-blind to actual group status. A second chi squared analysis was conducted based on predicted group and actual group status as described above. A description of the observational coding subsample is provided in Section 2.3. Group differences for the demographic and clinical scores were calculated using univariate ANOVA. Post hoc tests were carried out to allow for multiple comparisons. Levene's test of variances determined Tukey and Games-Howell post hoc tests.

2.2.7 MACHINE LEARNING

In order to validate the observational coding framework and predicted group results, machine learning was undertaken on the whole dataset (n=43). Demographics for the whole dataset are presented in Section 3.4.1. PK informed on the approach based on observation and coding framework by guiding the possible spatio-temporal eye- gaze patterns that were loaded

into the machine-learning algorithm. Data models were then processed independently by an expert in machine-learning, reducing any potential observer bias and improving validity via automation.

The eye tracking dataset was explored via a dynamic sequence model using MATLAB. This resembled the dynamic eye gaze patterns, providing a sequence of fixations over specified facial features. This model aimed to find discriminative sequences which frequently occurred in one diagnostic group but rarely occurred in other diagnostic groups. These sequences were defined as code word indices, whereby a sequence on the codes labelled 1–11 denoted a code word (see Figure 2.6). For example, the dynamic sequence of fixations over the codes 3463, denotes a fixation sequence on the left eye, then the right eye, then the mouth and then the left eye. The codes represented specific location of the facial features (forehead, left eye, right eye, the nose, mouth, etc.). The codes were selected such that they are located at the centre of these facial features, to make the sequences more interpretable. Codes were created based on the x and y positions of the fixations extracted from the eye tracking procedure described in Section 2.2.4. The 10 most frequently occurring sequences found for each group were used to compute a feature vector for each subject. The frequency count of each selected sequence in each subject determined the prevalence of the corresponding feature for that subject.

Sequence mining to discover frequent sequential patterns was performed on the eye tracking data from all the emotional faces. Only fixated positions (minimum fixation duration of 200ms) were used in the analysis. Consecutive repeated code words were merged into a single occurrence of

that word for example 1111225444 became 1254 (Figure 2.6). Only sequences which were of a length greater than 2 and those which had all unique elements with no elements repeated, were selected. The sequences were produced from the first 4 codes. Discriminative sequences were mined for each group separately. A score was computed for each sequence representing the accuracy obtained if only the presence of that specific sequence is used for classifying the subject into one and the rest of the groups. These scores were used for selecting the most frequently occurring 10 sequences for each group.

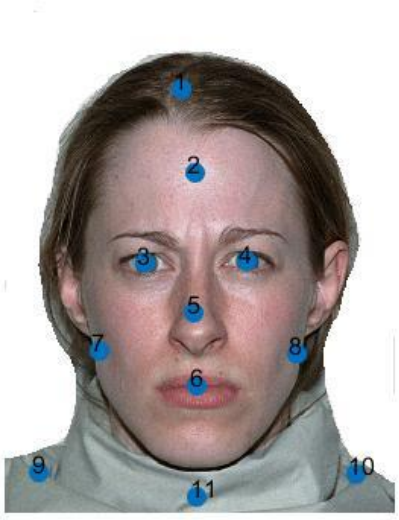


Figure 2. 6: Codes for dynamic sequencing

Each blue circle represents a code. Each code is denoted by a number (1–11) based on the position over the emotion face image. The dynamic sequence is defined by the order of codes (code word indices).

Machine learning models were trained based on feature vectors computed from the 10 most frequently occurring sequences found for each

group. Feature vectors were computed by counting how many times a sequence occurred for each subject. The resultant 40-dimensional feature vector representing each subject was created (based on the 4 codes within each of the 10 most frequently occurring sequences). An additional feature vector for 'scatter of eye gaze', based on the distance of fixation from the central fixation cross of the image was generated. Specifically, the 'scatter of eye gaze' was computed by calculating the standard deviation of the x and y locations.

These classification models were trained using SVM (Support Vector Machines) and KNN (K–Nearest Neighbours). To evaluate performance, the models were trained (including sequence selection) and tested using a leave-one-subject-out protocol in which one subject is used for testing and the rest of the subjects were used for training. This process was then repeated for each subject and the overall classification score was obtained by averaging over each test subject as described by Jaiswal et al. (2017). The model predicted (using the leave-one-subject-out approach) each case to belong to one of the groups (e.g. ADHD versus ASD+ADHD). The accuracy was then calculated as: accuracy=(number of cases correctly predicted)/(total number of cases).

2.3 RESULTS

A description of the subsample for observational coding is presented in Table 2.1. As shown in Table 2.1, groups were well matched for age (F (3, 29)=0.73, p>0.05, ηp^2=0.07) and there was a male predominance in all

groups (F (3, 29)=0.41, p>0.05, ηp^2=0.04). Groups differed in mean IQ (F (3, 29)=3.94, p<0.05, ηp^2=0.29) with significantly lower scores in the ADHD group (p<0.05) compared to the control group. The groups differed significantly on SCQ (F (3, 29)=30.26, p<0.001, ηp^2=0.76) with significantly higher scores in the ASD group (p<0.01) and ASD+ADHD group (p<0.001) compared to control group. Groups differed significantly on SAS (F (3, 24)=21.00, p<0.001, ηp^2=0.72) with significantly lower scores in all three clinical groups (p<0.001) compared to control group.

Groups differed significantly on the Conners' DSM-IV IA T-score (F (3, 27)=34.78, p<0.001, ηp^2=0.79) with significantly higher T-scores in all three clinical groups compared to control group (p<0.01). Conners' DSM-IV IA T-scores were significantly higher in the ADHD group (p<0.01) and ASD+ADHD group (p<0.01) compared to the ASD group. Groups also differed significantly on the Conners' DSM-IV HI T-score (F (3, 27)=47.10, p<0.001, ηp^2=0.84) with significantly higher T-scores in all three clinical groups compared to control group (p<0.05). Groups also differed significantly on the Conners' DSM-IV Oppositional T-score (F (3, 27)=12.66, p<0.001, ηp^2=0.59) with significantly higher T-scores in the ADHD group (p<0.001) and ASD+ADHD group (p<0.01) compared to control group.

Table 2. 1: Demographic and clinical characteristics of the subsample for observational coding (n= 33)

	Group				Group effect		
	ADHD (n=5)*	**ASD** (n=7)	**ASD+ADHD** (n=7)	**Controls** (n=14)	***F***	**p-value**	**Group differences** (post-hoc)
Mean age in years (SD; range)	11.21 (1.93; 9.16-13.76)	11.98 (1.49; 10.03-14.64)	12.78 (2.14; 9.22-15.66)	12.36 (1.96; 9.88-15.76)	0.73	p>0.05	n/s
Gender % male (n male)	80.0% (4)	85.7% (6)	100.0% (7)	85.7% (12)	0.41	p>0.05	n/s
Mean FSIQ (SD; range)	95.40 (12.58; 79.00-108.00)	107.14 (8.11; 94.00-116.00)	99.29 (13.02; 84.00-118.00)	111.64 (9.67; 95.00-127.00)	3.94	p<0.05	Controls > ADHD [c]
Total SCQ (SD; range)	13.00 (9.00; 2.00-26.00)	20.57 (8.00; 5.00-30.00)	24.14 (4.95; 16.00-30.00)	2.57 (2.17; 0.00-7.00)	30.26	p<0.001	Controls < ASD [b] / ASD+ADHD [a]
SAS (SD; range)	10.40 (6.35; 4.00-18.00)	7.29 (6.26; 0.00-16.00)	5.86 (2.67; 3.00-10.00)	24.56 (5.64; 15.00-33.00)	21.00	p<0.001	Controls > ADHD / ASD / ASD+ADHD [a]
Conners' IA T score (SD; range)	79.20 (7.33; 70.00-90.00)	62.14 (8.49; 52.00-77.00)	75.44 (6.43; 66.00-86.00)	47.58 (6.46; 40.00-60.00)	34.78	p<0.001	Controls < ASD [b] / ASD+ADHD / ADHD [a] ASD < ADHD / ASD+ADHD [b]

Conners' HI T score (SD; range)	89.40 (1.34; 87.00-90.00)	72.57 (13.79; 54.00-90.00)	83.57 (8.22; 68.00-90.00)	47.58 (4.17; 43.00-54.00)	47.10	p<0.001	Controls < ASD [c] / ADHD / ASD+ADHD [a]
Conners' OD T score (SD; range)	81.80 (8.11; 72.00-90.00)	71.43 (18.30; 49.00-90.00)	71.43 (10.47; 61.00-89.00)	49.00 (8.00; 39.00-64.00)	12.66	p<0.001	Controls < ADHD [a] /ASD+ADHD [b]
Oppositional and Conduct Disorders	3	4	3	0	-	n/a	-
Emotional Disorders†	0	1	3	0	-	n/a	-

FSIQ Full Scale Intelligence Quotient (WASI); SAS Social Aptitudes Scale (≤ 12 is suggestive of ASD); SCQ Social Communication Questionnaire (≥ 15 suggestive of ASD); Conners' Parent IA (Inattentive); HI (Hyperactive-Impulsive); OD (Oppositional) T scores (≥ 65 suggests difficulties in these areas). Rating scale scores shown are parent rated. †Emotional Disorders include general anxiety disorder, mild depressive episode, obsessive compulsive disorder or specific phobia. Note: participants could have more than one disorder. Emotional, oppositional and conduct disorders were based on DAWBA computer diagnoses and confirmed by clinical rating as described in methods section (2.2.2.3). *1 child from the ADHD group was not included in the observational coding analysis due to poor fixation to the screen. 1 child in the ADHD group could not complete the calibration so could not complete the task (as described in Section 2.2). [a]$p<0.001$; [b]$p<0.01$; [c]$p<0.05$

2.3.1 DEVELOPING AN OBSERVATIONAL CODING FRAMEWORK

Themes and models that emerged from the observation were noted and a coding framework was developed (example transcripts from four participants for the observation and coding framework are available in the appendix (Section A.II).

Important themes generated from observation of dynamic eye gaze:

1) **Core features of the face where most time is spent fixating**

Core features include the mouth, right and left eyes. For the purposes of this Thesis, the left eye refers to the eye in the left hemi space of the face stimulus and the right eye refers to the eye in the right hemi space of the face stimulus from the perspective of the viewer.

2) **Shapes and patterns generated by viewing core features of the face**

These can include:

- Fixating on the left eye and then the right eye and then the mouth and back to the left eye to produce an upside-down triangle (see Figure 2.7a);
- Fixating on the left eye, then the mouth and then the right eye to produce a V shape in the pattern of fixations (see Figure 2.7b);
- Fixating on the left eye and then mouth to produce a single, linear pattern (see Figure 2.7ci)

3) **First features viewed**

It would be useful to include areas e.g. left eye area to include left eye and eye brow rather than separately due to fixation patterns observed. Is fixating on the left eye a lot indicative of being a control or not having ASD?

4) **Other non-core face features that were viewed**

These non-core features include other facial features (not eyes and mouth) for example wrinkles in nose, forehead and raised eyebrows (facial muscles).

Natural distractors outside of the face that were viewed, for example hair, beard, pointy ears, bald head.

6) **Time spent in quadrants of the face**

Upper versus lower quadrants for example, some children spent very little time in the upper quadrant which includes the eyes and this may suggest ASD or poor performance on the task.

7) **Amount of 'scatter' on the eye gaze observation**

Increased 'scatter' looks like fixation circles all over the place, with these fixations not coalescing or overlapping on core features of the face (see Figure 2.9a). Fixation circles appeared very fast and covered a larger area much quicker. How much scatter is too much and indicative of ADHD?

8) **'Off task'**

There was some suggestion that the participants could be 'off task' e.g. fixations outside the photo as trials go on, may signify distractibility, fatigue or lack of vigilance. One child started doing this at

trial 30 (half-way through the task). One could hypothesise that this would happen earlier in ADHD and later in pure ASD?

9) **Heterogeneity or variability of gaze**

Sometimes children 'triangulate' but other times their eye gaze, indexed by blue fixation circles goes 'off' the photo. Could this be suggestive of pure ADHD with variable attention?

10) **Developing group profiles**

When observing the dynamic eye gaze, it was possible to get a potential control versus clinical profile of eye gaze within the first few face stimulus trials. For differentiation between the pure and comorbid groups, it takes more than 20 trials and so it was much more time consuming.

Models of face scanning generated by above themes:

Models of dynamic eye gaze that were generated by the themes during observation are shown in Figure 2.7. Model 1 includes the three fixation sequence patterns between the core features of the face. The 'upside down triangle' which includes fixations over the left eye moving to the mouth, moving to the right eye and then back to the left eye (as shown in Figure 2.7a). The 'V-shape' includes fixations over the left eye, moving to the mouth and then moving to the right eye (as shown in Figure 2.7b). The 'linear shape' include fixations over one core feature moving to another core feature for example the left eye to the mouth (as shown in Figure 2.7ci).

Model 2 includes fixations moving across quadrants of the face (as shown in Figure 2.8a). Model 3 includes fixations moving across the horizontal zones of the face (as shown in Figure 2.8b). Model 4 includes the 'scatter' of fixations over the face stimulus with increased 'scatter' of fixations being more widely spread across the face stimulus and moving across the face stimulus quickly (Figure 2.9a). Conversely, reduced 'scatter' of fixations include fixations that are close together, coalescing and appearing as individual fixations more slowly over the face stimulus (Figure 2.9b).

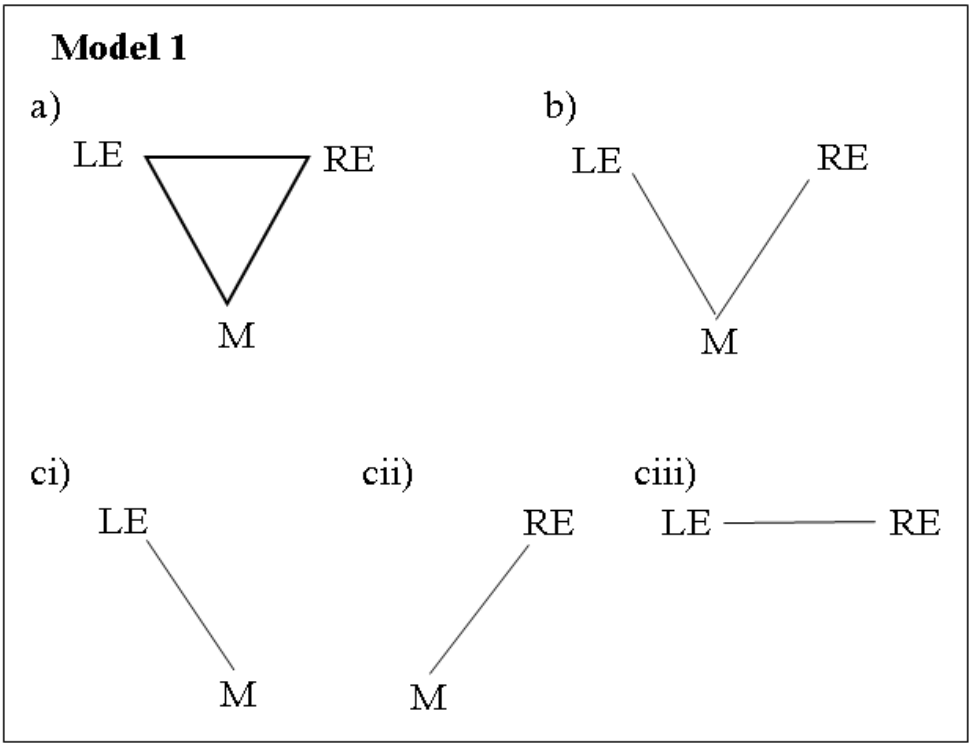


Figure 2. 7: Model 1 Fixation patterns between core face features

a) Upside down triangle includes fixation between LE, M, RE and back to LE, b) V-Shape includes fixation between LE, M and RE c) Linear shapes include fixations between ci) LE and M; cii) M and RE; and ciii) LE and RE (Left Eye (LE), Mouth (M), Right Eye (RE). The left eye is the eye in the left hemi space, the right eye is the eye in the right hemi space of the stimulus from the perspective of the viewer.

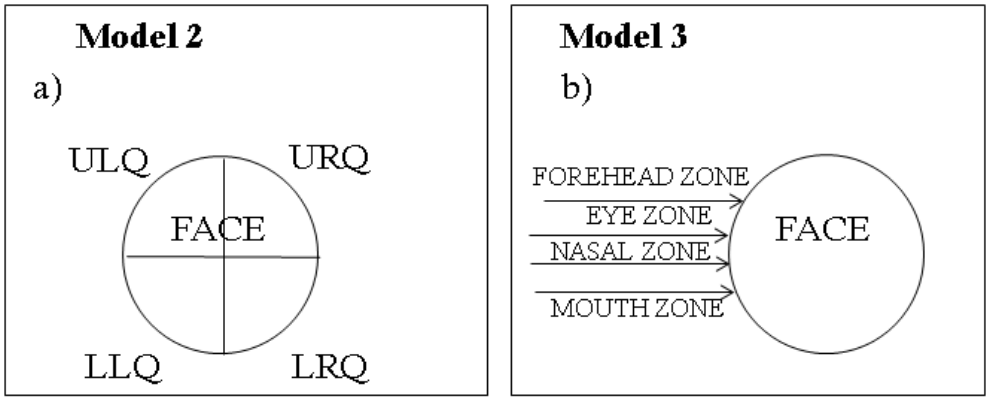


Figure 2. 8: Model 2 and Model 3 Fixations moving across the face

a) Model 2: Moving across quadrants of the face; b) Model 3: Moving across horizontal zones of the face. Upper Left Quadrant (ULQ); Upper Right Quadrant (URQ); Lower Left Quadrant (LLQ); and Lower Right Quadrant (LRQ).

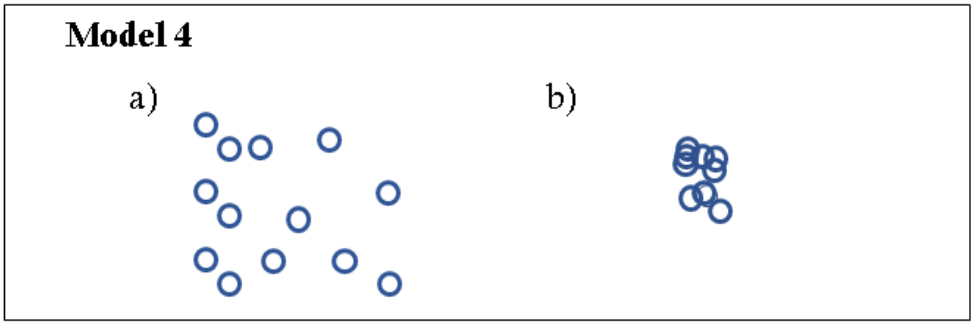


Figure 2. 9: Model 4 'Scatter' of fixations

a) Increased 'scatter' occurs when fixation circles shown in blue move very fast, are far apart and do not tend to overlap, b) Reduced 'scatter' occurs when fixation circles shown in blue are slower to appear, overlap and coalesce.

2.3.1.1 CODING FRAMEWORK

During the observation of dynamic eye gaze, the models which occurred most frequently were Model 1 (fixation patterns between core features) and Model 4 (amount of 'scatter' of fixations). Models 1 and 4 were used to develop a coding framework protocol to aid group classification based on observed dynamic eye gaze. The coding framework protocol incorporated elements from both Models 1 and 4 and was characterised by the following:

1) Patterns of eye gaze to core face features (triangulations, V-shape, linear or none);
2) 'Scatter' of dynamic eye gaze, includes speed and distance of fixations (increased or reduced).

Predicted group designation

Group predictions were based on the observed participant trials being assessed on the coding framework above, static eye gaze patterns from case studies (section 2.2.5.1) and the literature review in Chapter 1 as follows:

1) Control group: fixations to the core facial features (eyes and mouth) were triangulations and V shape patterns. Fixations showed reduced 'scatter' and a greater tendency to fixate on core feature of the face (eyes mouth) than non-core features (e.g. forehead, chin).
2) Clinical group: more linear fixation patterns, fewer triangular or V-shaped fixation patterns over core facial features. A greater tendency to fixate on non- core features compared with core features. Fixations have increased 'scatter' over the face stimulus:
    a. ADHD group: some linear patterns of fixation between core facial features and increased 'scatter' of fixations over the face stimulus.
    b. ASD group: few fixation sequence patterns between core facial features and more fixations to on non-core features of the face. Reduced 'scatter' of fixations over the face stimulus.

c. ADHD+ASD group: few fixation sequence patterns between core facial features and more fixations to on non-core features of the face. Increased 'scatter' of fixations over the face stimulus.

2.3.2 APPLICATION OF THE CODING FRAMEWORK

As stated in section 2.2.6, while the observation of dynamic eye gaze was completed, transcript notes were generated based on the themes and models that emerged for each participant. Once the observation of dynamic eye gaze was completed, the written transcripts were reviewed and the predicted group was designated based on the clinical coding framework protocol presented in the previous section. The initial analysis for the predicted groups are shown below. This was calculated by comparing the predicted group (based solely on the blinded gaze analysis above) to the actual group.

2.3.2.1 INITIAL ANALYSIS

Initially, the coding framework protocol was assessed to see if clinical cases could be separated from control cases based on the dynamic eye gaze patterns. Table 2.2 shows the chi squared results when the initial coding framework protocol was applied to the participants, in order to generate a proposed clinical versus proposed control case status. This procedure correctly classified 17/19 (89.5%) of the clinical group ($\chi^2(1)=5.3$, $p<0.05$) however, only 6/13 (46.2%) of the control group was correctly classified (see Table 2.2).

Table 2. 2: Initial analysis for clinical and control groups

		Actual Group		Total
		Clinical	**Control**	
Proposed Group (based on coded procedure)	**Clinical**	**17** *	7	24
	Control	2	**6**	8
Total		19	13	32

*$\chi^2(1)=5.3$, $p<0.05$

2.3.2.2 **REVISED PROTOCOL**

Once the blinded analysis was completed, those that were misdiagnosed using the initial coding framework protocol were checked by examining the thematic notes created during observation and coding. If the notes contained further information, for example documentation of 'scatter' of fixations suggesting ADHD grouping, then this would allow for the group reassignment (from control to ADHD). It was also noted in this secondary analysis that children with a predicted diagnosis of from the initial coding framework of ADHD that had an actual ASD+ADHD diagnosis had less triangulations between core features in their gaze patterns. Also, those children with an ASD+ADHD predicted diagnosis from the initial coding framework who had increased fixations on the left eye tended to have an actual diagnosis of ADHD. Based on this secondary analysis, it was thus noted that during the coding framework development and group predictions, there was a tendency to prioritise the 'scatter' of fixations over the sequence of fixations over the core features (e.g. V shape, linear etc.) so this was refined in the revised protocol.

Details of revised protocol:

1) patterns of eye gaze to salient core features (triangulations, V-shape, linear or none);
2) 'Scatter' of eye gaze, includes speed and distance of fixations over the face stimulus (increased or reduced).

Revised predicted group designation (changes shown in bold):

1) Control group: more fixations to the core facial features (eyes and mouth) were triangulations and V shape patterns. Fixations showed **much** reduced 'scatter' and a greater tendency to fixate on core features (eyes and mouth) than non-core features (other areas of the face).
2) Clinical group: more linear patterns of fixations to core features or no fixations to core features. Increased 'scatter' of fixations and fixations on non-core facial features:
    a. ADHD: Some linear patterns of fixations to core features **with more fixations on the left eye than the right eye** and increased 'scatter' of fixations.
    b. ASD: **fewer fixation sequence patterns between core facial features** and more fixations to on non-core features of the face. Reduced 'scatter' of fixations over the face stimulus
    c. ADHD+ASD: **fewer fixation sequence patterns between core facial features** and more fixations to on non-core features of the face. **Much increased** 'scatter' of fixations over the face stimulus.

2.3.2.3 SECONDARY ANALYSIS

The revised protocol described above was then used to create a secondary analysis that allowed for these changes. When the revised protocol was implemented, the procedure correctly classified 19/19 (100%) of the clinical group ($\chi^2(1)=15.6$, $p<0.001$) and, 8/13 (61.5%) of the control group was correctly classified (see Table 2.3).

Table 2. 3: Secondary analysis for clinical and control groups

		Actual Group		Total
		Clinical	**Control**	
Proposed Group (based on coded procedure)	**Clinical**	**19** *	5	24
	Control	0	**8**	8
Total		19	13	32

*$\chi^2(1)=15.6$, $p<0.001$

In order to evaluate how effective the revised protocol was at differentiating between groups, further analysis was completed as shown in Table 2.3. The highest classification accuracies were yielded for the ADHD group with 4/4 (100%) cases correctly classified ($\chi^2(9)=38.3$, $p<0.001$). 7/8 (87.5%) of the ADHD+ASD groups were correctly classified while only 3/7 (42.9%) of the ASD group were correctly classified. Interestingly, the protocol categorised children with ASD into the ADHD groups more frequently than the ASD group (see Table 2.4).

Table 2. 4: Analysis of diagnostic groups

		Actual Group				Total
		ADHD	**ASD**	**ASD+ ADHD**	**Control**	
Proposed Group (based on coded procedure)	**ADHD**	**4***	1	1	1	7
	ASD	0	**3**	0	2	5
	ASD+ ADHD	0	3	**7**	2	12
	Control	0	0	0	**8**	8
Total		4	7	8	13	32

*$\chi^2(9)=38.3$, $p<0.001$

2.3.3 VALIDATION OF OBSERVATIONAL RESULTS USING MACHINE LEARNING

As discussed in methods section 2.2.7, the whole eye tracking dataset was explored via dynamic sequence modelling and the most frequent classifying sequences for each group were generated. This section presents the results from the dynamic sequence patterns and the group classification accuracies using machine leaning.

2.3.3.1 SEQUENCES IN THE GROUPS

The most frequently occurring classifying sequence from each group is presented in Figure 2.10).

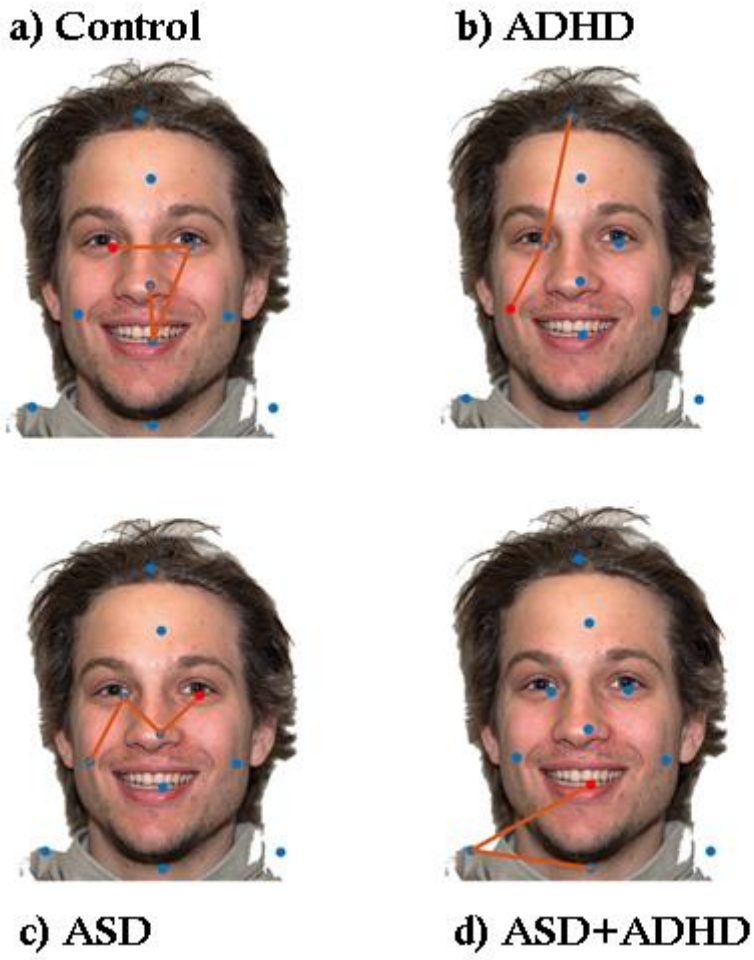


Figure 2. 10a–d): Most frequent sequence for each group

Each blue circle represents a code. Each code is denoted by its position over the emotion face image. The red circle is the end of the sequence and the red line represents the dynamic sequence as defined by the order of codes.

As shown in Figure 2.10b), the most frequently occurring sequence for the ADHD group is a linear pattern of eye gaze over the left hemi space of the emotional face from the viewers perspective. This is in line with the findings from the static fixation patterns shown in Figure 2.5 and, the observation coding framework protocol described in Section 2.3.1. The most frequently occurring sequence for ADHD also differs from that of the other groups. The most frequently occurring sequence in the ASD+ADHD group showed more fixated features over the lower half of the emotional

face image (Figure 2.10d), while those with ASD showed the most frequently occurring sequence of fixations in a zig-zag like configuration across the mid-zone of the image (Figure 2.10c). The most frequently occurring sequence for typically developing controls showed a triangular configuration of fixations between core features (eyes and mouth; Figure 2.10a), which was also observed qualitatively in section 2.3.1.

In summary, the automated sequences from machine learning showed similarities to the qualitative observations in the previous section. This included a linear pattern of fixations between the left eye and the mouth in children with ADHD and, a triangular configuration of fixations between core features (eyes and mouth) in the typically developing control children. The sequences also appear to differ amongst the clinical groups. The next section presents the group classification accuracies for the most frequent fixation sequences.

2.3.3.2 MACHINE LEARNING SEQUENCE AND SCATTER ACCURACIES IN THE GROUPS

Table 2.5 presents the group accuracies from the most frequently occurring sequences and scatter features derived from machine learning.

Table 2. 5: Group accuracies from sequence and scatter features

Group comparison	Accuracy from sequence features	Accuracy from sequences and scatter features
Controls versus ADHD	0.83	No improvement
Controls versus ASD	0.69	No improvement
Controls versus ASD+ADHD	0.68	No improvement
ADHD versus ASD	0.78	No improvement
ADHD versus ASD+ADHD	0.71	No improvement
ASD versus ASD+ADHD	0.79	0.84

The codes generated by the machine-learning approach yielded the highest accuracy, 83%, when distinguishing ADHD from controls (Table 2.5). This supports the finding the observation detailed in section 2.3.1, that a linear eye gaze pattern found in ADHD differs from the triangulation gaze pattern found in typically developing controls. When the 'scatter' feature was added to the model, accuracies between the ASD and the ASD+ADHD group increased from 79% to 84%, suggesting that dispersal of fixations helps to further differentiate ASD+ADHD from ASD. This machine learning approach supports the hypothesis of visual social-emotional attention differentiating ADHD from ASD and ASD+ADHD and, begins to answer the third question of this thesis regarding the potential for eye tracking measures to differentiate the groups.

2.4 SUMMARY AND DISCUSSION OF FINDINGS

This chapter described a novel approach to eye gaze analysis to faces including: results from dynamic eye gaze to emotions; observational coding of eye fixation patterns from an emotion recognition task; generation of models; and a set of fixation patterns that differentiate children with neurodevelopmental conditions from typically developing control children. The models that were most frequently observed and included in the coding framework protocol were fixations to core features (left eye, right eye and mouth) of the face and 'scatter' of fixations over the face stimulus. This eye gaze coding framework protocol designated children as control participants if they had more triangulations and V shape fixation patterns between the eyes and mouth and reduced 'scatter' and fixation on non-core features of the face. This protocol designated children as clinical participants if their eye gaze had more linear fixation patterns or no fixation sequences between eyes and the mouth and had increased 'scatter' of fixation and fixations on non-core features of the face.

The initial protocol correctly classified the clinical group (89.5%) more accurately than the control group (46.2%; ($\chi^2(1)=5.3$, $p<0.05$)). A revised protocol which was more stringent on controls, having much less 'scatter' of fixation improved these results; correctly classifying 100% of the clinical group and 61.5% of the control group ($\chi^2(1)=15.6$, $p<0.001$). The dynamic sequence eye gaze coding framework protocol to differentiate between clinical groups, included participants designated to the ADHD group if their eye gaze had increased 'scatter' of fixations and linear fixation patterns between the left eye and mouth. Participants were designated

to the ASD group if their eye gaze had less triangulation of fixations between core features (eyes and mouth), more fixations to non-core features and reduced 'scatter' of fixations over the face stimulus. Participants were designated to the ADHD+ASD group if their eye gaze had less triangulation of fixations between core features (eyes and mouth), more fixations to non-core features and increased 'scatter' of fixations over the face. This protocol generated classification accuracies of 100%, 87.5% and 42.5% in the ADHD, ADHD+ASD and ASD group(s) respectively ($\chi^2(9)=38.3$, $p<0.001$). A limitation of the chi-square test used to analyse the observational coding was that cell sizes were less than 10 in some cases and therefore, Fisher's exact test may have been more appropriate for the analysis in the small sub-sample. As Fisher's exact test is usually performed for 2x2 contingency tables, chi-squared was used here as it is more suitable for all dimensions including 4x4 contingency tables; allowing for testing in all four groups. Machine learning approaches in the whole sample improved differentiation in the ASD group and, validated the observer based coding framework results.

In conclusion, this chapter presented a novel approach to eye gaze analysis and proof of concept that visual social-emotional attention (VSA) may help to differentiate between clinical groups such as ADHD and ASD. Machine learning on the whole dataset provided validated differing visual social-emotional attention and face processing in the groups. This procedure was not only designed to gain greater insights into eye gaze patterns but also as a guide to select eye tracking measures that could quantitatively

capture some of the qualitative differences found amongst the groups.

These quantitative eye tracking measures are described in the next chapter.

3 STUDY OF VISUAL ATTENTION TO EMOTIONAL FACES IN SAMPLE 1

3.1 OVERVIEW

This chapter extends the work of the previous chapter which started to answer the questions of the thesis. The previous chapter demonstrated that observed eye gaze patterns distinguished the groups, helping to provide evidence for visual attention differentiating ADHD, ASD and ASD+ADHD on an emotion recognition task. Such qualitative observations do not however, allow for questions regarding association or comorbidity at a symptom level to be adequately addressed. The enquiry in this chapter, was to investigate whether quantitative eye tracking measures to emotional faces in ADHD are associated with emotion recognition deficits on a prompted emotion recognition task, analyse any association of visual attention to emotional faces with clinical symptom severity and, compare visual social-emotional attention amongst the groups. This seeks to address the questions of the thesis on the association of visual attention to emotional faces on a prompted emotion recognition task; a commonly used task in the study of ASD.

Quantitative eye tracking measures reviewed in the literature (section 1.5.1; visual social-emotional attention in ADHD) were analysed in this chapter. As described below, the quantitative eye tracking measures capture different aspects of visual social-emotional attention. In the ASD literature, the eye tracking measures used include fixation duration to interest areas (otherwise known as Dwell Time (DT)) to eyes and mouth. Eye

tracking measures from the ADHD literature also capture temporal (speed of attention across the stimulus) and spatial (breadth of attention across the stimulus) indicies to face stimuli separately. As discussed in Section 1.5.1, additional eye tracking measures to DT could yield important information and give clues to underlying neuro-circuitry and cognitive processes. This may help characterise visual social-emotional attention in the groups and differentiate ADHD, ASD and ASD+ADHD on the emotion recognition task, addressing question 3 of this Thesis. Eye tracking measures were analysed to clarify if emotion recognition deficits in ADHD are primary to ADHD or secondary to co-occurring ASD, addressing question 2 of this Thesis. Models of comorbidity were considered within the hypotheses and mixed design ANOVA two-factor model (with ADHD and ASD as fixed factors) was used for the analyses as described below.

The relationship between emotion recognition accuracy, symptom severity and the quantitative eye tracking measures were also analysed. This was done to address question 1 of this Thesis; to find out if visual social-emotional attention can elucidate emotion recognition problems in ADHD.

3.1.1 CHAPTER OUTLINE

The hypotheses specific to this chapter and the methods for calculating eye tracking measures are presented first. This is followed by the results from this chapter which are divided and presented as 3 sections: 1) emotion recognition accuracy, 2) dwell time (indexing fixation duration to interest areas of the face) and, 3) temporal and spatial measures (indexing speed

and breadth of attention to the face stimulus). A brief discussion of visual social-emotional attention in children with comorbidity and its impact conclude this chapter.

3.2 HYPOTHESES

The hypotheses for the groups are presented in 3 subsections based on the dependent variable being tested in the mixed design ANOVA two-factor model (with ADHD and ASD as fixed factors; see Section 3.3.2 for detailed methodology of statistical analysis).

3.2.1 EMOTION RECOGNITION ACCURACY

Based on the literature (Sinzig, Morsch, and Lehmkuhl 2008), it was predicted that emotion recognition accuracy for faces would be greatest in the following descending order: happy, sad, anger, fear, disgust and surprise. Thus, emotion recognition accuracy would be highest for happy and lowest for surprise.

It was hypothesised that this order of accuracy would be similar in all the groups but that the differences between groups would be significantly greater for certain emotions as presented in the literature review (section 1.4.1)

1) **ADHD**

It was hypothesised that ADHD would have reduced accuracy to all emotions compared with typically developing controls, but that this effect would be greatest for negative emotions, namely anger.

2) **ASD**

It was hypothesised that ASD would have reduced accuracy to all emotions compared with typically developing controls, but this difference would be significantly greater for fear and more complex emotions e.g. surprise and disgust.

3) **ASD+ADHD**

It was hypothesised that ASD+ADHD would have the lowest accuracy to all emotions compared with typically developing controls, with particular impairment to negative emotions including both anger and fear.

It was also hypothesised that emotion recognition accuracy to stimuli in the 'eyes only' condition would follow a similar group pattern to the face hypotheses above. However, overall accuracy would be reduced in the 'eyes only' condition compared to the 'faces' condition based on the findings by Sinzig et al. (2008).

3.2.2 DWELL TIME TO INTEREST AREAS

Dwell time (DT) is defined as the fixation duration to the specified interest areas e.g. eyes and mouth of the face. Based on findings from the literature review in Chapter 1, it was hypothesised that dwell time (DT) to eyes and mouth would differ based on emotion type, with more mouth viewing for positive emotions such as happy.

1) **ADHD**

It was hypothesised that ADHD would have reduced DT to eyes and mouth for negative emotions such as anger compared with typically developing controls.

2) ASD

Based on the literature presented in Chapter 1, it was hypothesised that ASD would have reduced DT to eyes and mouth for all emotions and that this would be most pronounced for emotions fear and surprise compared with typically developing controls.

3) ASD+ADHD

There is a lack of literature in the comorbid population. However, it was hypothesised that if the comorbid group have both ASD and ADHD, they will have the additive effects of both conditions. This will lead to significantly reduced DT to the eyes and mouth of most emotions compared with typically developing controls.

It was also hypothesised that reduced DT to eyes and mouth would be associated with increased symptom severity in the social reciprocal interaction and the communication domains of the SCQ. It was also hypothesised that there could be a weak association with reduced DT to eyes and mouth and the Conners' rating scale inattentive but not hyperactive symptoms. It was also hypothesised that reduced DT to eyes and mouth would be related to poorer emotion recognition accuracy.

3.2.3 TEMPORAL AND SPATIAL MEASURES

In addition to dwell time to the eyes and mouth of the face, eye tracking measures from the ADHD literature also capture temporal (speed of attention across the stimulus) and spatial (breadth of attention across the stimulus) analyses to face stimuli separately. Based on the literature on visual social-emotional attention in ADHD presented in Section 1.5.1, it was hypothesised that temporal measures (including total fixation duration; mean fixation duration; and fixation number to emotional faces) would be greater for positive emotions such as happy and reduced for more negative emotions. It was also hypothesised that spatial measures (fixation scanpath length; mean length between fixations; and standard deviation of fixation length) would be greater for negative emotions overall.

1) **ADHD**

Based on the observed findings in Chapter 2 of more 'scattered' fixations in ADHD, it was hypothesised that children with ADHD would have shorter and more dispersed fixations when viewing emotional faces compared with typically developing control children and children with ASD. This would be indicative of a 'hyper-extensive' scanning style as described in the literature (section 1.5.1). It was therefore hypothesised that those with ADHD would have: reduced mean fixation duration with increased fixation number; increased fixation scanpath length; increased mean length between fixations; and increased standard deviation of fixation

length to emotional faces compared with typically developing controls and children with ASD. It was also hypothesised that if this 'hyper-extensive' pattern is specific to emotion type, for example angry faces in ADHD compared with typically developing controls and children with ASD, then there would be an interaction between ADHD factor and 'Emotion' on the dependent variable.

2) ASD

Based on the literature described in section 1.5.1, it was hypothesised that children with ASD would have a 'restricted' scanning style when viewing emotional faces compared to typically developing control children and children with ADHD. It was hypothesised that this would result in a profile of increased mean fixation duration with reduced fixation numbers; reduced fixation scanpath length; reduced mean length between fixations; and reduced standard deviation of fixation length to emotional faces compared with the typically developing children and the children with ADHD. It was hypothesised that if this 'restricted' pattern is specific to emotion type e.g. fearful faces in ASD compared to typically developing children and children with ADHD, then there would be an interaction between ASD factor and 'Emotion' on the dependent variable.

3) ASD+ADHD

As described previously, at the time of writing there is a lack of literature on the comorbid population. It was difficult to predict if comorbidity would result in a scanning profile midway between a 'hyper-extensive' or 'restricted' style. Specific hypotheses were not

put forward for the comorbid group. It was suggested that if the comorbid group had a significantly different scanning style to either of the pure groups, then this would result in an interaction of ADHD by ASD factor on the specified dependent variable.

It was also hypothesised that an 'hyper- extensive' scanning style in children with ADHD would be associated with symptom severity on the Conners' rating scale inattentive and hyperactive-impulsive subscales and, a 'restricted' scanning style in ASD would be associated with repetitive stereotyped behaviours on the SCQ. It was difficult to hypothesise which scanning style would be associated with poor emotion accuracy. However, it was suggested that both extremes of temporal and spatial visual attention could be associated with poor emotion recognition accuracy.

3.3 METHODS

Participants, measures and tasks are described in Chapter 2 (Section 2.2).

3.3.1 EYE MOVEMENT DATA PROCESSING

Raw eye tracking data collected during the emotional faces task was processed using ILAB which contains open source MATLAB functions for post-experimental eye movement analysis (Gitelman 2002). Eye locations and pupil values from the raw data samples were converted to text files for pre-processing in ILAB. Coordinate transformation allowed visualisation in ILAB by entering calibration points from the eye tracker, computer

screen resolution and distances in the task (as described in Chapter 2 (Section 2.2.4)) into the ILAB parameters setup.

A trial length of 4500ms was analysed as this is the length of time participants had to view emotional faces prior to the words appearing prompting emotion accuracy response. A minimum fixation duration of 200ms was set in line with the literature on face viewing in ADHD (Marsh 2008). The basic definition of a fixation, is a set of eye locations within a defined area for a selected amount of time (Gitelman 2002). As described by Widdel (1984), fixations were calculated using the dispersion algorithm in ILAB which is relatively resistant to missing points including blinks (Widdel 1984). Thus, in this instance, a fixation was defined as within a dispersion threshold of 2.68 degrees for a duration of 200ms. Participants' eyes are allowed to drift as long as this was for less than the minimum fixation duration (200ms). Blink artefacts were removed in ILAB using a combination of pupil size being equal to 0 and eye position being incorrect (off the computer screen) (Gitelman 2002).

Trials with fewer than two fixations were discarded as fixation durations were too long, potentially invalidating the trial data. Trials were removed if eye movement data was not continuously recorded for at least 1125ms (at least 25% of the trial time). Trial adequacy was verified using a two-step approach; firstly, the data was visually assessed in ILAB and secondly, a percentage acquisition was computed by ILAB for cross checking. Participants with more than 50% invalid trial data were removed from the analysis, as has previously been documented in the literature with similar

trial numbers in ASD and disruptive disorders (Bours et al. 2018). Participants with less than 50% of valid trial data included two control participants; both of whom were recruited at the beginning of the study and less data was collected due to a computer capacity error that was promptly corrected. Of the initial 44 children recruited, one child with ADHD could not complete the calibration (see Chapter 2 for details) and two control children did not have adequate eye movement data so, in total, 41 children were included in the final eye movement data analysis.

The emotional faces for each trial were imported into ILAB by creating a JPEG directory containing the scaled images, and interest areas were designated using the region of interest function in ILAB. A template for the interest area of the emotional faces was created for the core facial features (the right eye, left eye and mouth). The interest area for the eyes includes the eye lashes and brows, and for the mouth contains the philtrum (Figure 3.1). The interest area to the eyes and mouth were designed to be large enough to allow for offsets (such as head movements) in the data that are found when conducting studies with children (Guillon et al. 2015).

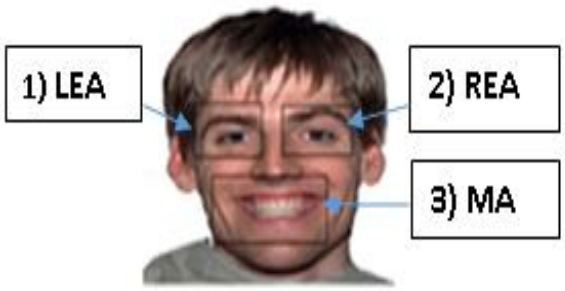


Figure 3. 1: Interest areas for emotional faces

Rectangles for core features: 1) Left Eye Area in left hemi-space (LEA); 2) Right Eye Area in right hemi-space (REA); and 3) Mouth Area (MA)

Interest areas for the whole face, photograph and the screen were also defined so that fixation duration to the screen and fixation to other regions of the face could be calculated. Interest area statistics for each trial were calculated from the defined fixations in ILAB to provide a DT to the designated interest area (DT is defined as the fixation duration to the designated interest area). Mean DT per participant and mean DT percentage (DT/Trial time (4500ms)) were also calculated for subsequent analysis.

Socially salient features include both eyes and mouth and DT is a measure of the amount of time spent fixating during the trial. Times spent fixating at specific interest areas are most commonly performed in the ASD literature (see Section 1.5.2 for details). In addition to the socially salient features of the face (eyes and mouth), other features of the face such as the nasal bridge, forehead and other creases of the face are also important to look at when recognising emotions (Boucher and Ekman 1975). An interest area which contained these other facial features (without the eyes and mouth) was created and termed 'other'.

In addition to the interest area statistics, fixation analysis based on the defined fixations described above were also extracted from ILAB. For each fixation per trial, the fixation duration, fixation number and distance to next fixation were extracted. These fixation data were used to calculate the temporal and spatial measures providing quantitative variables of visual scanning (Table 3.1). Planned contrasts of each measure to specific hypothesis (in this case extensive versus restricted scanpaths to emotional faces) were made. Temporal measures include; total fixation number, total

fixation duration (ms) and mean fixation duration (ms). Spatial measures (in degrees of visual angle) include; fixation scanpath length (total distance between fixations), mean distance between fixations and SD of distance between fixations.

Table 3. 1: Temporal and spatial measures and calculations

Eye tracking measure		Calculation	What these measures signify
Temporal			How much information processing has occurred—an estimate of processing rate.
1)	Total fixation number (TFN)	Sum of the number of fixations per trial.	
2)	Total fixation duration (TFD; ms)	Sum of fixation duration per trial.	
3)	Mean fixation duration (MFD; ms)	Average fixation duration per trial.	
Spatial			Where the attention in allocated—breadth of attention (e.g. extensive scanpath length signified by relatively greater distances between fixations).
4)	Fixation scanpath length (FSPL; distance)	Sum of the distances from fixation to fixation per trial.	
5)	Mean length between fixations (MLBF; distance)	Average distance between fixations per trial.	
6)	SD length between fixations (SDLBF; distance)	Standard deviation of the distance between fixations.	

Trial temporal and spatial measures were calculated as shown in Table 3.1 and then the mean values for each participant for each emotion type were calculated for statistical analysis.

3.3.2 STATISTICAL ANALYSIS

As described in Section 2.2, group differences for the demographic and clinical scores were calculated using univariate ANOVA. Post hoc tests were carried out to allow for multiple comparisons. Levene's test of variances determined Tukey and Games-Howell post hoc tests.

The effects of ASD and ADHD on emotion accuracy and eye tracking measures were tested using mixed-design ANOVA two-factor model comprising ASD and ADHD as fixed factors and 'Emotion' as a repeated measures factor. ASD and ADHD factors are computed in SPSS from the diagnostic category (control group, ADHD group, ASD group, ASD+ADHD group). ASD factor (yes) includes children from the ASD group and ASD+ADHD group. ASD (no) includes children from the ADHD group and control group. ADHD factor (yes) includes children from the ADHD and ASD+ADHD group and ADHD (no) includes children from the ASD and control groups.

This two factor analysis method has been used to test comorbidity in ERP data by our group (Groom et al. 2017) and other groups (Tye et al. 2014; Shephard et al. 2019). This two factor analysis method allows comparison of the eye tracking and ERP results as participants from this data set were tested using eye tracking and EEG. Results of the ERP data from this sample have been presented in Groom et al. (2017). Importantly, duplicating this method of analysis in the eye tracking data in this way, serves to answer question 2 of this Thesis relating to comorbidity. Specifically, this design helps to disentangle the influences of ASD versus ADHD in the case of comorbidity. The two factor design tests the main effect of ASD and ADHD factors on variables of interest in addition to an interaction between ASD and ADHD factors (Banaschewski et al. 2007; Groom et al. 2017). In particular, an interaction between ASD and ADHD factors could suggest a model compatible with the comorbid group belonging to a third separate nosology to either of the pure groups as described by Rutter and

Taylor (2002). Alternatively, a main effect of ASD and/or ADHD factors, with a lack of interaction between ASD and ADHD factors could suggest an 'additive model' of comorbidity, especially if a double dissociation exists (Banaschewski et al. 2007) . This additive model would be in keeping with the comorbid group sharing a profile with both the pure groups and potentially shared risk factors within the comorbid group as discussed in Section 1.3.

In addition to the fixed factors described above, the mixed design ANOVAs also included a repeated measures 'Emotion' factor comprising 6 levels (happy, sad, anger, fear, disgust and surprise). Planned repeated contrasts were applied as described by Field (Field 2005) in accordance with the hypothesis of group effects on the dependent variable (emotion recognition accuracy or eye tracking measure). It was hypothesised that the order of accuracy of emotion recognition would be as follows: happy would be the easiest; followed by sad; then anger; then fear; then disgust; and finally, surprise would be the most difficult to detect. The contrast was specified such that: Level 1 corresponds to happy; Level 2 corresponds to sad; Level 3 to Anger; Level 4 to fear; Level 5 to disgust; and Level 6 to surprise. Repeated contrast is reported as Level 1 versus Level 2; Level 2 versus Level 3; Level 3 versus Level 4; Level 4 versus Level 5 and Level 5 versus Level 6. Thus, the first comparison would be between happy and sad. The second comparison would be between sad and anger. The third comparison between anger and fear. The fourth comparison between fear and disgust and the fifth comparison between disgust and surprise. ASD

factor and ADHD factor were entered as between-subject fixed factors. Significant findings relating to the fixed factors (ASD Factor and ADHD Factor) will be reported in detail. However, significant effects that do not interact with the ASD and ADHD factors will be summarised and tabulated but not reported in the main text.

Significant interactions were followed up by simple effects analysis. As DT percentage gave a similar pattern of results to DT, only results for DT are reported for brevity. Controlling for multiple comparisons for the eye tracking variables was not done as they were planned prior, to test the hypotheses. Testing these eye tracking variables individually without controlling for multiple comparisons, has been done in previous eye tracking literature and is appropriate when the variables are conceptually separate (e.g. spatial versus temporal) (Marsh 2008; Guillon et al. 2015). Pearson's correlation co-efficient was conducted to analyse associations between significant eye tracking variables, symptom severity subscales and emotion recognition accuracy.

To examine the possible effects of covariates, hierarchical linear regression was used to test if IQ (WASI scores) or oppositional symptoms (Conners' parent rating scale oppositional subscale T scores) had significant contributions to the dependent variable over and above ADHD and ASD factors. Hierarchical linear regression models were applied to the dependent visual attention variable being tested (e.g. emotion accuracy and DT to the mouth). This analysis was performed only on dependent variables that were found to be significant in the main analyses described above. If ADHD factor had a main effect on the dependent variable (e.g. emotion

accuracy), then ADHD factor was entered in the first block and ASD factor entered in the second block. If ASD factor had a main effect on the dependent variable (e.g. DT to the mouth) then ASD factor was entered in the first block and ADHD factor entered in the second block. Full scale IQ was entered in the third block and oppositional problems on the Conners' parent rating scale was entered in the final block. The model was tested at each step to determine whether the covariates explained additional variance over and above the variance explained by ADHD and ASD. This approach to testing the effects of covariates was chosen in preference to entering multiple covariates into the repeated measures models described above, because the use of ANCOVA has been shown to be a poor way of covarying for IQ in psychiatric and developmental disorders especially if IQ is tightly bound to the clinical profile of the disorder as is the case for both ASD and ADHD (Miller and Chapman 2001). Miller and Chapman (2001) highlighted that entering multiple covariates into the ANOVA model removed too much of the variable of interest (in this case ADHD), potentially leading to a false negative result. For these reasons, a hierarchical linear regression approach was taken to be most informative of the variables of interest.

As described in section 2.2.1, a power calculation to estimate the number of participants required in each group was calculated using G*power software (version 3.1.9.2). As the projected sample size based on four groups was not achieved (Section 3.4.1), a post hoc power calculation based on the 2x2 factorial design described in this section was calculated using G*power in order to calculate the power to detect an interaction of

medium effect size. Based on the actual sample size of 41, it was calculated there was 87.7% power to find an interaction between the ASD and ADHD factors with a medium effect size at an alpha criterion of 0.05.

3.4 RESULTS

3.4.1 DEMOGRAPHIC AND SYMPTOMS SCORES IN THE SAMPLE GROUPS

As shown in Table 3.2, groups were well matched for age (F (3, 39)=0.16, p>0.05, ηp^2=0.01) and there was a male predominance in all groups except the groups differed in the ratio of males to females (F (3, 39)=3.38, p<0.05, ηp^2=0.21). Groups differed in mean IQ (F (3, 39)=4.04, p<0.05, ηp^2=0.24) with significantly lower scores in the ADHD group (p<0.05) and ASD+ADHD group (p<0.01) compared to the control group.

As expected, the groups differed significantly on SCQ (F (3, 39)=29.65, p<0.001, ηp^2=0.85) with significantly higher scores in the ASD group (p<0.001) and ADHD+ASD group (p<0.001) compared to control group. Significantly higher total SCQ scores were also found in the ASD group (p<0.01) and ADHD+ASD group (p<0.001) compared to the ADHD group. Groups differed significantly on SAS (F (3, 33)=26.57, p<0.001, ηp^2=0.71) with significantly lower scores in all three clinical groups (p<0.001) compared to control group.

Groups differed significantly on the Conners' DSM-IV IA T-score (F (3, 37)=37.4, p<0.001, ηp^2=0.75) with significantly higher T-scores in all three clinical groups compared to control group (p<0.001). Conners' DSM-IV IA T-scores were significantly higher in the ADHD group (p<0.001) and ADHD+ASD group (p<0.01) compared to the ASD group.

Groups also differed significantly on the Conners' DSM-IV HI T-score (F (3, 37)=65.95, p<0.001, ηp^2=0.84) with significantly higher T-scores

in all three clinical groups compared to control group ($p<0.001$). Conners' DSM-IV HI T-scores were significantly higher in the ADHD group ($p<0.001$) and ADHD+ASD group ($p<0.01$) compared to the ASD group. Groups also differed significantly on the Conners' DSM-IV Oppositional T-score ($F(3, 37)=17.63$, $p<0.001$, $\eta p^2=0.59$) with significantly higher T-scores in all three clinical groups compared to control group ($p<0.001$). OD and CD were common in all the clinical groups. However, Emotional Disorders were mainly present in the combined ASD+ADHD group (Table 3.2). Emotional, oppositional and conduct disorders were based on DAWBA computer diagnoses and confirmed by clinical rating as described in methods section (2.2.2.3).

Based on parental report, four children in the ADHD group and four children in the ASD+ADHD group were regularly taking prescribed stimulant medication. Of the four children prescribed stimulant medication in the ADHD group, one child was prescribed Concerta XL, two children were prescribed Medikinet XL and one child was prescribed short acting Methylphenidate Hydrochloride. Of the four children in the ASD+ADHD group, three children were prescribed Concerta XL and one child was prescribed Equasym XL. As described in Section 2.2, all children were withdrawn from any stimulant medication 24 hours prior to testing. Two children in the ASD+ADHD group, one child in the ASD group and one child in the ADHD group were prescribed melatonin for sleep problems. One child in the ASD group was prescribed low dose anti-psychotic medication (Aripiprazole) for behavioural problems. None of the children from any of the groups were on non-stimulant or anti-depressant medication.

Raw emotion recognition scores, eye tracking data and excluded trials per group are presented in Appendix VI., Table A.24. For the eye tracking analysis, excluded number of face trials as described in the methods (Section 3.3.1) were not significantly different amongst the groups (F (3, 37)=2.69, p>0.05, ηp^2=0.18).

Table 3. 2: Demographic and clinical characteristics of the sample (n= 43)

	Group				Group effect		
	ADHD (n=8)	**ASD** (n=10)	**ASD+ADHD** (n=9)	**Controls** (n=16)*	***F***	**p-value**	**Group differences** (post-hoc)
Mean age in years (SD; range)	11.95 (2.50; 9.16-15.42)	12.52 (1.76; 10.03-15.88)	12.46 (2.06; 9.22-15.66)	12.14 (1.95; 9.67-15.76)	0.16	p>0.05	n/s
Gender % male (n male)	50.0% (4)	90.0% (9)	100.0% (9)	87.5% (14)	3.38	p<0.05	n/a
Mean FSIQ (SD; range)	99.13 (11.21; 79.00-111.00)	106.00 (8.52; 94.00-116.00)	96.78 (16.19; 70.00-118.00)	111.44 (9.60; 95.00-127.00)	4.04	p<0.05	Controls > ADHD [c] / ASD+ADHD [b]
Total SCQ (SD; range)	9.25 (8.66; 0.00-26.00)	21.40 (8.90; 5.00-32.00)	25.67 (4.95; 16.00-32.00)	3.38 (3.70; 0.00-15.00)	29.65	p<0.001	Controls < ASD / ASD+ADHD [a] ADHD < ASD [b] / ASD+ADHD [a]
SAS (SD; range)	10.25 (6.07; 4.00-18.00)	7.80 (5.45; 0.00-16.00)	6.22 (2.99; 3.00-11.00)	24.50 (5.32; 15.00-33.00)	26.57	p<0.001	Controls > ADHD / ASD /ASD+ADHD [a]
Conners' IA T score (SD; range)	78.00 (9.26; 63.00-90.00)	63.20 (9.51; 51.00-77.00)	75.44 (6.21; 66.00-86.00)	47.00 (6.28; 40.00-60.00)	37.40	p<0.001	Controls < ADHD / ASD /ASD+ADHD [a] ASD < ADHD [a] / ASD+ADHD [b]

Conners' HI T score (SD; range)	88.88 (1.89; 85.00-90.00)	74.10 (11.87; 54.00-90.00)	85.00 (7.66; 68.00-90.00)	48.36 (5.57; 43.00-62.00)	65.95	p<0.001	Controls < ADHD / ASD /ASD+ADHD [a] ASD < ADHD [a] / ASD+ADHD [b]
Conners' OD T score (SD; range)	81.25 (9.79; 64.00-90.00)	70.70 (17.54; 49.00-90.00)	73.11 (10.12; 61.00-89.00)	47.57 (8.00; 39.00-64.00)	17.63	p<0.001	Controls < ADHD / ASD /ASD+ADHD [a]
Oppositional and Conduct Disorders	5	5	5	0	-	n/a	-
Emotional Disorders†	1	1	6	0	-	n/a	-

FSIQ Full Scale Intelligence Quotient (WASI); SAS Social Aptitudes Scale (≤ 12 is suggestive of ASD); SCQ Social Communication Questionnaire (≥ 15 suggestive of ASD); Conners' Parent IA (Inattentive); HI (Hyperactive-Impulsive); OD (Oppositional) T scores (≥ 65 suggests difficulties in these areas). Rating scale scores shown are parent rated. †Emotional Disorders include general anxiety disorder, mild depressive episode, obsessive compulsive disorder or specific phobia. Note: participants could have more than one disorder. Emotional, oppositional and conduct disorders were based on DAWBA computer diagnoses and confirmed by clinical rating as described in methods section (2.2.2.3). *2 control children were not included in the eye movement analysis due to inadequate data acquisition (as described in Section 3.3). 1 child in the ADHD group could not complete the calibration so could not complete the task (as described in Section 2.2.4). [a]$p<0.001$; [b]$p<0.01$; [c]$p<0.05$

3.4.2 EMOTION RECOGNITION

3.4.2.1 FACES

As described in section 3.2.2, a mixed-design ANOVA was performed to identify effects of ASD, ADHD and emotion type on the accuracy of emotion recognition. Accuracy was the dependent variable. Emotion, with 6 levels (happy, sad, anger, fear, disgust and surprise) was entered as a repeated measures factor and ASD and ADHD entered as fixed factors.

There was a significant main effect of ADHD ($F(1, 39)=4.78$, $p<0.05$, $\eta p^2=0.11$) with lower accuracy in those with (mean=0.69) than without (mean=0.76) ADHD. No other main effects or interaction for ASD or ADHD were significant for emotion accuracy. Significant main effects and interactions independent of fixed factors are tabulated at the end of the results Section 3.4.3.2. (Table 3.3).

3.4.2.2 EYES-ONLY

A mixed-design ANOVA was performed to identify the effects of ASD and ADHD on emotion accuracy between the 'faces' condition and the 'eyes-only' condition. There was a main effect, with all children showing reduced accuracy on the 'eyes-only' condition (mean accuracy=0.59) compared with the 'faces' condition (mean accuracy=0.74; $F(1, 35)=75.47$, $p<0.001$, $\eta p^2=0.68$). There were no significant effects between or within subjects for ASD or ADHD factor suggesting that accuracy for the 'eyes-only' condition does not differ in children with ADHD, ASD, ASD+ADHD and typically developing children.

A mixed-design ANOVA was performed to identify effects of ASD, ADHD and emotion type on the accuracy of emotion recognition in the 'eyes-only' condition as described for the 'faces' condition in section 3.4.2.1. Unlike the 'faces' condition, there was no main effects of ADHD on accuracy to the 'eyes-only' condition. There were no significant main effects or interactions for the ASD and ADHD fixed factors for accuracy to 'eyes-only'.

In summary, ADHD factor has a main effect on emotion accuracy of 'faces' but not the 'eyes-only' condition. No interaction with ADHD factor and emotion in faces was found, indicative of reduced accuracy to faces irrespective of emotion type. Emotion accuracy findings suggests that children with ADHD (ADHD and ASD+ADHD) have reduced general emotion recognition accuracy to 'faces' but not 'eyes-only' compared to children without ADHD (ASD and typically developing controls).

In the next Section, results of visual attention to the emotional faces will be analysed to elucidate if visual social-emotional attention is associated with emotion accuracy deficits in ADHD. ADHD will be compared with ASD as discussed in the planned contrasts detailed in the methods Section (3.3.2).

3.4.3 EYE TRACKING MEASURES FOR EMOTIONAL FACES

3.4.3.1 INTEREST AREAS OF EMOTIONAL FACES

Eyes and Mouth

A mixed-design ANOVA was performed to identify effects of ASD, ADHD and emotion type on DT to each interest area. DT was the dependent variable and interest area, with 3 levels (left eye, right eye and mouth) was entered as the first repeated measure. Emotion, with 6 levels (happy, sad, anger, fear, disgust and surprise) was entered as another repeated measures factor and ASD and ADHD entered as fixed factors. There was a significant main effect of ASD factor with reduced DT in those with ASD (mean=657.9ms) compared to those without ASD (mean= 779.4ms; $F(1, 37)=5.54$, $p<0.05$, $\eta p^2=0.13$). No interaction between ASD factor and 'Emotion' was found suggesting that reduced DT to eyes and mouth in those with ASD (ASD and ASD+ADHD) is not specific to emotion type.

There were no other significant effects between or within subjects for ASD or ADHD factor. Significant main effects and interactions independent of fixed factors are tabulated at the end of the chapter (Table 3.3).

Other facial features

The same analytical model was applied to identify effects of ASD, ADHD and emotion on DT to other facial features; to determine whether the effect of ASD on DT to the eyes and mouth interest area is also reflected in reduced DT to other features of the face. The aim of this was to determine whether the effect was specific to the eye and mouth interest area of the face. There was a main effect of ADHD on DT to other facial features with

those with ADHD looking at other facial features less (mean=957.6ms) than those without ADHD (mean=1229.8ms; $F(1, 36)=8.70$, $p<0.01$, $\eta p^2=0.20$). The effect of ASD fell just short of significant with greater DT to other facial features in those with (mean=1184.3ms) than those without ASD (mean=1003.1ms; $F(1, 36)=3.86$, $p=0.06$, $\eta p^2=0.10$). This suggests that those with ASD have specific reduced fixation to eyes and mouth rather than reduced fixation to all facial features. ADHD however, showed reduced fixation duration to other facial features but not to eyes and mouth.

CORRELATIONS WITH CLINICAL SYMPTOMS

Correlations between Dwell Time (DT; indexing viewing time) to interest areas, emotion recognition accuracy, SCQ, SAS and Conners' subscores were performed. DT to the mouth was significantly negatively correlated with repetitive and stereotyped behaviours ($r=–0.41$; $p<0.01$) and communication ($r=–0.35$; $p<0.05$) but, not social reciprocal interaction subscores ($r=–0.30$; $p>0.05$) on the SCQ. Although, it is noteworthy that the size of the correlation is similar for all SCQ subscores. DT to the mouth significantly correlated with SAS ($r=0.34$; $p<0.05$), but did not significantly correlate with emotion accuracy ($r=0.21$; $p>0.05$) or Conners' IA or HI T-scores ($r=–0.08$; $p>0.05$).

DT to the right eye was significantly negatively correlated with Conners' IA T-score ($r=–0.40$; $p<0.05$) and Conners' HI T-score ($r=–0.39$; $p<0.05$). DT to the left eye was not significantly correlated Conners' subscores ($p>0.05$). Neither DT to the left eye nor right eye significantly correlated with SCQ or SAS ($p>0.05$).

DT to other facial features (not eyes or mouth) significantly correlated with Conners' IA T-score ($r=–0.39$; $p<0.05$), Conners' HI T-score ($r=–0.39$; $p<0.05$) and SAS ($r=0.35$; $p<0.05$). DT to other facial features was not significantly correlated with SCQ subscores or emotion accuracy ($p>0.05$). This finding is interesting as it suggests reduced DT to other facial features is associated with ADHD symptoms and more social skills deficits on the SAS (a broader measure of social skills) but not the SCQ (more specific to ASD).

Total emotion accuracy was significantly negatively correlated with Conners' IA T-score ($r=–0.44$; $p<0.01$) and Conners' HI T-score ($r=–0.34$; $p<0.05$) but not SCQ subscores or SAS ($p>0.05$). Total emotion accuracy was also significantly negatively correlated with DT to left eye ($r=–0.36$; $p<0.05$) and positively correlated with DT to the right eye ($r=0.47$; $p<0.01$).

In summary, DT to the mouth showed significant correlations with SCQ subscores and SAS but, no significant correlations with Conners' subscores or emotion accuracy. DT to the right eye correlated negatively with Conners' IA and HI subscores and positively with emotion accuracy. This is an interesting finding as it suggests that the right visuospatial bias typically found in ADHD on non-face tasks (as described in Chapter 1) does not extend to faces. Furthermore, reduced DT to other facial features was associated with ADHD symptoms and social skills deficits on the SAS (a broader measure of social skills) but not SCQ (more specific to ASD). This

later finding is indicative of an association with atypical visual social-emotional attention with broader social skills deficits in ADHD, rather than social skills specific to ASD.

In the next section, temporal and spatial eye tracking measures previously reported in the ADHD literature (presented in section 1.5.1) will be analysed to test if these quantitative measures to emotional faces differ in those with and without ADHD and ASD.

3.4.3.2 TEMPORAL AND SPATIAL MEASURES TO EMOTIONAL FACES

In Chapter 2, eye gaze patterns derived from observational coding of eye-tracking data suggested that children from a subsample with ADHD had more 'scattered' fixations over the face stimuli in addition to more linear patterns between the left eye and mouth rather than triangulating between the eyes and the mouth. The findings in the previous section on DT showed that those with ADHD had typical viewing times to eyes and mouth but viewing time to the other areas of the face such as facial creases were reduced. DT does not give an indication of speed and distance of fixations that could be relevant to the qualitative finding of scattered eye gaze across the whole face stimulus. This section therefore tests temporal and spatial eye tracking measures to quantify the findings from Chapter 2.

TEMPORAL MEASURES

Temporal eye tracking measures are described in Table 3.1 and are an indication of fixation rate.

Total fixation number

A mixed-design ANOVA was performed to identify effects of ASD, ADHD and emotion type on mean total fixation number to the face stimuli. Total fixation number was the dependent variable. Emotion, with 6 levels (happy, sad, anger, fear, disgust and surprise) was entered as a repeated measures factor and ASD and ADHD entered as fixed factors. There was a borderline significant main effect of ADHD ($F(1, 37)=4.10$,

p=0.05, ηp^2=0.10) between subjects, with higher mean total fixation number in those with (mean=7.61) than without (mean=6.73) ADHD.

There was also a significant interaction between emotion and ASD by ADHD factor (F(5, 37)=2.71, p<0.05, ηp^2=0.07). To establish the basis of the interaction, the data file was split to analyse the main effect of ASD within each level of the ADHD factor (no and yes) at each level of emotion. This analysis showed a significant main effect of ASD when ADHD factor was 'yes', for the disgust emotion only (F(1, 16)=4.69, p<0.05, ηp^2=0.24). The effect was not statistically significant for 'ADHD-no' nor was it significant for any other emotion. Pairwise comparisons from simple effects analysis were conducted. Children with ADHD-only had significantly more total fixation numbers to disgust emotion faces (mean = 8.31) than typically developing children (mean = 6.75) and children with ASD-only (mean = 6.75) (p<0.05). There was a trend for those with ADHD-only to have a higher number of total fixations to disgust emotion faces than children with ASD+ADHD (mean = 7.16) however this did not reach significance (p=0.15). The ASD+ADHD group did not significantly differ on total fixation numbers to disgust emotion faces compared with ASD-only or typically developing children (p=0.60) as shown in Figure 3.2

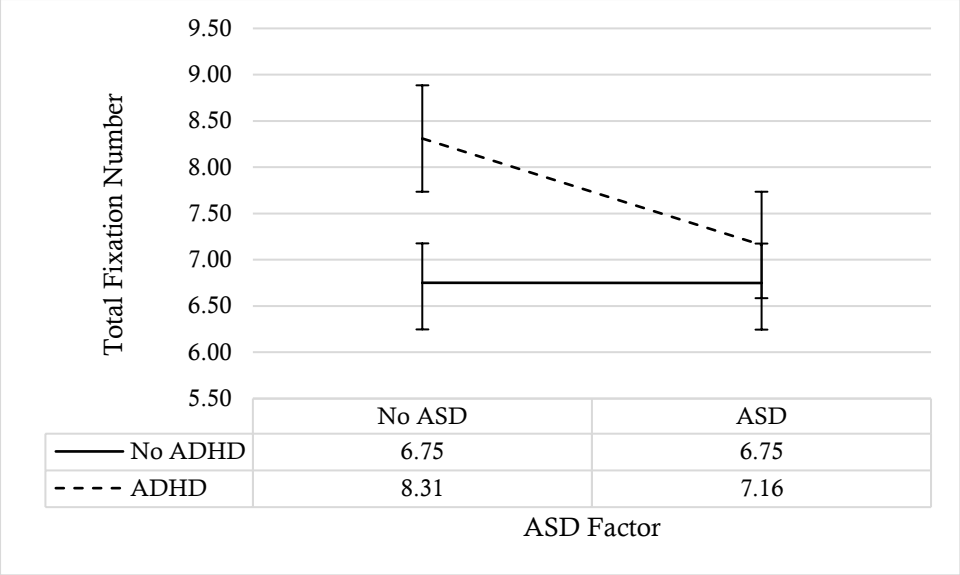


Figure 3. 2: ASD Factor by ADHD factor on Total Fixation Number (TFN) to faces showing disgust (Error Bars 95% CI)

Significant main effects and interactions independent of fixed factors are tabulated at the end of the Section (Table 3.3).

Total fixation duration

A mixed-design ANOVA was performed to identify effects of ASD, ADHD and emotion type on total fixation duration to the face stimuli as described in the previous section for total fixation number. There was no significant effect between or within subjects on any of the factors for total fixation duration to the stimuli. This is useful to note as it shows that children did not differ significantly on how long they fixated at the stimuli overall.

Mean fixation duration

A mixed-design ANOVA was performed to identify effects of ASD, ADHD and emotion type on mean fixation duration to the face stimuli as described for total fixation number. There was a significant main effect of ADHD (F (1, 37)=4.86, p<0.05, ηp^2=0.12) with lower mean fixation duration in those with (mean=612.6) than without (mean=782.9) ADHD. There were no other significant effects or interactions. As no interaction between ADHD Factor and Emotion on mean fixation duration was found, this suggests that fixation duration is reduced across all face stimuli independent of emotion type in those with ADHD (ADHD and ASD+ADHD) compared to those without ADHD (ASD and typically developing controls).

In summary, ADHD showed a significant main effect on temporal eye tracking measures. Specifically, mean fixation duration to facial stimuli was significantly lower in those with ADHD than in those without. Total fixation number was higher in those with ADHD than with those without. However, this effect was mitigated by ADHD with ASD having a lower fixation number for disgust (and thus the overall main effect for ADHD on total fixation number being of borderline significance). Children did not significantly differ on total fixation duration to facial stimuli, suggesting that the findings for the other temporal measures found in ADHD are not due to a lack of general attention to the stimuli but rather due to a tendency for faster fixations (and therefore shorter durations). In order to determine the distance between the fixations, spatial measures were covered in the next Section.

SPATIAL MEASURES

Spatial eye tracking measures are described in Table 3.1 and are an indication of the distance between the fixations (breadth of attention).

Fixation scanpath length

A mixed-design ANOVA was performed to identify effects of ASD, ADHD and emotion type on fixation scanpath length when viewing face stimuli as described for total fixation number. There was a significant main effect of ADHD ($F(1, 37)=7.72$, $p<0.01$, $\eta p^2=0.17$) between subjects, with longer scanpath lengths in those with (mean=174.6) than without (mean=139.1) ADHD. As no interaction between ADHD factor and 'Emotion' on fixation scanpath length was found, this suggests that fixation scanpath length is increased across all face stimuli independent of emotion type in those with ADHD (ADHD and ASD+ADHD) compared to those without ADHD (ASD and typically developing controls). As fixation scanpath length gives a measure of the total distance between all fixations, this suggests that the total scanpath length of those with ADHD is longer than those without ADHD.

Mean length between fixations

In addition to the total scanpath length described above, the mean distance between fixations gives an indication of the average distance between each fixation providing further fixation information over the trial time. A mixed-design ANOVA was performed to identify effects of ASD, ADHD

and emotion type on mean length between fixations when viewing face stimuli. There was a significant main effect of ADHD (F(1, 37)=4.35, $p<0.05$, $\eta p^2=0.11$) between subjects, with longer mean length between fixations in those with (mean=22.50) than without (mean=20.03) ADHD. This suggests that in addition to the total scan path length being longer as shown by fixation scanpath length in the previous subsection, the mean distance between the fixations is also increased indicative of all fixations within the scanpath being increased in those with ADHD compared to those without. As no interaction between ADHD Factor and Emotion on mean fixation length was found, this suggests that mean fixation length is increased across all face stimuli independent of emotion type in those with ADHD (ADHD and ASD+ADHD) compared to those without ADHD (ASD and typically developing controls).

SD of length between fixations

A mixed-design ANOVA was performed to identify effects of ASD, ADHD and emotion type on SD of distance between fixations when viewing face stimuli. There was no effect of ADHD (F(1, 36)=0.51, $p>0.05$, $\eta p^2=0.01$) . This suggests there is no significant variability of distance between fixations in those with ADHD. There was no significant effect between or within subjects for the other factors, including ASD.

In summary, ADHD factor showed a significant main effect on spatial eye tracking measures. Specifically, fixation scanpath length and mean length between fixations to facial stimuli were significantly longer in those

with ADHD than in those without. There was no main effect of SD length between fixations, suggesting no significant difference in variability in the distance between fixations in those with ADHD or ASD. There was no within-subjects effect for spatial measures on the type of emotion, suggesting that those with ADHD have an atypically extensive scanpath to facial stimuli regardless of emotion type.

In summary, findings for the temporal and spatial measures indicated that the scanning of emotional faces was both rapid and long in those with ADHD (ADHD and ASD+ADHD) compared to those without ADHD (ASD and typically developing controls). Although rapid and longer scanning has been linked with increased processing and broader attention, excessively extensive scanning could be indicative of atypical processing. This is also consistent with the qualitative effects of increased scatter in ADHD, described in Chapter 2. In the next section, correlates of significant temporal and spatial measures with ADHD symptoms and emotion accuracy scores were presented.

Table 3.3 shows the significant main effects and interactions independent of ASD and ADHD fixed factors for the repeated measures ANOVA analyses described thus far in this chapter.

Table 3. 3: Summary of significant main effects for emotional faces independent of fixed factors for all children

Dependent variable(s)	Independent variable/ Interaction	Main effect (F)	Direction of effect[a] (mean dependent variable)
Accuracy to faces	Emotion	47.35[d]	Happy (0.95) > sad (0.82)[d] > anger (0.63)[d] > fear (0.43) < disgust (0.71)[d] < surprise (0.81)[f]
Accuracy to eyes only	Emotion	40.55[d]	Happy (0.89) > sad (0.58)[d] < anger (0.70) > fear (0.27)[d] < disgust (0.42)[d] < surprise (0.72)[d]
DT to faces (ms)	Interest Area	12.45[d]	Left eye (635.96) > right eye (489.82) < mouth (1030.30)[d]
	Emotion	4.69 [d]	Happy (719.73) > sad (700.22) <anger (740.98)[f] > fear (670.38)[f] < disgust (706.15) < surprise (774.70)[e]
	Interest Area* Emotion[c]	5.76[d]	Left eye (635.96) >right eye (489.82) for fear[f] Happy (574.2) < sad (600.98) < anger (688.43)[f] > fear (649.48) > disgust (597.91) < surprise (704.68)[f] for left eye Happy (425.63) <sad (477.99) < anger (559.23) > fear (439.14)[e] > disgust (402.80) < surprise (634.13)[d] for right eye Happy (1159.28) > sad (1021.68)[f] > anger (975.28) >fear (922.51) < disgust (1117.72)[e] > surprise (985.29)[f] for mouth
TFN to faces	Emotion	5.73[d]	Happy (6.82) < sad (7.11) > anger (6.97) < fear (7.41)[e] > disgust (7.24) < surprise (7.60)
MFD to faces (ms)	Emotion	2.74[f]	Happy(730.28)>sad(708.34)<anger(727.86) >fear(679.53) <disgust (682.88)>surprise(657.83)[b] Happy > fear[f]; happy > surprise[e]; Anger > disgust[f]; anger > surprise[f]
FSPL to faces	Emotion	4.23[e]	Happy (165.18) > sad (154.36) > anger (145.02) < fear (161.36)[f] > disgust (147.36) <surprise (167.65)[e]

[a]For significant main effects, planned contrasts were performed to identify which emotions differed from one another. For repeated planned contrasts, each category (except the first) is compared to the previous category (Field 2005). [b] If planned contrasts failed to show any significant differences between emotions, pairwise comparisons (LSD - Least Significant Difference) from simple effects analysis were conducted to identify the cause of the main effect. [c]Significant interactions were followed up by simple effects analysis and pairwise comparisons (LSD) [d]$p<0.001$; [e]$p<0.01$; [f]$p<0.05$; DT (Dwell Time); TFN (Total Fixation Number); MFD (Mean Fixation Duration); FSPL (Fixation Scanpath Length)

CORRELATION WITH CLINICAL SYMPTOMS

Correlations between the significant temporal/spatial measures, symptom scores and emotion accuracy were performed. Correlations were not significant for temporal or spatial measures with SCQ, SAS or Conners' HI and IA subscores ($p>0.05$). However, mean length between fixations correlated significantly with emotion accuracy ($r=–0.36$; $p<0.05$) with increased length of fixations associated with reduced emotion accuracy. No other spatial or temporal measures were significant with emotion accuracy ($p>0.05$).

Although mean length between fixations did not correlate directly with parent rated ADHD symptoms it was associated with ADHD diagnoses in the previous section. In section 3.4.3.1, reduced DT to other facial features was associated with ADHD symptoms and poor social skills on the SAS but not emotion accuracy. As it could be conceived that a 'hyper-extensive' scanning of face stimuli, indexed by increased mean length between fixations could be associated with DT to other (non-core) facial features, this was tested. DT to other facial features significantly negatively correlated with mean length between fixations ($r=–0.38$; $p<0.05$); suggesting that 'hyper-extensive' scanning of face stimulus indexed by increased mean length between fixations is associated with reduced DT to other facial features. In summary, these correlations could suggest a link between ADHD symptoms, atypical visual social-emotion attention (reduced DT to other facial features with increased mean length between fixations over the face stimulus), poor emotion recognition accuracy and social skills deficits on the SAS. This association is represented in Figure 3.3.

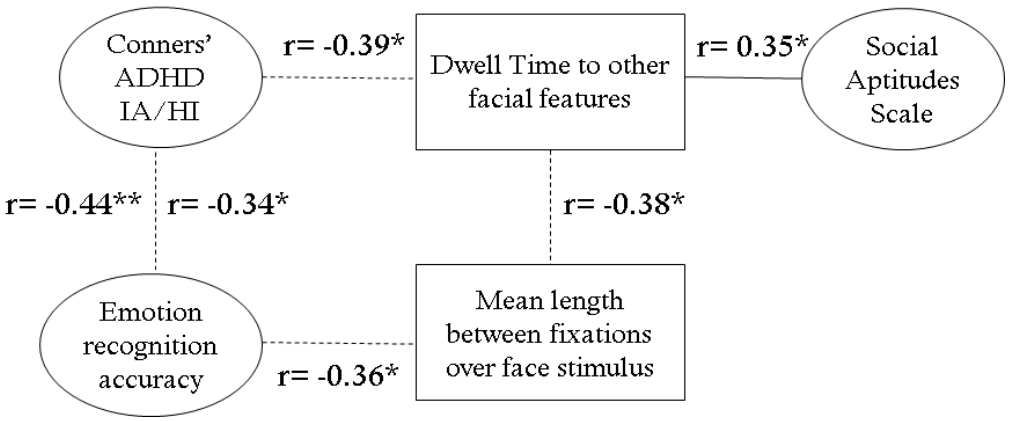


Figure 3. 3: Visual social-emotional attention correlates

ADHD IA (Inattentive) and HI (Hyperactive-Impulsive) symptoms on Conners' parent rating scale, Social Aptitudes Scale (SAS) and emotion recognition; (**p<0.01, *p<0.05); Dwell time to other facial features = non-core features: face – (eyes +mouth)

3.4.3.3 HIERARCHICAL REGRESSION

In order to test if IQ or oppositional symptoms had significant contributions to the dependent variable over and above ADHD and ASD factors, hierarchical linear regression was applied to the dependent variable as described in Section 3.3.2. In order to reduce the number of linear regression models, only significant variables presented in Section 3.4.2.1, 3.4.3.1 and 3.4.3.2 were entered as the dependent variable for each analysis.

With regards to the dependent variable total emotional accuracy, hierarchical linear regression revealed that ADHD significantly explained 15% of the variance ($p<0.05$). When ASD factor was added into the analysis, it explained a further 2% of the variance ($p>0.05$). When IQ was added, this explained a significant further 11% of the variance ($p<0.05$) over and above ADHD and ASD to the total emotional accuracy score. When oppositional symptoms were added in the final model, they explained a further nonsignificant 2% of the variance ($p>0.05$) over and

above ADHD, ASD and IQ. These results suggested that both ADHD and low IQ were significantly associated with lower emotional accuracy scores (see Appendix.V.; Table A.2). When accounting for other variables (ASD factor, IQ and oppositional symptoms) in the final model, although there was a trend for ADHD factor on the total emotional accuracy score, this no longer remained significant ($p=0.13$). IQ remained significant ($p<0.05$) for total emotional accuracy when accounting for the other variables.

In order to explore this further, hierarchical linear regression models were run separately using each significant eye tracking measure as the dependent variable. Hierarchical linear regression revealed that IQ significantly explained 22% of the variance ($p<0.01$) for DT to the right eye, over and above ADHD and ASD factors. ADHD Factor no longer remained significant in the final model when the other variables were entered ($p>0.15$) however, IQ remained significant ($p<0.01$) for DT to the right eye. For all other visual attention variables, neither IQ nor ODD symptoms explained a significant amount of the variance over and above ADHD or ASD factors. When accounting for ASD factor, IQ and oppositional symptoms in the final model, ADHD factor remained significant for DT to other facial features, mean fixation duration and fixation scanpath length ($p<0.05$). There was a trend for ADHD factor to remain significant when other variables were entered for total fixation number ($p=0.06$) however, ADHD factor was no longer significant for mean length between fixations ($p>0.15$). The significance of ADHD factor in the final hierarchical linear regression models when accounting for the other variables therefore provided mixed results related to the dependent variable being analysed.

Hierarchical linear regression model results tables for each dependent variable were presented in the Appendix.V.

3.5 DISCUSSION

The objective of this chapter was to determine if quantitative eye tracking measures during emotional face viewing are associated with emotion recognition deficits and symptom severity scores in ADHD and, if these eye tracking measures differ amongst the groups. Findings from this chapter extends the work from chapter 2 on observational coding of atypical attention to emotional faces in ADHD. To the author's knowledge, this is one of the first studies to use eye tracking to investigate quantitative visual attention to emotional faces in ADHD, ASD and ASD+ADHD and typically developing children. A 2x2 factorial approach was used to investigate the effects of ADHD and ASD on visual attention to emotional faces. This section provides a discussion of main findings followed by the limitations and strengths of the study.

3.5.1 DISCUSSION OF MAIN FINDINGS

Reduced total emotional recognition accuracy was found in children with ADHD (ADHD and ASD+ADHD) compared to children without ADHD (ASD and typically developing controls). Global emotion recognition deficits have been reported in ADHD (Da Fonseca et al. 2009; Kats-Gold, Besser, and Priel 2007; Seymour et al. 2013). However, other studies (Singh et al. 1998; Pelc et al. 2006; Aspan et al. 2014; Sinzig, Morsch, and Lehmkuhl 2008) have also reported specific emotion recognition deficits.

Findings from this study do not support specific deficits (e.g. towards anger) as hypothesised, yet this could be related to differences in task type. In this study, only emotional faces were studied but Sinzig et al. (2008) found emotion-specific deficits and also included a neutral faces during emotion testing. Additionally, the lack of a neutral face or graded emotional intensity stimuli could be part of the reason why children with ASD without comorbid ADHD did not show emotion recognition deficits in this study. It should however be noted that a similar pattern of group effects on global facial emotion recognition were found in our study and Sinzig et al. (2008), with better total emotion recognition in children with ASD and typically developing children compared to children with ADHD and ASD+ADHD. This similarity would argue against the lack of a neutral face contributing to better total emotion recognition accuracy in the pure ASD group compared to those with ADHD and ASD+ADHD.

When measuring visual social-emotional attention using eye tracking in this study, children with ASD (ASD and ASD+ADHD) had reduced Dwell Tine (DT; indexing viewing time) to the eyes and mouth of the face regardless of the type of emotion shown on the face. Furthermore, reduced DT to the mouth significantly correlated with repetitive stereotyped behaviours and communication subscores on the SCQ; suggesting that reduced DT to the eyes and mouth is core to repetitive stereotyped behaviours and communication difficulties in ASD. These findings are in keeping with reduced visual social-emotional attention in ASD (Chawarska and Shic 2009). As children with ASD had atypical visual social-emotional attention to core features, despite intact emotion recognition accuracy this could be

suggestive of compensatory emotion recognition strategies in ASD (Harms, Martin, and Wallace 2010).

In this study, those with ADHD fixated significantly less (indexed by DT) on other features of the face (forehead, nasal bridge and creases of the face) which are also important for emotion recognition (Boucher and Ekman 1975). This would suggest that children with ASD potentially find the core facial features (eyes and mouth) less salient when doing the task. Conversely, children with ADHD find the core facial features salient but do not utilise additional, more subtle information in the face during the emotion recognition task. As there were no interactions between the effects of ADHD and ASD on these eye tracking measures, those children with both ADHD and ASD have the additive effect of reduced DT to both core (eyes and mouth) and other facial features (forehead, nasal bridge, creases of the face). This would suggest that the comorbid group have additive effects from both disorders, suggestive of true comorbidity. These findings are in keeping with EEG studies investigating comorbidity between ADHD and ASD (Tye et al. 2014; Groom et al. 2017).

In this study, hierarchical linear regression showed that lower IQ was also associated with reduced emotion recognition and viewing (indexed by DT) of the eye in right hemi-space; explaining a significant amount of variance over above ADHD and ASD factors. This suggests that children with ADHD and lower IQ that do not meet threshold for intellectual disability services (IQ<70) have additional difficulties with emotion recognition and visual social-emotional attention, which merit recognition and intervention in addition to ADHD and ASD. Contrary to the literature (Santosh and

Mijovic 2004; Airdrie et al. 2018), oppositional symptoms did not explain any of the findings over and above ADHD or ASD factors, suggesting disruptive externalising problems do not significantly explain differences found in this sample.

Face scanning over space and time were quantified in this study by spatial and temporal eye tracking measures to emotional faces. Visual scanpaths were much longer in those with ADHD and mean length between fixations also correlated negatively with emotion accuracy. Overall, this was apparent across all emotions, suggesting an atypical 'hyper-extensive' scanning style in those with ADHD which is associated with the lower emotion accuracy that was found in this group. It is important to note that mean length between fixations did not directly correlate with parent rated ADHD symptoms but an effect was found with ADHD Factor. This could be because ADHD diagnoses also include more information including impairment and more detail about difficulties in more than one environment e.g. school. Unfortunately teacher ADHD ratings were not available for correlation analysis in this study. Findings from Serrano et al. (2018) however corroborate an association between visual attention and teacher but not parent rated ADHD symptoms.

Although a direct association with emotion recognition and social skills severity (e.g. on the SAS or SCQ) was not found, findings from this chapter suggest an indirect link with emotion recognition accuracy and social kills. Visual social-emotional attention correlates revealed an association with ADHD symptoms and emotion recognition accuracy and DT to other facial features. DT to other facial features was also associated with

social aptitude scores suggesting a possible association between ADHD symptoms, visual attention and social aptitude (as shown in Figure 3.3). As these correlates were not formally tested as pathways, findings should be considered preliminary until replication with structural equation modelling has been undertaken. Findings from this chapter, extend the findings of Buitelaar et al. (1999) who found an association with emotion recognition and performance IQ but not ASD symptom severity in children with ASD and ADHD. Buitelaar et al. (1999) suggested that emotion recognition deficits could be linked with visuospatial abilities and we have found an association with poor emotion recognition and atypical spatial eye tracking measures suggestive of 'hyper-extensive' scanning in children with ADHD.

In addition, we found a link with ADHD symptom severity, reduced Dwell Time (DT) to other facial features and reduced social skills on the SAS but not the SCQ. This suggests social difficulties in children with ADHD are primary to ADHD symptom severity rather than core ASD symptoms. This is important as it answers one of the main questions of the thesis providing further insight into social difficulties in ADHD.

3.5.2 Limitations, strengths and future directions

Despite two further rounds of recruitment, the sample size remained small; after which funding and time limitations ensued. Although the sample size was small compared with the projected estimated sample size calculated in section 2.2.1, the analytical 2x2 factorial approach increased the power of the study. A post hoc power calculation based on this 2x2 analytical approach showed there was sufficient power (87.7%) to find an interaction

with a medium effect size as described in section 3.2.2. Furthermore, an interaction for emotion type by ASD by ADHD on total fixation count was found with a medium effect size (ηp^2=0.07); substantiating sufficient power to detect an interaction of medium effect size. Nevertheless, this is the first study to the author's knowledge that has investigated quantitative visual social-emotional attention using eye tracking in children with ADHD, ASD, ADHD+ASD and typically developing controls, making it an important pilot study.

Due to study time limitations, the ADOS was only performed in a subset of children. However, ADOS confirmed the diagnosis from the DAWBA in all cases. The participants were well categorised and all children with ADHD were either stimulant naive or off the stimulant medication minimising confound due to medication.

As described above, task stimuli included exaggerated emotional faces without exclusion of a neutral face. The task was, however, an adapted version of the Frankfurt test and training of social affect (FEFA) (Bolte et al. 2002), improving potential clinical transferability. The neutral face was excluded as it was hypothesised that children with ADHD may pick this emotion when they were not sure about the emotion or when they were bored, potentially biasing accuracy scores. In order to consider visual attention to neutral faces, this will be examined specifically in Chapter 5 of this Thesis. The importance of future studies testing the effects of stimulant and non-stimulant medication for ADHD and social skills training on atypical visual social-emotional attention and social skills deficits are discussed in Chapter 7.

Surprisingly, ASD did not have an effect on any of the temporal and spatial eye tracking measures presented in section 3.3.3.2, contrary to our prediction of restricted scanpaths in ASD. As our findings relates to static faces, future studies using interacting dynamic stimuli such as videos are more likely to reveal restrictive scanpaths in ASD, as shown in the recent case study by Tsang et al (2018).

Finally, as the task in this study prompted children to look at faces and select emotions, spontaneous emotion recognition and understanding without any prompts could lead to differing results in children with ASD who benefit from such scaffolding. In Chapter 4, visual social-emotional attention will be measured using eye tracking during free viewing of social scenes from the ADOS without prompting or priming to look at faces.

3.5.3 IMPLICATIONS

In conclusion, findings suggest that children with ADHD have atypical 'hyper-extensive' scanpaths when viewing emotional faces and that this correlated with poorer emotion recognition accuracy. ADHD symptom severity was also associated with reduced Dwell Time (DT; indexing visual attention) to other facial features which was associated with reduced social skills on the SAS but not the SCQ. This later finding suggests an independent pathway for poor social skills linked to ADHD symptom severity which is separate to core ASD symptoms on the SCQ. This is a very interesting finding as it provides evidence of social difficulties in children with ADHD primary to ADHD symptom severity rather than core ASD symptoms. This has important clinical implications, suggesting that these social

skills deficits could be amenable to treatment primarily for ADHD; providing further evidence for the importance of early identification and treatment of ADHD (Sayal et al. 2018).

On the whole, the atypical 'hyper-extensive' scanpaths and reduced DT to other facial features in those with ADHD was not mitigated by co-occurring ASD. ASD (ASD and ASD+ADHD) was characterised by reduced looking to core features of the face (particularly the mouth). These findings suggest that having ASD+ADHD leads to an additive effect across different aspects of visual attention to emotional faces, specifically 'hyper-extensive' scanpaths with reduced looking to core and other facial features. This could explain the poorer long-term prognosis of children with both disorders. Improving emotion recognition may have significant benefits in the comorbid group in particular and the inclusion of strategies for recognising deficits in emotion recognition including looking to both core and other facial features may be helpful in practice. As the emotional faces task in this study was an adapted version of the Frankfurt test and training of social affect (FEFA), which also teaches emotions (Bolte et al. 2002), the effect of intervention on atypical visual social-emotional attention in future studies are discussed further in Chapter 7.

In the next chapter, visual social-emotional attention to a commonly used tool in ASD assessment is examined in a new sample of children with ADHD, ASD, ASD+ADHD and typical development.

4 STUDY OF VISUAL ATTENTION TO AUTISM DIAGNOSTIC OBSERVATION SCHEDULE IMAGES IN SAMPLE 2

In the previous chapter, visual attention to emotional faces in an emotion recognition task was tested and children with ADHD showed atypical visual social-emotional attention and reduced accuracy in emotion recognition. As the emotions task specifically asked the children to name emotions, this required an element of active judgment and priming to look at the faces. Furthermore, in the previous chapter although children with ASD showed reduced dwell time to core facial features (eyes and mouth), this did not relate to emotion recognition ability.

In clinical and research settings the Autism Diagnostic Observation Schedule (ADOS) is commonly used to aid with diagnostic assessment of ASD. In order to increase the likelihood of finding both atypical emotion recognition and visual social-emotional attention in ASD, images from the ADOS were used in this chapter as it was predicted that children with ASD would show deficits on the ADOS which includes testing of spontaneous emotion recognition. Visual social-emotional attention was measured using eye tracking during free viewing of social scenes selected from images used in the ADOS. Children were not given an explicit task to complete during eye tracking. ADOS images consisted of 3 pictures and 2 cartoons, described in Section 4.1.3. The full ADOS was then administered after eye tracking of ADOS images. As the ADOS is a commonly used assessment tool for ASD, the potential association of visual social-emotional attention and ADOS scores is of interest to clinicians. This could provide

additional objective measurement about where and how a child looks at the images alongside ADOS scores.

Quantitative visual social-emotional attention to social scenes have been studied in ASD using eye tracking. However, to the author's knowledge, visual social-emotional attention to ADOS images has not yet been investigated. Previously studied eye tracking measures from social scene perception in ASD literature were used. These eye tracking measures included Dwell Time (fixation duration to faces), Fixation Count (exploration and processing within faces) and First Fixation Time (latency to orient and attend to a face). A supplementary measure, Run Count which indexes exploration and processing between faces was also measured in the ADOS cartoon images which depict interactions between two characters in the scene.

In this chapter, visual social-emotional attention during free viewing of social scenes in the ADOS was compared amongst the groups and, association of visual attention to ADOS images with clinical symptom severity including spontaneous emotion recognition was analysed. This seeks to address the questions of the thesis on the association of visual attention to social scenes from the ADOS and spontaneous emotion recognition difficulties on the ADOS; a commonly used clinical tool in the assessment of ASD. This chapter presents findings from a new sample of children (ADHD, ASD, ASD+ADHD and typically developing controls).

4.1 STUDY METHODS

4.1.1 PARTICIPANTS

Participants were recruited as part of a larger study called the Study of Attention and Arousal in Neurodevelopmental Disorders—SAAND, funded by The Baily Thomas Charitable Fund and The Waterloo Foundation (grant number 980-365) within the Division of Psychiatry and Applied Psychology at the University of Nottingham. Participant recruitment and inclusion and exclusion criteria were very similar to those described for the SOCCA study as described in Chapter 2 (Section 2.2). Important differences in recruitment include the expansion of geographical sites from Nottinghamshire to the wider East Midlands region. This yielded a larger sample size than the previous study. Children aged 7-15 years were recruited to the study. Although many children had prior diagnoses of ASD or ADHD, some children (awaiting assessment) who were deemed high risk by CAMHS of a neurodevelopmental disorder were recruited as long as they met study inclusion criteria as described in Section 2.2. Ethical approval for the study was given by the East Midlands Research Ethics Committee (REC) (17/EM/0193), IRAS project number 220158.

4.1.2 SYMPTOM AND DIAGNOSTIC MEASURES

Methods for symptom and diagnostic measures were very similar to those described for the SOCCA study, described in Chapter 2 (Section 2.2). The main exceptions being, that in addition to parent informants, teacher Conners' rating scale and SCQ were requested for the participants in this study. Furthermore, in this study, parents completed the DAWBA directly

online. Updated versions of the Conners' rating scale (Conners' 3rd Edition, Conners' 3 and DSM-5 update, 2014) and ADOS (ADOS-2, Autism Diagnostic Observation Schedule 2nd Edition, 2014) were also used in this study; which has also been updated with the DSM-5 criteria. ADOS-2 assessments were carried out by PK and IA, who have research reliability accreditation. The ADOS-2 modules 3 and 4 were used as described for ADOS in Chapter 2 (Section 2.2 and below). As the ADOS is very similar to ADOS-2, the term ADOS will be used interchangeably to include the second version for the rest of the Thesis.

As this chapter presents visual social-emotional attention to images taken directly from the ADOS, further details of the ADOS tasks are described here. The ADOS module 3 consists of 14 activities with 29 accompanying items and module 4 consists of up to 15 activities with 32 accompanying items (Lord C 2012). Both modules are examined in a manualised fashion and take approximately 45-minutes to complete. Both modules contain the activities 'Description of a Picture task' and the 'Cartoons' task'.

Throughout the ADOS activities, the child's behaviour is observed and scored on several items within each of the 5 domains. As an example, domains for module 3 include: A—Language and Communication (9 items); B—Reciprocal Social Interaction (11 items); C—Imagination (1 item); D—Stereotyped Behaviours and Restricted Interests (5 items); and E—Other Abnormal Behaviours (3 items). Each item is given a code from 0 to 3 which is then converted to a score.

Based on the module 3 algorithm, only certain item scores from domains A, B and D are then summed to provide the ADOS total score. Autism spectrum disorder (ASD) is suggested on the ADOS if the participant scores at or above 7 based on the module algorithm (Lord C 2012).

Within the reciprocal social interaction domain, the ADOS also has scores related to emotion recognition. For the purposes of this Thesis, the 'Comments on Others' Emotions/Empathy' subscore was used in the analysis. This emotion subscore reflects the participants' spontaneous emotion recognition, understanding and response to feelings of others throughout a series of tasks. It is scored from 0 to 2 with higher scores reflecting less spontaneous emotion recognition. Further details of how this ADOS emotion recognition subscore is generated in the ADOS scoring procedure, are presented in the Appendix.III.

In contrast to the facial emotion recognition task described in Chapters 2 and 3, the ADOS emotion recognition subscore relies on spontaneous recognition of emotion in complex social scenes and stories without prompting. Therefore, it was predicted that this particular subscore would be closely related to visual attention to faces within the ADOS images.

Although the emotion recognition subscore is generated in modules 3 and 4, only module 4 includes the subscore in the final domain and total diagnostic algorithm scores. As described in Section 2.2.2.4, the module chosen is based on the child's verbal ability and maturation. Module 3 was designed to be administered to verbally fluent children up to the age of 15-years-old. Module 4 was designed for verbally fluent, older adolescents but

can be used in younger adolescents based on their maturity and attitude to play materials. In this study sample, 18.6% had a module 4 compared with 81.4% who had a module 3. As the central aim of this Thesis was to investigate emotion recognition in ADHD, it was important to analyse the ADOS emotion recognition subscore, in addition to the total ADOS score as emotion recognition may not be reflected in the total ADOS score in those who were administered Module 3.

The ADOS image stimuli for eye tracking described below in Section 4.1.3 were chosen from the 'Description of a picture task' and 'Cartoons task'. The images were chosen as they lend themselves particularly well to visual social-emotional attention and, provide many opportunities to label or comment on emotions during the ADOS examination. The images were predicted to provide the most likely chance of finding a relationship between visual social-emotional attention and emotion recognition subscore; which was one of the primary questions of this Thesis.

The 'Description of a Picture Task' requires the child to simply describe what they see in the picture and is designed to test what captures the child's interest and give examples of their spontaneous communication in the ADOS examination. 3 pictures are available for this task and all 3 were used in the eye tracking study but only 1 picture is required in the ADOS examination which was carried out after the eye tracking procedure (see Section 4.1.4 which shows the 3 pictures).

In the ADOS 'Cartoons task', 2 cartoon series ('Cat' and 'Monkeys') which contain 6 cards each are available for use in the ADOS examination. This task provides an opportunity for the child to comment on the emotions of the characters in the stories and observes how they narrate a story (Lord C 2012). Again, one card from each Cartoon series available was used in the eye tracking procedure of the study but only one Cartoon series (either A or B) is required in the ADOS examination which was carried out after the eye tracking procedure. Each cartoon series depicts a sequence containing two characters; the cat and the fisherman in the Cat Cartoon (Series A) and the two monkeys in the Monkeys Cartoon (Series B; see Section 4.1.4 which shows the card used from each of the Cartoon series).

In order to understand the reasoning for the particular cartoon cards from each series that were chosen for eye tracking and the subsequent visual attention measures extracted, a brief explanation of the cartoon series is given below. Both cartoons series show interaction between the characters and include items being taken and characters getting angry in response. The Cat Cartoon depicts a man fishing who is unaware of the cat behind him who wants to steal the fish. The man puts the fish in the bucket and the cat steals it and then places it in another bucket that turns out to be the beak of a pelican, who then flies off with the fish. The card chosen for the eye tracking from the Cat Cartoon is the first in this series where the man is happy fishing and the cat is wanting to steal the fish. This card was chosen because it contains positive emotions with both characters smiling. The man is the potential victim and the cat is the potential perpetrator.

In the Monkeys Cartoon series, the first monkey in the tree is collecting coconuts and then a second monkey comes along unaware how coconuts got there and starts taking them. The first monkey then realises his coconut has been taken and so he hits the second monkey on the head with one of the coconuts (see Appendix.IV, for full series' of cartoons from the ADOS examination). The card chosen for the eye tracking from the Monkeys Cartoon is the last in this series where the angry monkey in the tree has hit the monkey on the ground, who is in pain. This card was chosen because it contains negative emotions. The monkey in pain on the ground is the victim and the angry monkey in the tree is the perpetrator.

Although the eye tracking of ADOS images was tested in all participants (see next Section), it was only possible to complete the full ADOS examination in the clinical participants of the study. The ADOS examination was completed in 95.16% of clinical participants (n=59/62).

4.1.3 EYE TRACKING PROCEDURE AND TASK STIMULI

Participants viewed stimuli while their eye gaze was measured on the EyeLink 1000 Plus eye tracker (SR Research Ltd. 2017). The EyeLink 1000 Plus eye tracker has a sampling rate of up to 2000Hz binocular with head supported and accuracies up to 0.15 degrees and resolution of 0.01 degrees. In this study, the sampling rate was 500Hz (sampling every 2ms) which is double the rate of the eye tracker used in the first study described in Chapter 2. The eye tracking apparatus was set up as described in the first study (with head supported). However, the EyeLink eye tracker was placed near the viewing screen rather than over the headrest.

Stimuli were presented on a screen (48cm wide x 27cm height), 60cm from the participant. Participants had their head supported using a chin mount and head rest during the testing and a 9-point calibration was completed prior to the task. Laboratory room luminance was measured using a photometer to ensure luminance consistency (between 70–90 lux) for each testing session. Participants were verbally instructed to look at the stimuli whichever way they liked.

Stimuli consisted of the three pictures selected from the ADOS 'description of a picture' task (Holiday, Hollywood and Meal) and two cartoon cards from the ADOS cartoons task (one card from each card set; images are shown in Section 4.1.4). ADOS images were resized to 16cm wide x 10cm height. A central fixation cross was presented for 100ms interspersed by the ADOS images which were presented in a random order for 20 seconds each.

As shown in Section 4.1.4, the pictures from the ADOS are colourful, content dense with many faces and other objects such as vehicles or planes that can take the participants interest. The faces were deemed the most social parts while the vehicles and buildings were the most non-social parts of the pictures. The majority of the faces in the pictures range from neutral to positive. The 3 pictures range slightly in content density with the most faces in the Holiday picture, the least number of faces in the Meal picture and the Hollywood picture having a number midway, between the other two pictures. The crowding of the components and the contrast of

colours was also deemed to be in a similar descending order for the 3 pictures (with the Holiday picture having the most components and brightest colours and the Meal the least).

The cartoons on the other hand are black and white and depict social interactions between two characters. The emotions vary among the characters with more positive emotions in the Cat Cartoon image and more negative emotions in the Monkeys Cartoon image (Figures 4.4 and 4.5). For the purposes of this study, the Cat Cartoon image was classed as positive valence and the Monkeys Cartoon image as negative valance. As described in the previous Section, the specified cartoon image depicts future and current victim and perpetrator status of the characters in the cat and the Monkeys cartoons, respectively.

The eye tracking tasks to the ADOS images was completed before the full ADOS assessment which was completed in full separately. The majority of participants did not have prior knowledge of the ADOS images before doing the eye tracking tasks. The eye tracking tasks, including the calibration took approximately 5 minutes for participants to complete.

4.1.4 DATA EXTRACTION

Raw eye tracking data was processed using the EyeLink 1000 Plus accompanying software EyeLink Data Viewer. This software allows for interest areas such as faces to be isolated from the rest of the image and visual attention to be measured within the specified interest area. In addition to DT described in Chapter 3, this software provides automated extraction of a

wide range of additional eye tracking measures defined within the specified interest area.

For the ADOS pictures, two types of interest areas were created a priori, faces (denoted by circles) and non-social areas (denoted by rectangles). Faces needed to be in full view to be selected as a social interest area (for example the back of the head or faces obscured by a large hat or glasses were not selected). Non-social areas included any vehicle or building in the pictures and were selected as they were deemed as the most non-social 'mechanical' areas of the pictures (see Figures 4.1–4.3). Although food and trees could be classed as non-social, these were not included as they are more organic in nature and could be visualised for other reasons for example food due to hunger in the participant. Interest areas were created for the faces in the cartoons (see Figures 4.4–4.5).

Interest areas over ADOS images



Figure 4. 1: Holiday ADOS Picture

Interest areas denoted as purple circles for faces and purple rectangles for vehicles and buildings.



Figure 4. 2: Hollywood ADOS Picture

Interest areas denoted as purple circles for faces and purple rectangles for vehicles and buildings.



Figure 4. 3: Meal ADOS Picture

Interest areas denoted as purple circles for faces and purple rectangles for buildings.

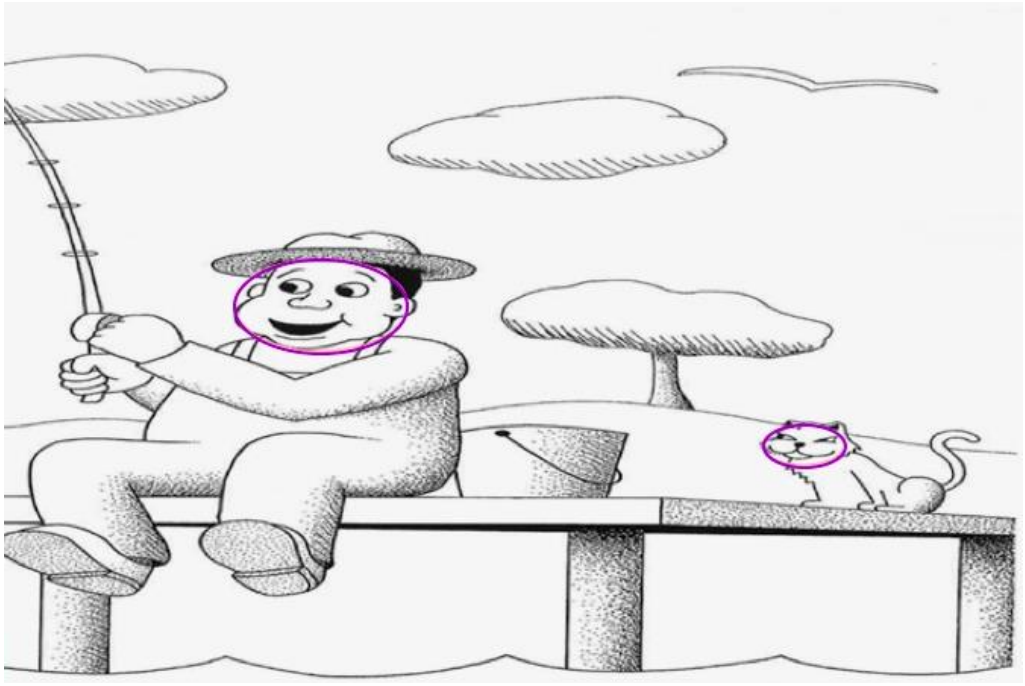


Figure 4. 4: ADOS Cat Cartoon (positive valence)

Interest areas denoted as purple circles for faces. Figure shows cat (future perpetrator) and happy man fishing (future victim).



Figure 4. 5: ADOS Monkeys Cartoon (negative valence)

Interest areas denoted as purple circles for faces. Monkey 1 is angry in the tree (current perpetrator), monkey 2 is in pain (current victim).

Total stimulus length was analysed which corresponds to 20 seconds for the ADOS images. A minimum fixation duration of 100ms was set to allow for shorter fixations while scanning complex pictures. Blink artefacts were removed by defining these as any periods of data where pupil size was equal to 0mm.

Trials were removed if eye movement data was not continuously recorded for at least 25% of the trial time. Trial adequacy was verified using a two-step approach; firstly, the data was visually assessed in Data Viewer and secondly, a percentage acquisition was computed by Data Viewer for cross checking. The mean number of trials excluded per group are presented in the Appendix IV, Table A.25.

Participants with more than 50% invalid trial data were removed from the analysis as described in Section 3.3.1. Of the initial 87 eligible

children recruited, two control children and one child in the ASD+ADHD group did not have adequate eye movement data using the described procedure so 84 children were included in the final eye movement data analysis.

As the stimuli vary based on colour, emotions and density, it can be conceived that using one single visual attention measure may fail to disentangle what might be driving viewing patterns to these stimuli. As described in Chapter 1, a range of eye tracking measures is likely to be required to distinguish complex neurodevelopmental disorders. This certainly appeared to be the case in the emotion recognition task in Chapter 3 where, DT to interest areas in faces and spatial/temporal eye tracking measures gave additive findings, allowing for a fuller profile of visual social-emotional attention in ADHD. Furthermore, attentional patterns and priorities to people in scenes have been analysed by multiple eye tracking measures in ASD (Freeth et al. 2010). Eye tracking measures from social scene perception literature in ASD were included for extraction in this chapter as described below.

In addition to Dwell Time (DT) which is an indication of viewing time to the specified interest area, two additional eye tracking measures were chosen for the main analysis. These included the First Fixation Time (FFT) and the Fixation Count (FC). The FFT to an interest area is indicative of orientation to an interest area, for example time to orient to a face. This was important to test as faces are not preselected in everyday life and those with ASD have been shown to have slower orientation to faces (Freeth et al. 2010; Frost-Karlsson et al. 2019). The FC which is a measure of the number of fixations within an interest area was also extracted. The

FC allows for the estimation of the exploration and processing of a face (Table 4.1).

A supplementary eye tracking variable, Run Count (RC) was extracted (a measure of the number of fixations between interest areas, e.g. between the faces in the cartoons) was also extracted for the cartoon images as these cartoon images contained complex interactions between characters displaying varying emotions. This is important as it allows for a measure of the exploration and processing between faces in the cartoons compared to the FC which only gives a measure of attention within a face. Processing within and between faces is important in complex social scene perception and may have relevance to higher order social cognition such as ToM (Itier and Batty 2009).

The pre-selected eye tracking measures described above were extracted using the interest area report function in EyeLink and are summarised in Table 4.1. Trial eye tracking measures were extracted for each participant as shown in Table 4.1. For the ADOS images, the sum of all the variables was calculated, except the FFT which was the minimum value.

Table 4. 1: Eye tracking measures, calculations and significance

Eye tracking measure *	Calculation	What the measure indicates	Possible interpretation of social processing**
Viewing Time			
1) Dwell Time (DT)	The sum of the duration of all the fixations that fell in the interest area.	Amount of time spent viewing the corresponding interest area.	**Interest/Saliency** Increased viewing time to face interest area could be associated with increased saliency to faces.
2) Dwell Time percentage (DT %)	Interest area DT/trial DT (the latter is the summed duration of all fixations within the trial time).		Conversely, decreased viewing time to faces could be associated with decreased saliency of faces to the participant.
Exploration			
3) Fixation Count (FC)	Total number of fixations falling in interest area.	Exploration and processing of information in interest area.	**1st order ToM** Decreased processing within faces interest area could suggest decreased 1st order ToM.
4) Run Count (RC)†	Total runs of fixations in the trial (two consecutive fixations in the same interest area belong to the same run).	Exploration and processing between interest area (RC=next fixation in another interest area relative to the current fixation).	**2nd order ToM** Reduced RC indicates reduced processing across interest area in ADOS images & could indicate reduced 2nd order ToM.
Orienting			
5) First Fixation Time (FFT)	Start time (in milliseconds relative to the start time of the current trial) of the first fixation to enter the specified interest area.	Speed of orienting the minimum time to fixate to a face or a specified non-social interest area	**Central coherence** Increased FFT to a face indicates slower orientation which could be related to weak central coherence.

* Eye tracking measures are defined as stipulated in the EyeLink Data Viewer manual.
**Tentative interpretation of eye tracking measures and social processing. †Supplementary eye tracking measure extracted from cartoons.

4.1.5 RATIONALE AND HYPOTHESES

Based on the findings from Chapter 3, children with ADHD showed atypical global visual social-emotional attention which differed from children with ASD. Although children with ASD had atypical visual social emotional attention, emotion recognition on the task was normal. Furthermore, the predicted emotion-specific findings, such as poorer processing of negative emotions in ADHD were not found. This could be because of the type of task used, which required active judgements of emotion within the face and eye stimuli, and the comparison of 6 emotions rather than testing positive versus negative emotions.

Hyper-activation of the medial prefrontal cortex to positive emotions and hypo-activation to negative emotions has been reported in a study using fMRI to assess emotion processing during an emotional Stroop test in ADHD (Posner et al. 2011). Furthermore, in children with ADHD, haemodynamic cerebral activation of temporal brain regions when viewing expressions has been found to happy faces compared to angry faces which, was related to preserved ability to recognise happy but not angry emotions (Ichikawa et al. 2014). It has been postulated that atypical emotion processing in ADHD may arise from deficits in orienting toward, recognising or allocating attention to emotional stimuli (Shaw et al. 2014). As described in Section 4.1.4, eye tracking measures in this chapter were extracted based on those previously studied in the ASD social scene perception literature which also include measures relating to orienting and allocating attention to social stimuli. In particular, orienting to faces in social

scenes has been shown to be atypically slower in ASD compared to typically developing individuals (Freeth et al. 2010) and also compared to those with ADHD (Frost-Karlsson et al. 2019). The main aim of this chapter is to compare visual social-emotional attention to ADOS images amongst the groups to analyse if the eye tracking measures can differentiate ADHD from ASD and identify the basis of comorbidity between the two disorders.

In summary, atypical visual social-emotional attention to social scenes (fixation duration and orienting to faces) has been found in those with ASD. However, this has not yet been studied in using the ADOS images from the ADOS which is a commonly used clinical tool, to assess for ASD. As free viewing of ADOS images which contain social-emotional scenes, allow for fixation duration and orienting to faces to be measured, it was predicted that the ADOS images would have most chance of differentiating the groups. As the ADOS also tests for spontaneous emotion recognition, the aim was also to address the other questions of the thesis, whether emotion recognition deficits are primary to ADHD or secondary to ASD and, if these eye tracking measures can help to explain the comorbidity between them. In order to expand visual social-emotional attention to include orienting and to potentially enhance the ecological and clinical validity of the Thesis, social-emotional scenes from the ADOS were used as stimuli.

4.1.5.1 **ADOS PICTURES**

As described in section 4.1.4, the ADOS pictures are colourful and content dense and mainly of positive valence. In order to quantify visual social-

emotional attention to ADOS pictures, eye tracking measures that tap into attention duration (reflected in Dwell Time; DT); exploration and processing (reflected in Fixation Count; FC); and orienting (First Fixation Time; FFT) to social areas (faces) versus non-social areas (vehicles/buildings) were derived and compared between the groups.

HYPOTHESES

It was hypothesised that visual attention to social areas (faces) would be greater than non-social areas (vehicles/buildings). The predicted profile would include increased DT (indexing viewing time/interest), increased FC (indexing exploration) and, quicker FFT (indexing faster orienting) to social areas (faces) compared with non-social areas in the pictures.

1) **ADHD**

Based on the findings in Chapter 3 on typical visual attention to core social features of the face and the literature on typical processing of positive valence described above, it was hypothesised that children with ADHD would have intact visual social-emotional attention to predominantly positive valence ADOS pictures. Based on the findings from Chapter 3, with reduced visual attention to non-core facial features, it was hypothesised that children with ADHD would have reduced visual attention to non-social areas compared with typically developing control children and children with ASD. This would lead to reduced DT, FC and slower FFT to the non-social areas.

2) ASD

Based on the findings from Chapter 3 and the literature presented above, it was hypothesised that children with ASD would have reduced viewing time/interest (DT), exploration (FC) and slower orienting (FFT) to the social areas (faces) than the non-social areas of the pictures compared to typically developing children and children with ADHD. It was also hypothesised that this profile of atypical visual social-emotional attention would be more pronounced in the pictures with highest content density.

3) ASD+ADHD

There is a lack of literature on the comorbid group although, it is hypothesised that if the comorbid group have both ASD and ADHD, they will have the additive effects of both conditions. This could lead to less viewing time/interest, exploration and increased orienting in both faces and non-social objects with reduced DT, FC and increased FFT in all pictures.

4.1.5.2 **ADOS CARTOONS**

In order to test if atypical processing of emotional valence was present in ADHD, eye tracking measures (DT, FC and FFT) to faces were compared between the Cat Cartoon (positive valence) and the Monkeys Cartoon (negative valence). As the cartoons contained complex social interaction between two characters, measures to victim's face versus perpetrator's face in the cartoons was also compared. Furthermore, the Run Count (RC), indexing exploration and processing between faces was also compared amongst the groups.

HYPOTHESES

Based on the literature described in section 1.5.1, it was hypothesised that intact social-emotional processing indexed by typical visual social-emotional attention to faces would indicate similar levels of DT, FC, RC, FFT to both cartoons independent of valence of the cartoon.

1) **ADHD**

Based on the literature on reduced processing of negative emotions described in the literature review in Chapter 1, it was hypothesised that children with ADHD have atypical visual social-emotional attention to the negative valence (Monkeys) cartoon compared to the positive valence (Cat) cartoon. Atypical visual social-emotional attention would include decreased DT, FC and RC to faces in the negative valence (Monkeys) cartoon compared to the positive valence (Cat) cartoon.

2) **ASD**

It was hypothesised that the complex social content of the cartoons would lead to a global emotion and face processing deficit. It was therefore predicted that children with ASD would have atypical emotion processing of both positive and negative valence emotions with, atypical visual social-emotional attention to faces in both cartoons compared to typically developing children and children with ADHD. The predicted visual social-emotional attention profile would include decreased DT, FC, RC and slower FFT to faces in both cartoons compared to typically developing children and children with ADHD.

3) ASD+ADHD

There is a lack of literature on the comorbid group yet, it is hypothesised that if the comorbid group have both ASD and ADHD, they will have the additive effects of both conditions. This will lead to potentially more pronounced atypical visual social-emotional attention than that seen in the ASD group and the ADHD group. However, if the comorbid group has a different visual social-emotional attention profile to the pure groups then it was predicted that an interaction between ASD by ADHD fixed factors would be found.

4.1.6 STATISTICAL ANALYSIS

Group differences for the demographic and clinical scores was calculated using univariate ANOVA. Group differences were followed up using post hoc tests which were carried out to allow for multiple comparisons. If Levene's test of difference between group variances was significant, the Games-Howell post hoc test was used; otherwise Tukey's test was used.

The effects of ASD and ADHD on eye tracking measures were tested using mixed design ANOVA two-factor model, comprising ASD and ADHD as fixed factors (as described in Section 3.3.2). Significant findings relating to the fixed factors (ASD Factor and ADHD Factor) will be reported in detail. However, significant effects that do not interact with the ASD and ADHD factors will be summarised and tabulated but not reported in the main text. A detailed description of each analysis is given in

the corresponding subsections. It should be noted that all the mixed design ANOVAs described below are based on diagnostic groups derived from clinical consensus described in section 2.2.1 rather than ADOS scores alone.

PICTURES

Multivariate mixed design ANOVA was performed to test the effects of ASD and ADHD on eye tracking variables (DT, FC and FFT) to faces (social) versus non-social areas (vehicles/buildings) among the 3 ADOS pictures. Picture, a within-subjects factor with 3 levels (picture 1: Meal, picture 2: Hollywood and picture 3: Holiday) was entered. The factor was created in this way to reflect increasing image content density (defined by the number of faces, the crowding of the components and the contrast of colours in the ADOS pictures) as it was hypothesised that visual attention would differ based on content density. Interest area was entered as the second within-subjects factor and comprised two levels, faces and non-social, as it was hypothesised that visual attention to the face would differ from the selected non-social areas. ASD factor and ADHD factor were entered as between-subject fixed factors. This model was applied to three dependent variables: DT, FC and FFT. Significant interactions were followed up by simple effects analysis. As DT percentage gave a similar pattern of results to DT, only results for DT are reported for brevity.

CARTOONS

A Multivariate mixed design ANOVA was performed to identify effects of ASD and ADHD on eye tracking variables (DT, FC and FFT) to faces of

perpetrator versus victim status in the ADOS Cartoons. Cartoon with two levels (Cat - positive valence cartoon and Monkeys – negative valence cartoon) was entered as the first repeated measure. Face with two levels (Face 1=perpetrator and Face 2=victim) was entered as the second repeated measure. The dependent eye tracking variables were entered individually (DT, FC and FFT). ASD factor and ADHD factor were entered as between-subject fixed factors. Significant interactions were followed up by simple effects analysis. A mixed design ANOVA was also run separately to compare the cartoons on Run Count indexing exploration between faces, as described in the corresponding results section. Pearson's correlation coefficient was conducted to analyse associations between significant eye tracking variables and symptom severity subscales including the ADOS emotion recognition subscore. In order to test if IQ or oppositional symptoms had significant contributions to the dependent variable over and above ADHD and ASD factors, hierarchical linear regression was applied to the dependent variable as described in Section 3.3.2.

Multiple linear regression was used to test how all the eye tracking variables described above, relate to the ADOS emotion recognition subscore and the total ADOS score, in order to test for the independent effects of the eye tracking variables in each ADOS image on ADOS scores. All of the eye tracking variables for each ADOS image were entered as independent variables using the stepwise method and the ADOS emotion recognition sub score or the total ADOS score was entered as the dependent variable.

A power calculation to estimate the number of participants required in each group was calculated using G*power software (version 3.1.9.2). In the literature, medium to large effect sizes (Cohen's d= 0.4-0.7) have been found in the ADHD group compared to the control group for fixation latencies to negative emotional faces in social scenes (Serrano, Owens, and Hallowell 2018). Similar effect sizes have also been found for fixation latencies to faces and people in scenes in children with ASD versus children without ASD (Cohen's d=0.5-0.8) (Chita-Tegmark 2016; Frost-Karlsson et al. 2019). Effect sizes were not presented by Frost- Karlsson et al. (2019) so, the effect size was derived using G*power based on the mean, standard deviation and group sample numbers provided by the author in the original article. Using G*power, 25-30 participants per group were calculated as required in order to detect a medium to large effect size, with 80% power and an alpha criterion of 0.05.

As the projected sample size based described above was not achieved in all the groups (Section 4.2.1), a post hoc power calculation based on the 2x2 factorial design described in this section was calculated using G*power in order to calculate the power to detect an interaction of medium effect size. Based on the actual sample size of 84, it was calculated there was 99.5% power to find an interaction between the ASD and ADHD factors with a medium effect size at an alpha criterion of 0.05.

4.2 RESULTS

4.2.1 DEMOGRAPHIC AND CLINICAL CHARACTERISTICS IN THE SAMPLE GROUPS

As shown in Table 4.2, groups were well matched for age and there was a male predominance in all groups. Groups differed in mean Full Scale IQ (F (3, 79)=5.66, $p<0.01$, $\eta p^2=0.18$) with significantly lower scores in the ASD group ($p<0.01$) and ASD+ADHD group ($p<0.01$) compared to the control group. Groups also differed in mean Verbal IQ (F (3, 79)=5.49, $p<0.01$, $\eta p^2=0.17$) with significantly lower scores in the ASD group ($p<0.05$) and ASD+ADHD group ($p<0.01$) compared to the control group. Groups were better matched for Performance IQ (F (3, 79)=3.18, $p<0.05$, $\eta p^2=0.11$) with significantly lower scores between the ASD+ADHD group ($p<0.05$) compared to the control group but not the other clinical groups ($p>0.05$; Table 4.2).

Groups differed significantly on the Conners' DSM-5 IA T-score (F (3, 78)=52.38, $p<0.001$, $\eta p^2=0.67$) with significantly higher T-scores in all three clinical groups compared to control group ($p<0.001$). Groups also differed significantly on the Conners' DSM-5 HI T-score (F (3, 78)=50.74, $p<0.001$, $\eta p^2=0.66$) with significantly higher T-scores in all three clinical groups compared to control group ($p<0.001$). Conners' DSM-5 HI T-scores were significantly higher in the ADHD group ($p<0.05$) and the ASD+ADHD group ($p<0.05$) compared to the ASD group. Groups differed significantly on the Conners' DSM-5 Oppositional T-score (F (3, 78)=32.31,

$p<0.001$, $\eta p^2=0.55$) with significantly higher T-scores in all three clinical groups compared to control group ($p<0.001$).

The groups differed significantly on SCQ ($F(3, 77)=34.11$, $p<0.001$, $\eta p^2=0.57$) with significantly higher scores in all the clinical groups ($p<0.001$) compared to the control group. SCQ scores were also significantly higher in the ASD+ADHD group ($p<0.05$) compared to the ADHD group. Groups differed significantly on the SAS ($F(3, 74)=37.70$, $p<0.001$, $\eta p^2=0.60$) with significantly lower scores in all three clinical groups compared to control group ($p<0.001$).

The clinical groups differed significantly on total ADOS scores ($F(2, 53)=21.76$, $p<0.001$, $\eta p^2=0.45$) with significantly higher scores in the ASD group ($p<0.001$) and the ASD+ADHD group ($p<0.001$) compared to the ADHD group. The clinical groups did not differ significantly on the ADOS emotion recognition subscore ($F(2, 53)=1.73$, $p>0.05$, $\eta p^2=0.06$). Other disorders including conduct and emotional disorders were present in all the clinical groups (Table 4.2).

Based on parental report, seven children in the ADHD group and eight children in the ASD+ADHD group were regularly taking prescribed stimulant medication. Of the seven children in the ADHD group prescribed stimulant medication, three children were prescribed Medikinet XL, one child was prescribed Concerta XL, one child was prescribed Equasym XL, two children were prescribed Elvanse and, one child was also prescribed short acting Methylphenidate Hydrochloride in addition a long acting preparation. Of the eight children in the ASD+ADHD group, four children were

prescribed Medikinet XL, two children were prescribed Elvanse and two children were prescribed stimulants where the preparation was not recorded. As described in Section 2.2, all children were withdrawn from any stimulant medication 24 hours prior to testing. Four children in the ASD+ADHD group and three children in the ADHD group were prescribed melatonin for sleep problems. 1 child in the ASD group was prescribed anti-depressant medication (Fluoxetine) for anxiety. None of the children from any of the groups were on non-stimulant or anti-psychotic medication.

Raw eye tracking data and excluded trials per group are presented in Appendix VI., Table A.25. For the eye tracking analysis, excluded number of trials as described in the methods (Section 4.1.4) were not significantly different amongst the groups ($F(3, 80)=0.61$, $p>0.05$, $\eta p^2=0.02$).

Table 4. 2: Demographic and clinical characteristics of the sample (n=84)

	Group				Group effect		
	ADHD (n=16)	**ASD** (n=18)	**ASD+ADHD** (n=28)	**Controls** (n=22)	***F***	**p**	**Group differences** (post-hoc)
Mean age in years (SD; range)	10.17 (2.06; 7.00-14-17)	11.01 (2.11; 7.50-15.00)	10.82 (1.56; 8.58-13.92)	10.80 (2.40; 7.58-14.82)	0.55	>0.05	n/s
Gender % male (n male)	68.8% (11)	61.1% (11)	75.0% (21)	59.1% (13)	0.56	>0.05	n/a
Right hand dominance**	100% (14)	88.2% (15)	84.0% (21)	90% (19)	0.82	>0.05	n/a
Right eye dominance**	50.0% (7)	52.9% (9)	68.0% (17)	61.9% (13)	0.52	>0.05	n/a
Mean FSIQ (SD; range)	111.44 (10.37; 96.00-128.00)	103.53 (15.41; 75.00-125.00)	103.04 (19.47; 77.00-140.00)	119.00 (9.83; 100.00-138.00)	5.66	<0.01	Controls > ASD / ASD+ADHD [b]
Mean VIQ (SD; range)	113.19 (7.88; 102.00-128.00)	103.18 (19.03; 73.00-135.00)	102.04 (19.14; 78.00-144.00)	117.73 (9.52; 93.00-132.00)	5.49	<0.01	Controls > ASD [c] / ASD+ADHD [b]
Mean PIQ (SD; range)	106.87 (15.23; 84.00-136.00)	104.00 (13.87; 79.00-124.00)	102.74 (18.92; 76.00-133.00)	115.86 (12.79; 92.00-138.00)	3.18	<0.05	Controls > ASD+ADHD [c]
Conners' IA T score (SD; range)	83.50 (10.97; 52.00-90.00)	77.44 (12.47; 54.00-90.00)	84.04 (7.62; 60.00-90.00)	52.05 (5.98; 41.00-59.00)	52.38	<0.001	Controls < ADHD / ASD /ASD+ADHD [a]
Conners' HI T Score (SD; range)	85.69 (7.17; 69.00-90.00)	75.71 (12.57; 54.00-90.00)	84.70 (8.92; 57.00-90.00)	53.23 (5.56; 40.00-59.00)	50.74	<0.001	Controls < ADHD / ASD /ASD+ADHD [a] ASD < ADHD / ASD+ADHD [c]

Conners' OD T Score (SD; range)	81.75 (10.55; 61.00-90.00)	77.12 (15.08; 44.00-90.00)	83.48 (11.04: 50.00-90.00)	52.95 (7.20; 41.00-74.00)	32.31	<0.001	Controls < ADHD / ASD /ASD+ADHD [a]
SAS (SD; range)	11.38 (6.75; 3.00-23.00)	7.33 (5.64; 1.00-23.00)	7.42 (5.53; 0.00-22.00)	24.28 (4.87; 14.00-33.00)	37.70	<0.001	Controls > ADHD / ASD /ASD+ADHD [a]
Total SCQ (SD: range)	16.19 (7.22; 3.00-31.00)	19.31 (6.12; 11.00-31.00)	21.41 (6.48; 9.00-33.00)	4.45 (4.75; 0.00-12.00)	34.11	<0.001	Controls < ADHD / ASD / ASD+ADHD [a] ADHD < ASD+ADHD [c]
ADOS Total score* (SD; range)	5.00 (3.35; 0.00-14.00)	14.00 (4.86; 7.00-22.00)	14.08 (5.18; 5.00-23.00)	n/a	21.76	<0.001	ADHD < ASD / ASD+ADHD [a]
ADOS emotion recognition subscore* (SD; range)	0.37 (0.50; 0.00-1.00)	0.75 (0.68; 0.00-2.00)	0.67 (0.62; 0.00-2.00)	n/a	1.73	>0.05	n/s
Oppositional and Conduct Disorders	50.0% (8)	52.9% (9)	53.6% (15)	0	-	n/a	-
Emotional Disorders†	37.5% (6)	64.7% (11)	53.6% (15)	0	-	n/a	-

FSIQ=Full Scale Intelligence Quotient (WASI); VIQ=Verbal Intelligence Quotient; PIQ=Performance Intelligence Quotient; Conners' Parent Rating Scale: IA (Inattentive), HI (Hyperactive-Impulsive), OD (Oppositional) T scores (≥65 suggests difficulties in these areas).SAS=Social Aptitudes Scale (≤ 12 is suggestive of ASD); SCQ=Social Communication Questionnaire (≥15 suggestive of ASD); Rating scale scores shown are parent rated. ADOS=Autism Diagnostic Observation Schedule total score (Autism spectrum cut-off score ≥7).*ADOS total and emotion recognition scores not available for typically developing controls (n=22). **Missing data for hand and eye dominance (n=7). †Emotional Disorders include: general anxiety disorder, mild depressive episode, obsessive compulsive disorder or specific phobia (note: participants could have more than one disorder). Emotional, oppositional and conduct disorders were based on DAWBA computer diagnoses and confirmed by clinical rating as described in methods section (2.2.2.3). [a] $p<0.001$; [b] $p<0.01$; [c] $p<0.05$.

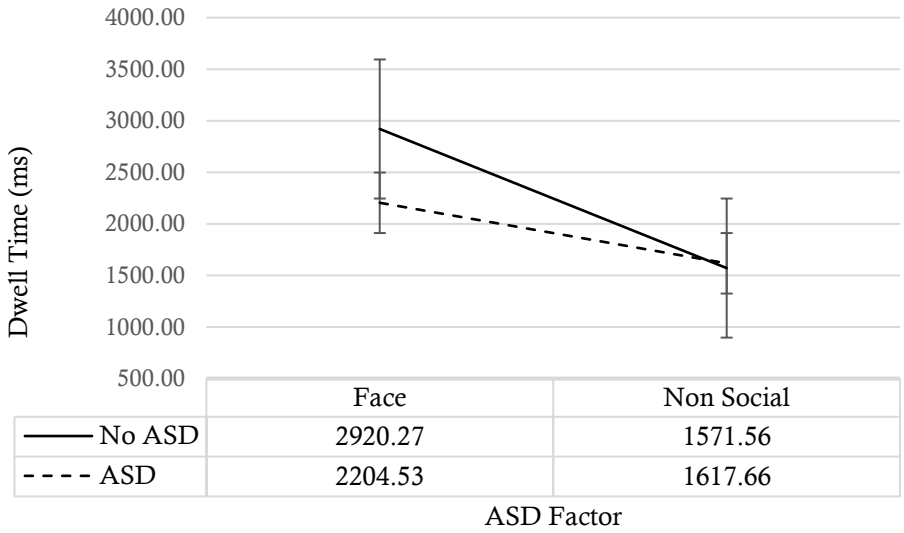
4.2.2 ADOS PICTURES

A multivariate mixed design ANOVA was performed to identify effects of ASD and ADHD on the 3 eye tracking variables to faces versus non-social areas in the three ADOS pictures as described in Section 4.1.6.

There was a trend for a multivariate between-subjects effect of ASD on all the eye tracking variables, but this did not quite reach significance (F (3, 76)=2.30, p=0.08, ηp^2=0.08). Univariate tests showed a significant effect of ASD factor for two out of the three dependent variables. Univariate analyses confirmed that DT was significantly reduced in those with ASD (1911.01ms) compared to those without ASD (2245.91ms; F (1, 78)=4.28, p<0.05, ηp^2=0.05). FFT was increased in those with ASD (4952.67ms) compared to those without ASD (3641.71ms; F (1, 78)=5.06, p<0.05, ηp^2=0.06). There was a trend for reduced FC in those with ASD (6.70) than without ASD (7.71; F (1, 78)=3.00, p=0.09, ηp^2=0.04). This suggests that DT is reduced and FFT is slower to both faces and non-social objects in ASD.

Although there was not an overall significant multivariate effect of interest area by ASD Factor across dependent variables (F (3, 76)=1.62, p>0.05, ηp^2=0.06), univariate tests showed a significant within-subjects effect for ASD factor by interest area on DT (F (1, 78)=4.16, p<0.05, ηp^2=0.05). There was no significant 3-way interaction with picture. Univariate tests showed trends for ASD Factor by interest area on FC (F (1, 78)=3.17, p=0.08, ηp^2=0.04) and FFT (F (1, 78)=2.42, p=0.12, ηp^2=0.03) but these did not reach significance.

The interaction between interest area and ASD factor on DT was followed up by simple effects analysis which showed a significantly reduced DT to faces in those with ASD (2204.53ms) than without ASD (2920.27ms; $F(1, 78)=5.45$, $p<0.05$, $\eta p^2=0.07$). There was no significant difference in DT to non-social areas in those with ASD compared to those without ASD. There was significantly increased DT to faces versus non-social areas within ASD ($p<0.05$) although, this finding was more robust in those without ASD ($p<0.001$), explaining the 2-way interaction between ASD and interest area. Overall, these findings suggest that DT to faces is specifically reduced in those with ASD compared to those without ASD (Figure 4.6).



	Face	Non Social
No ASD	2920.27	1571.56
ASD	2204.53	1617.66

Figure 4. 6: ASD Factor on DT to Faces versus Non-social areas of ADOS Pictures (Error Bars=95% CI).

The trend for an interaction for ASD by interest area on FC was also followed up on the basis it was an a priori hypothesis. Simple effects analysis showed a trend for reduced FC to faces in those with ASD (FC

mean=7.63) than those without ASD (FC mean=9.72; $F(1, 78)=3.92$, $p=0.05$, $\eta p^2=0.05$), however this just failed to reach significance. There was no significant difference in FC to non-social areas in those with ASD compared to those without ASD. There were significantly increased FCs to faces versus non-social areas within ASD ($p<0.05$), however, this finding was more robust in those without ASD ($p<0.001$; Figure 4.7)

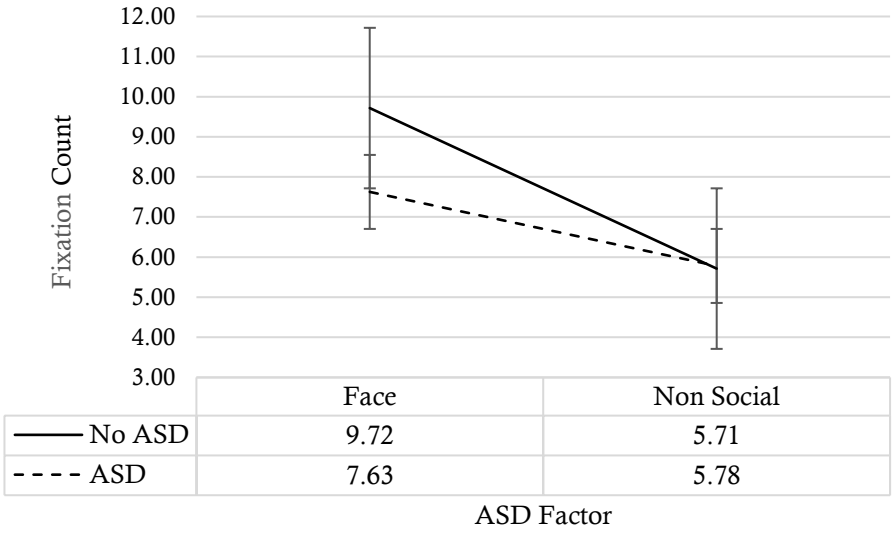
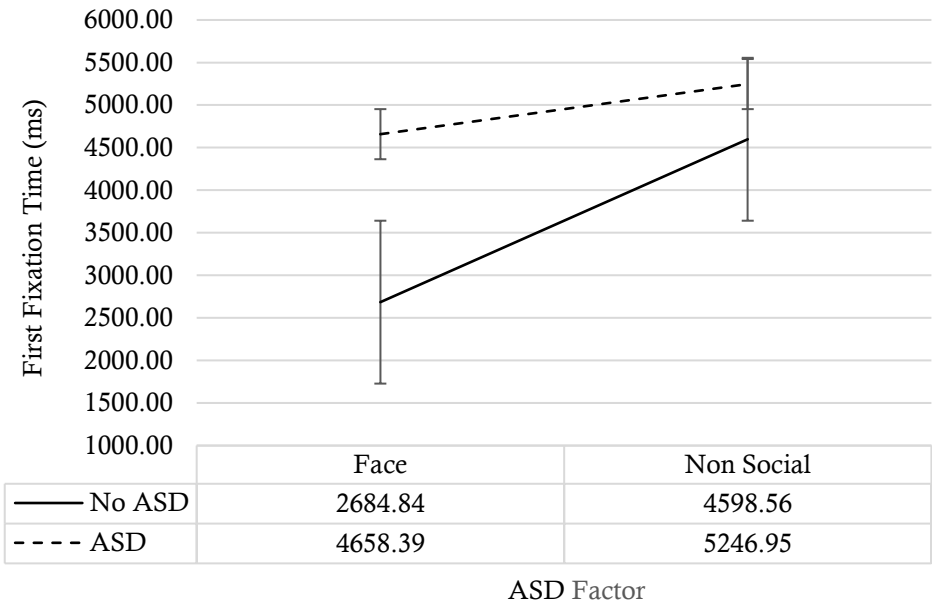


Figure 4. 7: ASD Factor on FC to Faces versus Non-social areas of ADOS Pictures (Error Bars=95% CI).

The trend for an interaction for ASD by interest area on FFT was also followed up as it was hypothesised that FFT is important in orienting which was hypothesised to be slower for faces in ASD. A similar follow up by simple effects analysis showed significantly increased FFT time to faces in those with ASD (mean=4658.39ms) compared to those without ASD (mean=2684.85ms; $F(1, 78)=8.73$, $p<0.01$, $\eta p^2=0.10$). There was no significant difference in FFT to non-social areas in those with ASD compared to

those without ASD. There were also no significant differences in FFT to faces versus non-social areas in those with ASD ($p>0.05$). However, in those without ASD, FFT to faces was significantly quicker than non-social areas ($p<0.01$; Figure 4.8). These results suggest that FFT to faces is slower than FFT to non-social areas in those with ASD compared to those without ASD.



	Face	Non Social
No ASD	2684.84	4598.56
ASD	4658.39	5246.95

Figure 4. 8: ASD Factor on FFT to Face versus Non-social areas in ADOS Pictures (Error Bars=95% CI).

There was no effect of ADHD factor by interest area or by picture or by ASD factor. Significant multivariate effects of interest area, picture and picture by interest area on all of the eye tracking variables that were independent of the fixed factors (ASD factor and ADHD factor) are summarised in Table 4.3.

In summary, DT and FFT differed for faces in those with ASD compared with those without ASD. DT and FFT to non-social areas did not differ significantly for those with and without ASD. This suggests that differences in viewing time/interest, indexed by DT and orienting, indexed by FFT in those with and without ASD are specific to faces in the ADOS pictures. As no effect of ADHD was found, this suggests typical visual social-emotional attention to ADOS pictures which are predominately of positive valence, in children with ADHD without ASD.

Table 4. 3: Summary of significant main effects independent of fixed factors in ADOS pictures for all children

Dependent variable (s)	Independent variable/ Interaction	Main effect (F)	Direction of effect[b] (mean dependent variable)
Multivariate tests on all eye tracking variables (DT, FC, FFT)	Interest Area	20.90[c]	-
	Picture	8.92[c]	-
	Interest Area*Picture	5.97[c]	-
Planned contrasts from univariate tests[a]			
DT (ms)	Interest Area	26.83[c]	Faces (2562.40) > non-social (1594.61)[c]
FC	Interest Area	23.30[c]	Faces (8.67) > non-social (5.75)[c]
FFT (ms)	Interest Area	8.63[c]	Faces (3671.62) < non-social (4922.76)[d]
DT (ms)	Picture	50.45[c]	Meal (1305.14) < Hollywood (2848.55)[c] > holiday (2081.83)[c]
FC	Picture	51.97[c]	Meal (4.55) < Hollywood (10.0)[c] > holiday (7.08)[c]
FFT (ms)	Picture	16.64[c]	Meal (5900.03) > Hollywood (3264.43)[c] < holiday (3727.11)
DT (ms)	Interest Area*Picture	0.01	-
FC	Interest Area*Picture	0.10	-
FFT (ms)	Interest Area*Picture	9.18[d]	Faces (3804.66) < non-social (7995.40) in holiday[c] Faces (3158.73) < non-social (4295.49) in meal[e] Faces (4051.47) > non-social (2477.39) in Hollywood[e]

[a]Planned contrasts were conducted on significant univariate tests from the multivariate analysis. For repeated planned contrasts, each category (except the first) is compared to the previous category (Field 2005)

[b]Significant univariate main effects from planned contrasts and significant interactions were followed up by pairwise comparisons (LSD) from simple effects analysis

[c]$p<0.001$; [d]$p<0.01$; [e]$p<0.05$.

DT (Dwell Time); FC (Fixation Count); FFT (First Fixation Time); ms (milliseconds)

4.2.2.1 *CORRELATIONS WITH CLINICAL SYMPTOMS*

Dwell time (DT; indexing viewing time) to faces in all the pictures significantly negatively correlated with the communication ($r=–0.32$; $p<0.01$) and, repetitive stereotyped behaviour subscores ($r=–0.27$; $p<0.05$) on the SCQ. DT to faces in all the pictures did not significantly correlate with the social reciprocal interaction subscore on the SCQ ($r=–0.09$; $p>0.05$). There was also a trend for an association with DT to faces and the SAS but this did not reach significance ($r=0.22$; $p=0.06$).

Fixation Count (FC; indexing exploration) to faces in all the pictures significantly negatively correlated with the communication ($r=–0.32$; $p<0.01$) and, repetitive stereotyped behaviour subscores ($r=–0.24$; $p<0.05$) on the SCQ. FC to faces in all the pictures did not significantly correlate with the social reciprocal interaction subscore on the SCQ ($r=–0.11$; $p>0.05$). There was also a trend for an association with FC to faces and the SAS but this did not reach significance ($r=0.20$; $p=0.08$).

First Fixation Time (FFT; indexing orienting) to faces in all pictures significantly correlated with the repetitive stereotyped behaviour subscore ($r=0.30$; $p<0.01$) on the SCQ. There was a trend with FFT to faces in all pictures with the communication subscale on the SCQ but this did not reach significance ($r=0.21$; $p=0.06$). FFT to faces in all the pictures did not significantly correlate with the social reciprocal interaction subscore on the SCQ ($r=0.12$; $p>0.05$) or the SAS ($r=–0.16$; $p>0.05$). Neither DT,FC nor FFT time significantly correlated with the ADOS emotion recognition subscore or Conners' IA or HI T-score ($p>0.05$).

In summary these finding suggest that atypical visual social-emotion attention to faces in ADOS pictures which are predominantly of positive emotional valence and content dense are associated ASD symptom severity rather that ADHD core symptoms.

4.2.3 ADOS CARTOONS

In this Section, visual social-emotional attention to faces in the positive valence Cat ADOS cartoon image versus the negative valence Monkeys ADOS cartoon image was compared. As described in Section 4.1.4, only the faces were defined as interest areas and the perpetrator or victim status of the face within each cartoon was also compared in line with the ADOS cartoons task. Non-social areas were not defined in this analysis as they differed across the cartoon types.

There was a trend for a within-subjects multivariate effect of ADHD factor by Cartoon (positive versus negative valence) but this did not quite reach significance ($F(3, 78)=2.62$, $p=0.06$, $\eta p^2=0.09$). Univariate tests showed a significant effect of ADHD factor by cartoon on DT ($F(1, 79)=4.89$, $p<0.05$, $\eta p^2=0.06$). Simple effects analysis showed a trend towards reduced DT to the faces in the negative valence Monkeys Cartoon (1850.41ms) compared with the positive valence Cat Cartoon (2241.19ms; $p=0.05$) in those with ADHD (Figure 4.9). The opposite pattern was seen in those without ADHD who had greater DT to faces in the Monkeys Cartoon. However, this was not significant ($p>0.05$). There were trends for increased DT to faces in the Cat Cartoon in those with ADHD compared

with those without ADHD and reduced DT to the faces in the Monkeys Cartoon in those with ADHD compared to those without ADHD but neither of these trends were significant (p>0.5; Figure 4.9). Overall, these findings suggest a trend for reduced DT to the faces in the negative (Monkeys Cartoon) versus positive (Cat Cartoon) emotional valence cartoons in those with ADHD.

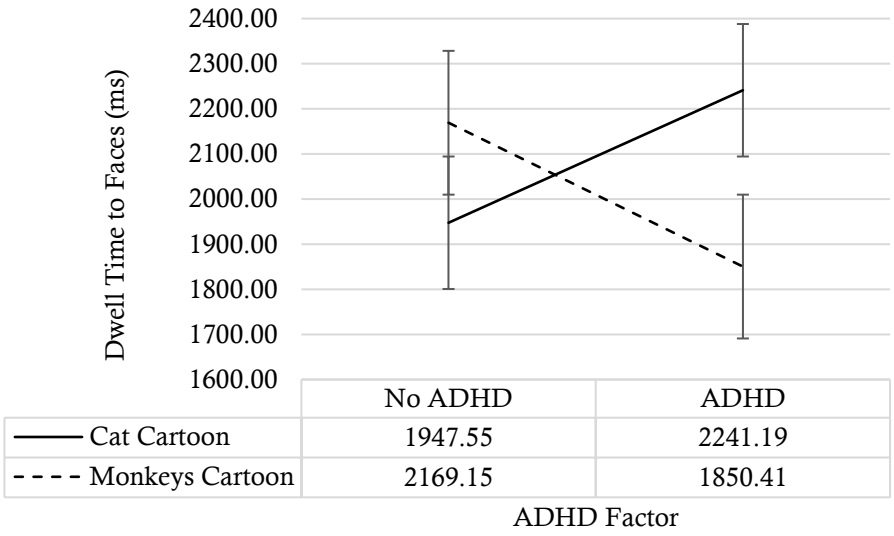


Figure 4. 9: ADHD factor on DT to Faces in Cartoons

Error Bars=95% CI, Cat Cartoon=positive emotional valence, Monkeys Cartoon=negative emotional valence.

There was also a trend for a within-subjects multivariate interaction between ASD factor, Cartoon and Face yet, this did not reach significance (F(3, 78)=2.00, p=0.12, ηp^2=0.07). Univariate tests showed a trend towards a significant effect of ASD factor by Cartoon by Face on FFT (F(1, 79)=3.47, p=0.07, ηp^2=0.04). Simple effects analysis showed significantly slower FFT to the perpetrator face in the negative valence Monkeys Cartoon (angry monkey) in those with ASD (6573.41ms) than those without ASD (3242.23ms; F(1, 79)=6.11, p<0.05, ηp^2=0.07). Those without ASD,

showed a significantly quicker FFT to the perpetrator face in the negative valence Monkeys Cartoon (angry monkey) compared to the future perpetrator face in the positive valence Cat Cartoon (cat face; 3242.23ms; $F(1, 79)=6.11$, $p<0.05$, $\eta p^2=0.07$). However, this pattern was not found in those with ASD who showed equally slow FFT to the perpetrator face regardless of Cartoon type ($p>0.05$). There were no significant differences between those with ASD or those without ASD for perpetrator face in positive valence cartoon (cat face; $p<0.05$; Figure 4.10). No significant differences were found for FFT either within ASD or between those with and without ASD for victim faces in the cartoons. Overall, these findings suggest that those with ASD are much slower to orientate, indexed by FFT to the perpetrator face in the negative valence Monkeys Cartoon (angry monkey) than those without ASD.

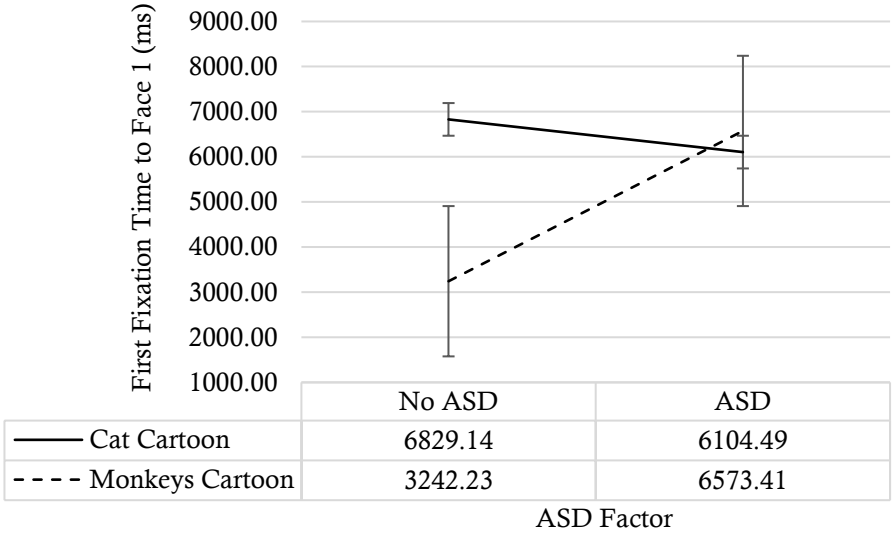


Figure 4. 10: ASD factor on FFT to Face 1 (perpetrator) in cartoons

Error Bars=95% CI, Cat Cartoon=positive emotional valence; Monkeys Cartoon=negative emotional valence.

On multivariate analysis, there was a significant between-subjects effect of ASD factor by ADHD factor on all the eye tracking variables in the main analysis (F(3, 78)=2.85, p<0.05, ηp^2=0.10). Univariate tests showed a significant interaction between ASD factor by ADHD factor on FC (F(1, 79)=7.10, p<0.01, ηp^2=0.08). Simple effects analysis showed significantly reduced FC in the ASD group (FC= 5.40; F(1, 79)=7.55, p<0.01, ηp^2=0.09) and the ADHD group (FC= 5.43; F(1, 79)=6.62, p<0.05, ηp^2=0.08) compared to the control group (FC= 7.70; Figure 4.11). Although there was a trend towards greater FC within faces in the ADHD+ASD group (FC= 6.29) compared to the pure groups, this was not statistically significant compared to the ASD group (F(1, 79)=1.79, p>0.05, ηp^2=0.02) or the ADHD group (F(1, 79)=1.05, p>0.05, ηp^2=0.01). This suggests that all the clinical groups had reduced FC, indexing reduced exploration and processing within faces in cartoons compared with the typically developing control group.

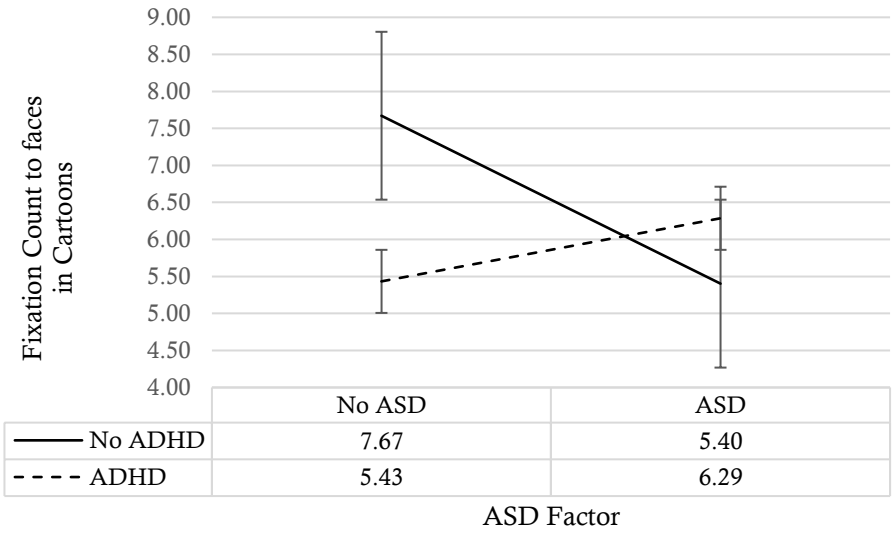


Figure 4. 11: ASD factor by ADHD factor on FC to faces in cartoons (Error Bars 95% CI).

Significant findings independent of ASD and ADHD fixed factors are summarised in Table 4.4.

Table 4. 4: Summary of significant main effects independent of fixed factors from main analysis in ADOS cartoons for all children

Face Status on Dependent variable (s)	Main effect (F)	Direction of effect[b] (mean dependent variable)
Multivariate tests on all eye tracking variables (DT, FC, FFT)	40.23[c]	-
Planned contrasts from univariate tests[a]		
DT (ms)	25.41[c]	Perpetrator (1599.86) < victim (2504.29)[c]
FC	78.74[c]	Perpetrator (4.43) < victim(7.97)[c]
FFT (ms)	55.44[c]	Perpetrator (5687.32) > victim(2046.74)[c]

[a]Planned contrasts were conducted on significant univariate tests from the multivariate analysis. For repeated planned contrasts, each category (except the first) is compared to the previous category (Field 2005)

[b]Significant univariate main effects from planned contrasts and significant interactions were followed up by pairwise comparisons from simple effects analysis

[c]$p<0.001$; [d]$p<0.01$; [e]$p<0.05$. Abbreviations as in Table 4.3

Summary of main findings for ASD and ADHD fixed factors in cartoons

In summary, there were subtle differences in visual social-emotional attention to the cartoon faces in those with ASD, ADHD and ASD+ADHD. Those with ADHD had a trend for reduced DT to faces in the negative valence Monkeys Cartoon compared to those without ADHD. Children with ASD had significantly slower FFT to the perpetrator face in the Monkeys Cartoon (angry monkey). Those with ADHD and those with ASD both had reduced FC to faces in the cartoons suggesting reduced exploration

and processing within faces. Exploration of faces in cartoons could be related to face processing and higher order social cognitive functions such as understanding the mental state of others (see below).

Exploration between faces in cartoons

Exploration within faces was tested using the FC to faces in the previous section and this was found to be significantly reduced for all faces in cartoons in those with ASD and ADHD. In order to understand a characters' desires or what one character is thinking about another character's thoughts, sufficient exploration between the faces and the other areas of the cartoons is likely to be important. The Run Count (RC) (as described in Methods Section table 4.1) to faces and the area outside the faces in cartoons was used to test the exploration between faces in cartoons.

A mixed design ANOVA was performed to identify effects of ADHD and ASD on the RC in the positive and negative emotional valence ADOS Cartoons. RC was entered as the dependent variable. Cartoon with two levels (Cat positive valence Cartoon and Monkeys negative valence Cartoon) was entered as the repeated measure and ASD factor and ADHD factor were entered as between-subject fixed factors.

There was a significant interaction between ASD factor and ADHD factor on RC ($F(1, 79)=4.01$, $p<0.05$, $\eta p^2=0.05$). Simple effects analysis showed significantly reduced RC in the cartoons in the ASD group (RC= 7.47; $F(1, 79)=4.00$, $p<0.05$, $\eta p^2=0.05$) and the ADHD group (RC= 7.27; $F(1, 79)=4.42$, $p<0.05$, $\eta p^2=0.05$) compared to the control group (RC= 9.39; Figure 4.12). Although there was a trend towards increased RC in the

cartoons in the combined group (RC= 8.10), compared to the pure groups this was not statistically significant compared to the ASD group (F (1, 79)=0.43, p>0.05, ηp^2=0.01) or the ADHD group (F (1, 79)=0.70, p>0.05, ηp^2=0.01). This suggests that all the clinical groups had reduced RC, indexing reduced exploration between faces and the area outside the faces in the cartoons compared with the typically developing control group. There were no other significant effects between or within subjects for the other factors.

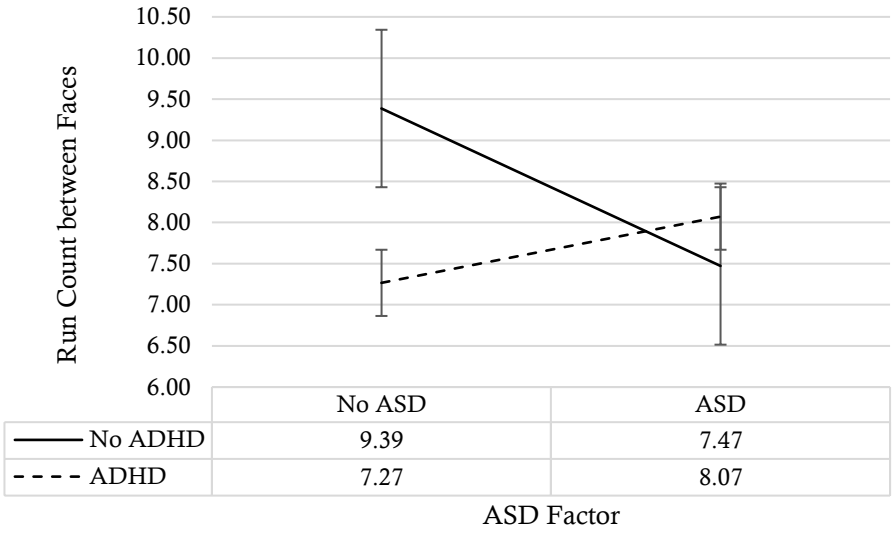


Figure 4. 12: ASD factor by ADHD factor on RC between faces and area outside the faces in cartoons (Error Bars 95% CI).

4.2.3.1 *CORRELATIONS WITH CLINICAL SYMPTOMS*

Correlations with clinical symptoms were conducted on eye tracking variables where a significant main effect was found in order to deduce association with clinical symptom severity. Dwell Time (DT; indexing viewing

time/interest) to faces in the negative emotional valence (Monkeys) cartoon was significantly negatively correlated with the communication ($r=-0.22$; $p<0.05$) but not the repetitive stereotyped behaviour ($r=-0.12$; $p>0.05$) or social reciprocal interaction subscores ($r=-0.14$; $p>0.05$) on the SCQ. DT also correlated with the SAS but this did not quite reach significance ($r=0.21$; $p=0.07$). DT did not significantly correlate with the Conners' IA ($r=-0.14$; $p>0.05$) or HI T-score ($r=-0.10$; $p>0.05$). These findings suggest that reduced DT, indexing viewing time/interest to faces in the negative emotional valence (Monkeys) cartoon is significantly associated with communication difficulties on the SCQ and not ADHD symptoms.

There were trends for an association between Fixation Count (FC; indexing exploration) to faces in all cartoons for the communication ($r=-0.21$; $p=0.06$) and repetitive stereotyped behaviour subscores on the SCQ ($r=-0.20$; $p=0.08$) and the SAS ($r=0.19$; $p=0.10$) but these did not reach significance. FC to faces in all cartoons did not significantly correlate with the Conners' IA ($r=-0.16$; $p>0.05$) or HI T-score ($r=-0.10$; $p>0.05$). It was conceived that as cartoon emotional valence affected DT, this could also be the case for the other eye tracking variables so, correlations between symptom severity subscales to FC to faces in the negative emotional valence (Monkeys) cartoon was analysed separately. FC to faces in the negative emotional valence (Monkeys) cartoon significantly correlated with the SAS ($r=0.29$; $p<0.05$), communication difficulties ($r=-0.25$; $p<0.05$) and repetitive stereotyped behaviours ($r=-0.26$; $p<0.05$) on the SCQ, with a trend for an association with the social reciprocal interaction subscore on the SCQ ($r=-0.20$; $p=0.07$). FC to faces in negative emotional valence

(Monkeys) cartoon did not significantly correlate with the Conners' HI T-score ($r=–0.12$; $p>0.05$) however, there was a trend for an association with the IA T score ($r=–0.20$; $p=0.07$) although this did not reach significance.

There was no significant association with Run Count (RC; indexing exploration between faces) in all cartoons and symptom severity scales ($p>0.10$). When RC in the negative emotional valence (Monkeys) cartoon was analysed separately, RC was significantly negatively correlated with the SCQ subscales (communication ($r=–0.26$; $p<0.05$), repetitive stereotyped behaviour ($r=–0.25$; $p<0.05$) and social reciprocal interaction ($r=–0.22$; $p<0.05$)). RC in the negative emotional valence (Monkeys) cartoon also significantly correlated with the SAS ($r=0.31$; $p<0.01$), Conners' IA ($r=–0.23$; $p<0.05$) but not the HI T-score ($r=–0.13$; $p>0.05$). Eye tracking variables (DT, FFT, FC, RC) to faces in the negative emotional valence (Monkeys) cartoons did not significantly correlate with the ADOS emotion recognition subscore ($p>0.05$).

In summary, findings suggest that atypical visual social-emotional attention to the negative valence emotional cartoon is associated with difficulties on the SAS and SCQ symptom severity. Only the RC which is a measures of exploration between faces was significantly associated with ADHD IA symptom severity and, none of the eye tracking variables correlated with ADHD HI symptoms. These findings suggest that atypical visual social-emotional attention to the negative valence emotional cartoon is not associated with ADHD core symptoms but rather, with social skills difficulties on the SAS and ASD symptom severity.

4.2.4 HIERARCHICAL REGRESSION

In order to test if IQ/oppositional symptoms had significant contributions to the dependent variable over and above ADHD and ASD factors, hierarchical linear regression was applied to the dependent variable as described in Section 3.2.2. In order to reduce the number of linear regression analyses, when possible; significant variables where a main effect was found (as presented in Section 4.2.2 and 4.2.3) were entered. Also, for the ADOS pictures the mean score for each significant dependent variable across the pictures was calculated and entered as the dependent variable in each analysis.

For ADOS emotion recognition subscore and eye tracking variables analysed in the pictures, neither IQ nor oppositional symptoms explained a significant amount of the variance over and above ASD or ADHD factors. For the cartoons, oppositional symptoms significantly explained 5% of the variance ($p<0.05$) for Dwell Time (DT) and Fixation Count (FC) to faces and, 6% of the variance for the Run Count (RC) between faces in the negative emotional valence (Monkeys) Cartoon over and above ADHD and ASD factors. For all other visual social-emotional variables, neither IQ nor oppositional symptoms explained a significant amount of the variance over and above ADHD or ASD factors. Hierarchical linear regression model results tables for each dependent variable are presented in the Appendix.V.

4.2.5 MULTIPLE LINEAR REGRESSION FOR VISUAL ATTENTION AND ADOS SCORES

ADOS emotion recognition subscore

Multiple linear regression was calculated with the ADOS emotion recognition subscore; it was entered as the dependent variable, and all the eye tracking variables to the individual pictures and cartoons were entered as the independent variables using the stepwise method (as described in Section 4.1.6). The final model was significant and explained 20% of the variance to the ADOS emotion recognition subscore (R^2=0.20; F (2, 55)=6.73, p<0.01). This model included two eye tracking variables (DT to the man face in the positive emotional valence (Cat) cartoon and, FFT to non-social areas in the holiday picture) (see Table 4.5). Model prediction, showed reduced DT to the man face in the positive valence cartoon and quicker FFT to non-social areas in the holiday picture would increase the ADOS emotion recognition subscore (reflecting worse emotion recognition).

Table 4. 5: Multiple linear regression models for ADOS emotion recognition subscore

Model	Variable(s)	R^2	R^2 change	F	p-value
1	DT to man face	0.11	0.11	6.67	<0.05
2	DT to man face FFT to NS in Holiday	0.20	0.09	6.73	<0.01

DT (Dwell Time) to man face in Cat Cartoon; FFT (First Fixation Time) to NS (non-social areas) in the Holiday picture.

ADOS Total score

Multiple linear regression was calculated with the total ADOS score entered as the dependent variable (as described in Section 4.1.6). The model was significant and explained 13% of the variance to the ADOS total score (R^2=0.13; F (1, 52) =7.79, p<0.01). This model included one eye tracking variable: DT% to non-social areas in the meal picture. Model prediction, showed increased dwell time percentage to non-social areas in the meal picture would increase the total ADOS score (reflecting more autistic behaviours). This result supports the notion that the total ADOS score relates to visual social-emotional attention in the ADOS picture. This finding differs with the ADOS emotion recognition subscore, described above which showed association with visual social-emotion attention to cartoon and picture.

4.3 DISCUSSION

This chapter included the comparison of visual social-emotional attention during free viewing of social scenes used in the ADOS amongst the groups and, analysed any association of visual attention to ADOS images with clinical symptom severity. This method, sought to address the questions of the thesis on the association of visual attention to social scenes from the ADOS and spontaneous emotion recognition difficulties on the ADOS; a commonly used clinical tool in the assessment of ASD. This chapter presents results extending findings from the previous chapter on the emotional recognition faces task and, also from the literature on social scene perception in children with ASD, ADHD and ASD+ADHD. To the author's knowledge, this is one of the first studies to use eye tracking to investigate visual social-emotional attention to ADOS images. As the ADOS is a commonly used diagnostic aid in the assessment of ASD, the findings of this study is of interest to clinicians. This section provides a discussion of main findings followed by the limitations and strengths of the study.

4.3.1 DISCUSSION OF MAIN FINDINGS

Visual social-emotional attention to ADOS pictures and cartoons showed several differences and some similarities in those with ASD and ADHD. Slower orientation, indexed by FFT (First Fixation Time) and reduced viewing time and exploration indexed by DT (Dwell Time) and FC (Fixation Count) to faces, which were deemed the most social areas of the pictures differentiated those with ASD (ASD and ASD+ADHD) compared to those without ASD (controls and ADHD). Both FFT, DT and FC to faces

in pictures was associated symptom severity on the SCQ but not the Conners' IA or HI subscales; suggestive of association of atypical visual social-emotional attention with ASD but not ADHD at the symptom level. Findings of slower orientation, indexed by FFT and reduced viewing time, indexed by DT to faces (social interest areas) in ADOS pictures in children with ASD (ASD and ASD+ADHD) is in line with the ASD eye tracking literature on social scene perception (Frost-Karlsson et al. 2019; Freeth et al. 2010; Riby and Hancock 2008). EEG studies have also found atypical ERP responses to faces in those with ASD (ASD and ASD+ADHD), supporting face processing deficits in ASD at the neural level (Groom et al. 2017; Tye et al. 2013).

Our findings from ADOS pictures suggest that the ASD+ADHD group genuinely have visual social-emotional attention like ASD rather than a 'phenocopy' or a severe form of ADHD. This adds to the findings from Chapter 3 regarding true comorbidity in the ASD+ADHD group, with reduced DT to the eyes and mouth of emotional faces in children with ASD and ASD+ADHD and, the association with reduced DT to the mouth and increased symptom severity on the SCQ.

In ADOS cartoons, exploration of faces, indexed by the FC and exploration between faces, indexed by the RC were significantly lower in the ASD and the ADHD groups compared to the typically developing control group. Visual social-emotional attention to faces in the negative emotional valence (Monkeys) cartoon was associated with social skills deficits on the SAS and communication difficulties and repetitive and stereotyped behaviours on the SCQ. Furthermore oppositional symptoms were significantly

associated with visual social-emotional attention to negative emotional valence cartoon. This contrasts with visual social-emotional attention correlates from the ADOS pictures, which correlated with ASD symptom severity on the SCQ however, oppositional symptoms did not explain significant variance over and above ASD factor.

Children with ADHD without comorbid ASD showed normal visual attention to ADOS pictures which were predominantly of positive emotional valence. In the ADOS positive and negative emotional valence cartoons there was a trend for reduced DT (indexing viewing time) to faces in the negative valence (Monkeys) cartoon in those with ADHD ($p=0.05$). Our findings are in keeping with Serrano et al. (2018) who found highest effect sizes for reduced visual attention to angry ($d=-0.73$) and scared faces ($d=-0.50$) in social scenes in children with ADHD. Pishyareh et al. (2015), however found reduced fixation latencies to pleasant versus unpleasant pictures, in children with, which differs from our findings albeit with different fixation latencies and methodology as they presented pictures stimuli side by side and did not capture attention to faces.

Additionally differences between studies could also be explained by the inclusion of children with oppositional symptoms in our study. Oppositional symptoms explained 5% of the variance to reduced DT and FC to the negative emotional valence cartoon, and these eye tracking measures were also associated with communication difficulties on the SCQ. Indeed, this association between social communication difficulties and conduct problems including oppositional behaviours in children with ADHD has been found in larger samples previously (Greene et al. 1996; Santosh and

Mijovic 2004; Mulligan et al. 2009). Furthermore, Santosh et al. (2004) also found an association with ADHD, social communication difficulties and conduct problems with relational difficulties with peers on parental report. As cartoons in our study contained interaction with characters, atypical visual social-emotional attention could be related to peer interactions (as described next).

ASD children had slower orientating, indexed by increased FFT to the perpetrator monkey face in the negative emotional valence cartoon and, as described above, ADHD children showed reduced DT to the faces (perpetrator and victim) in the negative valence (Monkeys) cartoon. Our findings on atypical visual social-emotional attention in negative valence cartoons could relate to bullying of those with ASD and, bullying of and by those with ADHD, in the context of oppositional symptoms (Chou et al. 2018; Chou et al. 2019; McQuade, Breslend, and Groff 2018). This is of interest, as it would suggest that that visual social-emotional attention differences to negative valence amongst the groups in this Thesis could relate to peer relation findings from previous literature.

Compared to findings from Chapter 3, we did not find an association with visual social-emotional attention and IQ in this study. This could be because of the free viewing task of shorter duration in this study, requiring minimal cognitive effort compared to the longer emotion recognition task in Chapter 3.

In this study, multiple linear regression showed that visual attention to ADOS images significantly accounted for 20% of the variance in the

ADOS emotion recognition score in children with ADHD, ASD and ASD+ADHD. These findings add to previous findings from Chapter 3, suggesting that increased FFT, indexing quicker orienting to non-social areas in the content dense holiday picture is associated with reduced spontaneous emotion recognition. Furthermore, slower orientating, indexed by increased FFT to faces in seems particularly specific to children with ASD as this was found in both the ADOS pictures and cartoons. As postulated in section 4.1.4, slower orientation to faces and faster orientation to non-social areas could be associated with weak central coherence, including detail focus and abilities in visual search tasks commonly found in those with ASD (Edmondson et al. 2020).

In summary, findings from this study suggest separable and shared visual social-emotional attention to ADOS pictures and cartoons amongst the groups. Slower orienting, indexed by increased FFT and reduced viewing time and exploration, indexed by DT and FC to faces in pictures associated with ASD (ASD and ASD+ADHD) and symptom severity on the SCQ. Conversely, atypical visual social-emotional attention (indexed by reduced DT, FC and RC) to faces in the negative valence (Monkeys) cartoon was associated with greater social skills difficulties on the SAS, ASD severity on the SCQ and oppositional symptoms. These findings suggest that atypical visual social-emotional attention to faces in the negative emotional valence cartoon found in ADHD is primarily associated with a combination of ASD and ODD symptoms rather than ADHD symptoms. Visual social-emotional attention to predominantly positive emotional valence

ADOS pictures specifically associated with ASD symptom severity, indicating true comorbidity with ASD in the ASD+ADHD group.

4.3.2 Limitations, strengths and future directions

Due to study time limitations, participants were subject to fewer trials (n=5) in this sample. However, this allows for more bottom-up processing and increased saliency with less habituation. Although sample sizes from this sample (n=84) are larger than Sample 1 (n=43), this sample is not big enough to look at subsamples (e.g. girls). Our findings are therefore potentially less generalisable to the whole neurodevelopmental population.

As a specific history of victimisation within participants was not available in this sample, only tentative conclusions can be made regarding peer relations and visual social emotional attention. All children had a parental DAWBA which asks about post-traumatic stress disorder (PTSD) and only one of the children met the threshold for a diagnosis of PTSD. Future studies including self-reports of trauma, for example bullying and victimisation, will also be important. Additionally, it could be conceived that findings relating the negative valence cartoons could be related to peer relations, arousal and emotional dysregulation in children with ADHD (Shaw et al. 2014; Bellato et al. 2020; Milledge et al. 2019) . Future avenues, incorporating the pupil as a measure of arousal and measures, of peer relations and emotional liability could help to uncover further insights into atypical visual social-emotional attention to the ADOS cartoons amongst the groups.

Visual social emotional-attention was measured using eye tracking to all available ADOS pictures from the 'description of a picture task' and one image for both cartoon series from the 'Cartoons' task. Due to limitations in time and laboratory equipment, eye tracking was only measured to ADOS images relating to two out of 14 ADOS tasks completed in the full ADOS examination. Future studies utilising portable eye tracking headset equipment while the full ADOS examination is being administered may provide a more accurate amount of variance explained by eye tracking variables and the ADOS scores.

It is also important to note that the ADOS emotion subscore on the ADOS does not differentiate between emotion recognition, understanding and empathy. Unfortunately, it is not possible to dissect the relationship between visual social-emotional attention and higher-order social cognitions based on the results of this study. Further studies incorporating a ToM battery of tests will help to improve understanding of the relationship of visual social-emotional attention and specific higher-order social cognitions in ADHD. In addition, visual search tasks to ascertain weak central coherence in order to strengthen the relationship with FFT, indexing speed of orienting to social versus non-social interest areas could be informative.

4.3.3 Implications

Findings of visual social-emotional attention to social-emotional scenes from ADOS images in this chapter provide further evidence that children with ASD+ADHD have true comorbidity with ASD rather than a 'phenocopy' or severe form of ADHD. In particular increased FFT, indexing

slower orientating and reduced DT and FC, indexing viewing time and exploration of faces in ADOS pictures differentiated those with ASD (ASD and ASD+ADHD) from those without ASD (ADHD and typically developing controls) and, were associated with symptom severity on the SCQ but not the Conners' rating scale. Furthermore, reduced FFT, indexing quicker orientating to non-social areas was associated with reduced spontaneous emotion recognition on the ADOS. Our findings provide some preliminary evidence for visual attention measurement during the ADOS examination assessment of ASD in the context of comorbidity with ADHD. For example, if a child with ADHD was found to have difficulties in orienting to faces in ADOS pictures this may suggest additive difficulties on the autism spectrum.

Our findings suggest that children with ADHD (without ASD) have normal face and emotion processing of positive emotional valence conditions compared with more negative ones during free viewing of ADOS images. Atypical visual social-emotional attention, indexed by reduced DT, FC to faces and reduced RC between faces in negative emotional valence cartoon was positively associated with social skills difficulties, ASD symptom severity and oppositional symptoms. This has implications for inclusion of treatments to help with social skills in children with ADHD and oppositional symptoms who may have particular difficulties with negative valence social-emotional processing.

Findings from this chapter emphasise the importance of a comprehensive assessment including ASD and oppositional defiant disorder in children presenting with ADHD in order to inform a multimodal treatment

plan (Connor, Steeber, and McBurnett 2010; Kolko, Bukstein, and Barron 1999; NICE 2018; Gillberg 2010). From a translational and formulaic perspective, these results also shed important insights into why children with ASD and ADHD may struggle in busy and complex social situations, both at a basic visual attentional level but also the potential follow on effects in relation to higher social cognitive functions and peer interactions.

Finally, atypical visual social-emotional attention to ADOS pictures is an indicator of ASD symptoms. Measuring atypical visual social-emotional attention could be a helpful adjunct to ADOS examination when assessing for neurodevelopmental conditions with social cognitive deficits. Furthermore, visual social-emotional attention measurement may have a role in those cases that are missed by standard clinical assessments or in cases where there is controversy or a second opinion is being sought.

With the exception of exploration within and between faces in ADOS cartoons reflected by FC and RC, the visual social-emotional attention profiles appear to be different in those with ADHD compared with those with ASD while ASD+ADHD show additive effects of both conditions. Findings suggest that atypical visual social-emotional attention to ADOS images could be a potential utility for differentiating the groups. Prediction of diagnoses from significant atypical visual social-emotional attention measures was tested directly using Discriminant Function Analysis in Chapter 6.

In summary, methodology in this chapter, sought to address the questions of the thesis on the association of visual attention to social scenes

from the ADOS and spontaneous emotion recognition difficulties in ADHD and, if these difficulties are primary to ADHD or ASD symptom severity. Findings suggest that atypical visual attention to ADOS images is associated with ASD symptom severity rather than ADHD symptom severity and, oppositional symptoms add to the variance over and above ASD and ADHD factors for negative valence cartoons. This extends the findings from Chapter 3 on prompted emotion recognition to faces, suggesting that spontaneous emotion recognition and social scenes from the ADOS used in clinical practice yield additional visual social-emotional difficulties amongst the groups.

5 STUDY OF VISUAL ATTENTION AND PROCESSING OF NEUTRAL FACES IN SAMPLE 2

5.1 BACKGROUND, OBJECTIVE AND RATIONALE

This chapter seeks to address the research questions of this Thesis during free viewing of neutral faces. This extends the methodology from the previous chapters by analysing visual attention and social processing to neutral faces without emotional expression. This was important to consider as visual attention to neutral faces was not tested during the emotion recognition task presented in Chapter 3. Both Chapters 3 and 4 presented findings in keeping with those with ADHD showing atypical visual attention to social-emotional stimuli, although findings could differ to social stimuli with less emotional content such as neutral faces. This may allow for further differentiation amongst the groups as, children with ASD showed reduced viewing time, indexed by DT to social compared with non-social elements of the stimulus compared to children with ADHD in Chapter 4.

As children with ADHD have been shown to be affected by the colour contrast of the stimulus (Tseng et al. 2013), the colour of the neutral face stimuli were manipulated to black and white images in order to reduce the saliency of the image due to brightness of the colours. Black and white neutral face stimuli were presented to the participants during a free viewing task in this study. Eye tracking measures, DT (Dwell Time; indexing viewing time/interest) and FC (Fixation Count; indexing exploration) to a priori interest areas as selected in Chapter 3 (right eye, left eye and mouth of

the face), were compared amongst the groups. This allowed for right eye versus left eye fixation measures of the participant to be considered in this sample as this was found to be atypical in the previous sample of children with ADHD. Although fixation duration to the right eye and the left eye viewing can provide an indication of right versus left face processing, this has produced mixed findings in the ASD literature. One study found increased fixation duration to the left eye in the left hemi field of the face (Yi et al. 2013) and another showed increased fixation duration to the right eye in the right hemi field of the face (Guillon et al. 2015) in those with ASD compared to controls. Neither of these studies discussed associated ADHD symptoms within the groups so mixed findings could be due to unknown variable ADHD comorbidity. In Chapter 3, reduced DT (Dwell Time; indexing viewing time/interest) to the right eye in emotional faces was associated with ADHD symptoms and lower IQ. Although visuospatial attention in those with ADHD has been associated with left visuospatial neglect on line bisection tasks (Manly et al. 2005), a left visuospatial neglect has not been found in ADHD when viewing faces (Klimkeit et al. 2003; Blaskey, Harris, and Nigg 2008). Unfortunately, these studies did not directly measure visual attention using eye tracking but the evidence suggests that differences in visuospatial attention in those with ADHD could be due to stimuli (e.g. social vs. non-social) and task type.

Simply testing the right eye versus left eye fixation duration may not be as accurate as the direction of fixation over the face stimulus when studying visuospatial attention and social processing amongst neurodevelopmental disorders (Guillon et al. 2015; Yi et al. 2013; Manor et al. 1999).

This could be because children with ASD have been found to have reduced fixation to the eyes as found in Chapter 3 and the literature (Chawarska and Shic 2009; Klin et al. 2002). A Laterality Index (LI), which is a measure of the number of fixations to the left versus the right, captures visuospatial attention across the whole face stimulus rather than just the eyes so this measure was also extracted for this study (Manor et al. 1999). In Chapter 3, children with ASD had a trend for increased fixations to other parts of the face so capturing direction of fixation to the whole face stimulus may improve detection of distinct attentional patterns amongst the groups. Face processing has been linked to specific neural networks that affect allocation of eye movements and, visual attention has been used to study lateral hemispheric differences in face processing in neurodevelopmental and neurotypical adult populations (Manor et al. 1999; Phillips and David 1997). More fixations to the left side of the face is suggestive of right hemisphere lateralisation bias in face processing which is typically found in right-handed adult control subjects (Butler et al. 2005).

Studies employing a chimeric face paradigm, where two halves of a face show a difference in appearance, suggest a bias to attending to the left-side of the face in typically developing children and those with ADHD (Klimkeit et al. 2003; Blaskey, Harris, and Nigg 2008). This bias in attending to the left-side of the face is not found in those at risk for ASD, suggesting that children with ASD do have the typical right hemisphere lateralisation bias during chimeric face processing tasks (Dundas et al. 2012; Dundas, Gastgeb, and Strauss 2012; Guillon, Hadjikhani, Baduel, Kruck,

et al. 2014). As these chimeric face studies have not investigated face processing amongst ASD, ADHD, ASD+ADHD and have not utilised eye tracking during face processing, this study seeks to address this gap to clarify visual attention to neutral faces amongst the groups.

Analysis of eye tracking measures between ADHD and ASD, including comorbidity using the two fixed factor approach described in Chapters 3 and 4, was used in this chapter to allow for comparison between findings amongst the studies. As findings on right eye viewing were associated with IQ on hierarchical linear regression in the previous sample in Chapter 3, a similar analysis was carried out in this study sample. The association of visual attention measures to neutral faces and to ADHD sub scores and ADOS scores was also tested to investigate the relationship between visual social processing and symptom severity sub scores in order to address the thesis questions.

5.1.1 HYPOTHESES

Based on the literature described above, more leftward fixations over the face stimulus is suggestive of right hemisphere lateralisation bias in face processing which is typically found in right-handed adult control subjects (Butler et al. 2005).

1) **ADHD**

It was hypothesised that if children with ADHD have typical face processing then they would have more leftward fixations over the face stimulus. Additionally, if children with ADHD have typical

viewing of central features of neutral faces such as the eyes, they may also have more left than right eye viewing.

However, if children with ADHD have a general right hemisphere hypofunction as described in the previous literature in Chapter 1 (section 1.5), they would have atypical visuospatial attention to neutral faces. This would lead to reduced leftward fixations over the face stimulus and reduced fixations to the left eye compared to the right eye.

2) ASD

As children with ASD have shown reduced attention to the left-side of the face in the chimeric face paradigm, it was hypothesised that children with ASD would not show more leftward fixations over the face, as is expected with typical face processing which is right hemisphere dominant. This would result in more rightward fixations over the neutral face stimulus, indexed by a positive Laterality Index in children with ASD compared to typically developing control children and children with ADHD. Based on findings from Chapter 3 and the ASD literature described in Chapter 1, it was also hypothesised that children with ASD would also have reduced fixations to the eyes in neutral faces compared to typically developing children and children with ADHD.

3) ASD+ADHD

There is a lack of literature on the comorbid group; nevertheless, it is hypothesised that if the comorbid group is more like ADHD they will have a similar profile to the ADHD group. However, if the comorbid group is more like ASD then they will have a

similar visual attention profile to that group. If the comorbid group has additive effects of both conditions, the visual attention profile will be midway between ASD and ADHD. If the comorbid group represent a distinct group with a different visual attention profile to the pure groups, this will result in an interaction of fixed factors for the dependent eye tracking variable.

5.2 METHODS

The sample of participants for this study are the same as those described in Chapter 4 (Section 4.1).

5.2.1 TASK AND EYE TRACKING PROCEDURE

The eye tracking procedure for this sample was described in Chapter 4 (Section 4.1.3). The participants viewed the ADOS images described in Chapter 4 prior to the photos of neutral faces. Stimuli for this study consisted of three photos of neutral faces (black and white; one female and two male). Stimuli were selected from the Nimstim set of faces and were resized to 5cm wide x 6.5cm height (Tottenham et al. 2009) (an example photo is shown in Figure 5.1). A central fixation cross was presented for 100ms followed by a neutral face which were then presented for 5 seconds. The participant was asked to simply look at the photo during the experiment.

5.2.2 DATA EXTRACTION

Raw eye tracking data was processed using the EyeLink 1000 plus accompanying software, EyeLink Data Viewer. The corresponding eye movement data was automatically overlaid on the corresponding images, as programmed in EyeLink software. Interest areas were created for the neutral faces (both eyes, mouth and face area; Figure 5.1). The eyes include the eye lashes and the eyebrows and the mouth includes the philtrum (Figure 5.1). The areas of interest to the eyes and mouth were designed to be large enough to allow for offsets in the data, such as head movements as described in Section 3.3.1.

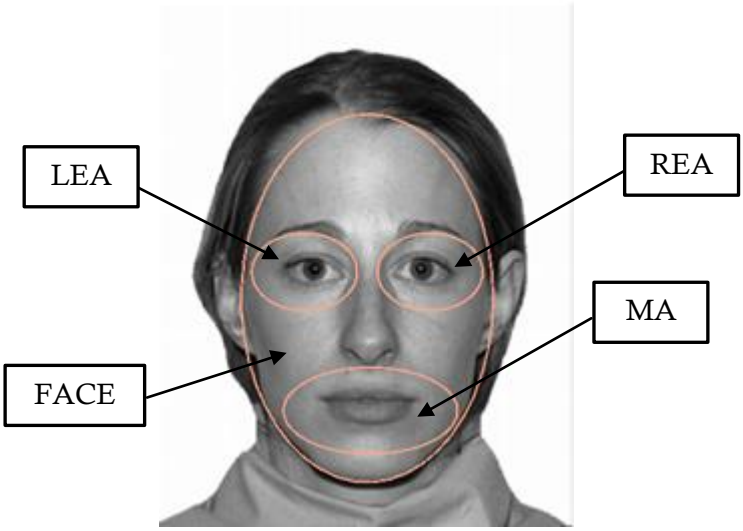


Figure 5. 1: Interest areas for neutral faces

1) Right Eye Area (REA); 2) Left Eye Area (LEA); 3) Mouth Area (MA)

Total stimuli presentation length was analysed which corresponds to 5000 milliseconds for the neutral faces. A minimum fixation duration of 100ms was set. Blink artefacts removal and eye tracking data processing was carried out as described for the ADOS images in Chapter 4 (Section

4.1.4). Pre-selected eye tracking variables were extracted using the interest area report function in EyeLink and are summarised in Table 5.1. The Trial report which gives information on individual fixation characteristics was also available.

Table 5. 1: Eye tracking measures, calculations and significance

Eye tracking measure *	Calculation	What these measures signify
Viewing Time		
1) Dwell Time (DT)	The sum of the duration of all the fixations that fell in the interest area.	Viewing time/interest to specified interest area.
Exploration		
2) Fixation Count (FC)	Total number of fixations falling in the interest area.	Exploration of specified interest area.
Additional		
3) Laterality Index (LI)**	(Nfx R – NfxL)/(NfxR + NfxL) (Number of fixations to the right minus number of fixations to the left divided by the total number of fixations)	An index of hemispheric lateralisation (a negative index=more leftward fixations associated with typical right hemisphere lateralisation in face processing)

* Eye tracking measures are defined as stipulated in the EyeLink Data Viewer manual.
** LI as stated in Manor et al. (1999).

Trial eye tracking measures were extracted for each participant as shown in Table 5.1. The mean values across stimuli were calculated for statistical analysis of the neutral face.

5.2.3 STATISTICAL ANALYSIS

A mixed design ANOVA was performed to identify effects of ASD and ADHD on DT (Dwell Time) to interest areas of neutral faces. DT was the dependent variable and interest area with three levels (right eye, left eye and mouth) was entered as the repeated measure with ASD and ADHD

entered as fixed factors. This mixed design ANOVA was also performed for dependent variables DT% (Dwell Time percentage) and FC (Fixation Count).

Univariate ANOVA was conducted to test the main effects of ADHD and ASD and the interaction between them on LI (Laterality Index) to the neutral faces. Pearson's correlation co-efficient was conducted to analyse associations between significant eye tracking variables and symptom severity subscales including the ADOS emotion recognition subscore. In order to test if IQ or oppositional symptoms had significant contributions to the dependent variable over and above ADHD and ASD factors, hierarchical linear regression was applied to the dependent variable as described in Section 3.3.2.

5.3 RESULTS

The demographic and clinical characteristics of this sample are presented in Chapter 4 (Section 4.2.1 (Table 4.2)). Raw eye tracking data and excluded trials per group are presented in Appendix VI., Table A.26. For the eye tracking analysis, excluded number of trials as described in the methods (Section 4.1.4) were not significantly different amongst the groups (F (3, 80)=2.32, p>0.05, ηp^2=0.08).

5.3.1 VIEWING TIME AND EXPLORATION OF INTEREST AREAS FOR NEUTRAL FACES

Eyes and Mouth

There was a significant effect of interest area on DT (F(1, 80)=4.68, $p<0.05$, $\eta p^2=0.06$), with a difference in DT between the eyes and the mouth (F(1, 80)=8.09, $p<0.01$, $\eta p^2=0.09$), for the children overall. This was followed up by simple effects analysis which showed that DT was significantly greater to the eye in the right visual field (mean=815.75ms) than the mouth (mean=495.77ms; $p<0.01$). There was also a significant interaction between interest area and ADHD factor (F(1, 80)=3.41, $p<0.05$, $\eta p^2=0.04$). When followed up by simple effects analysis, there was a difference in DT between the right and the left eye in those with ADHD (F(1, 80)=6.55, $p<0.05$, $\eta p^2=0.08$) and those with ADHD had less viewing time to the eye in the right visual field (mean=647.88ms) compared to those without ADHD (mean=983.62ms; F(1, 80)=4.75, $p<0.05$, $\eta p^2=0.06$), as shown in Figure 5.2. There were no other significant effects between or within subjects for the other factors.

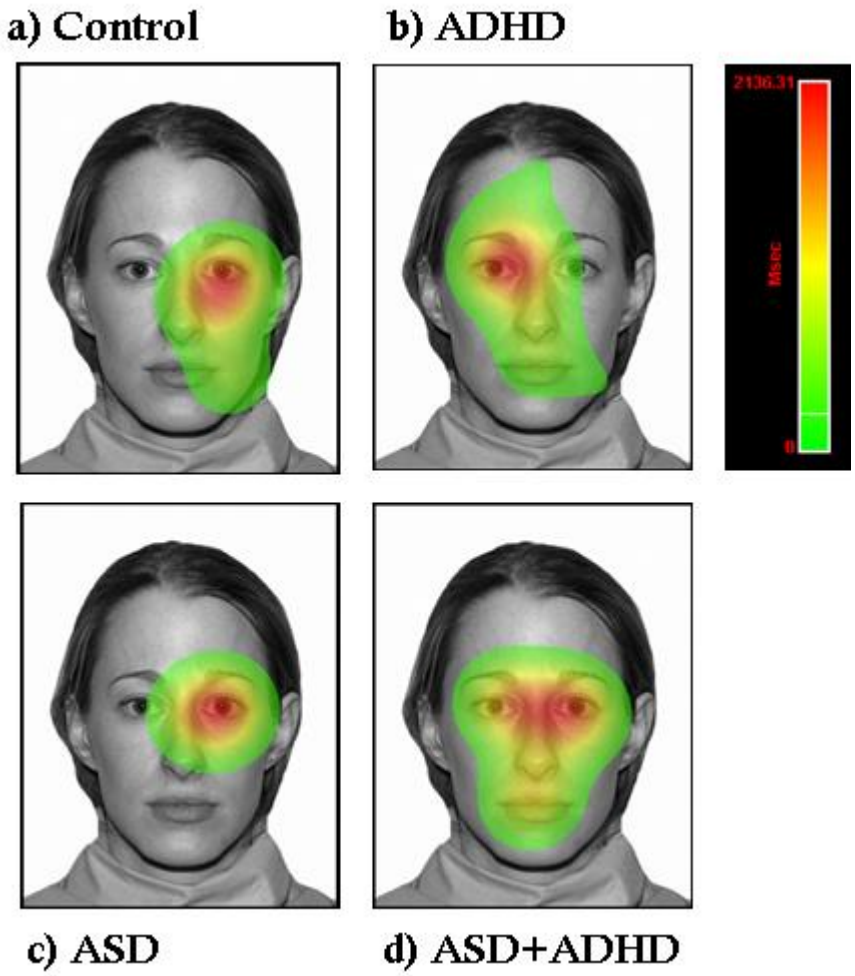


Figure 5. 2a–d): Example heat maps visualising DT to neutral faces

DT (Dwell Time) in Msec. (milliseconds); the colours of the heat map over each image denote the amount of time spent viewing areas on the image (Dwell Time). The black legend shows the colour scaling; when Dwell Time is approximately 100 milliseconds the heat map appears green over the corresponding area of the image; when the area of the heat map is red the Dwell Time is >2000 milliseconds; yellow areas of the heat map indicate Dwell Times half way between 100 milliseconds and 2000 milliseconds.

A similar pattern of effects was seen for FC. An interaction between interest area and ADHD factor $F(2, 80)=3.95$, $p<0.05$, $\eta p^2=0.05$) was found with significantly different FC between the right and left eye in those with ADHD $F(1, 80)=6.12$, $p<0.05$, $\eta p^2=0.07$) and significantly fewer FC to the right eye area (mean=1.50), compared to those without ADHD (mean=2.56; $F(1, 80)=8.77$, $p<0.01$, $\eta p^2=0.10$; see Figure 5.3).

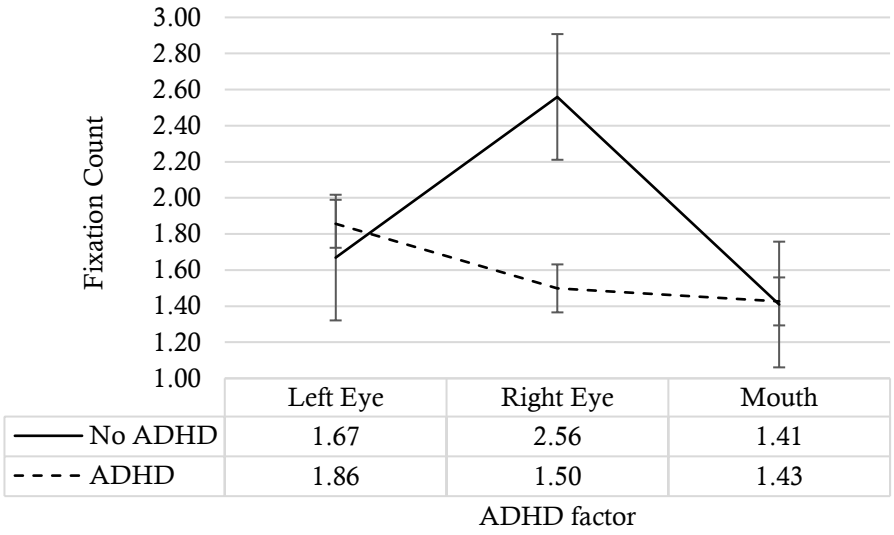


Figure 5. 3: ADHD factor on FC to interest areas on neutral faces (Error Bars=95% CI).

In summary, those with ADHD had reduced DT (Dwell Time; indexing viewing time) and FC (Fixation count; indexing exploration) to the right eye. This is consistent with results from the emotional faces in Chapter 3; showing a negative association between DT to the right eye and ADHD symptoms.

Other facial features

The same analytical model was applied to identify effects of ADHD, ASD on DT to other facial features (excluding core features: eyes and mouth) as described in section 3.4.3.1. In Chapter 3, children with ADHD (ADHD and ASD+ADHD) showed reduced DT to other facial features of emotional faces compared with children without ADHD (ASD and typically developing control children). Unlike findings from emotional faces, there was not a significant effect of ADHD on DT to other facial features versus

core features in neutral faces (F (1, 80)=0.11, p>0.05, ηp^2=0.001). This suggests that reduced DT to other facial features versus core features: eyes and mouth is specific to emotional faces in those with ADHD compared to those without ADHD.

CORRELATIONS WITH CLINICAL SYMPTOMS

Correlations between eye tracking variables to the right eye and the SCQ, SAS, ADOS and Conners' subscores were performed. DT to the right eye was significantly negatively correlated with Conners' ADHD HI subscore (r=–0.25; p<0.05), indicating that a higher severity of ADHD HI symptoms was associated with less DT to the right eye. DT to the right eye was also negatively correlated with Conners' ADHD IA subscore (r=–0.20; p=0.07), however, this did not reach significance. A similar pattern of results was found for FC to the right eye with Conners' ADHD HI (r=–0.26; p<0.05) and IA subscore (r=–0.19; p=0.08). There were no significant correlations with DT or FC to the right eye of neutral faces and SCQ, SAS or ADOS emotion recognition scores (p>0.10). These findings suggest that reduced DT and FC to the right eye of neutral faces is not associated with social cognitive deficits but rather ADHD symptom severity.

5.3.2 FACE PROCESSING AND LATERALITY INDEX (LI)

To measure direction of fixations to the whole face stimulus, a Laterality Index (LI) was computed (see Table 5.1). Univariate ANOVA was performed to identify the effects of ASD and ADHD on LI to the neutral face.

This showed a main effect of ASD on LI with a more positive LI indicating more rightward fixations in those with ASD (mean=0.01) than those without ASD (mean=–0.18; $F(1, 83)=8.13$; $p<0.01$, $\eta p^2=0.09$; Figure 5.4). There was no other significant effect or interaction between subjects for the ADHD factor.

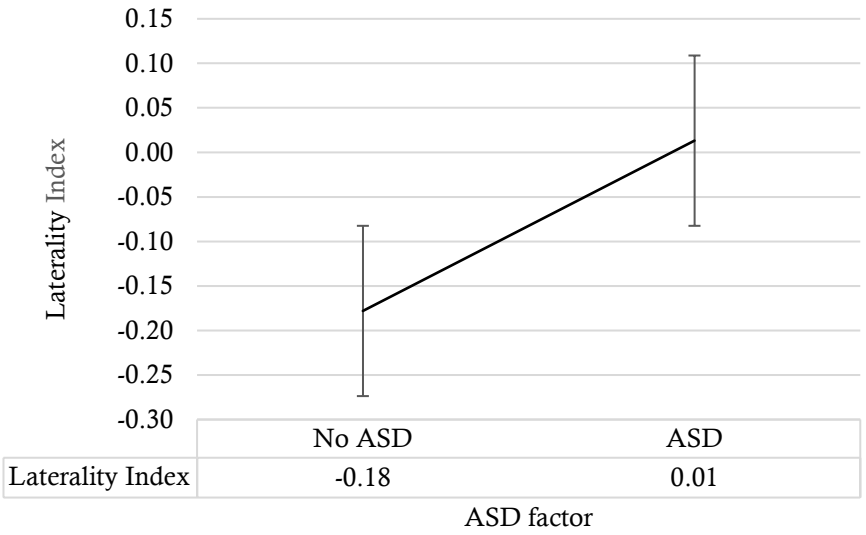


Figure 5. 4: ASD factor on LI to neutral faces (Error Bars 95% CI).

CORRELATIONS WITH CLINICAL SYMPTOMS

Correlations between LI, ADOS, SCQ, SAS and Conners' subscores were performed. A positive LI indicates a stronger rightward bias in fixations and is associated with atypical face processing. This correlated significantly with all the SCQ subscales (repetitive stereotyped behaviours ($r=0.31$; $p<0.01$), communication ($r=0.25$; $p<0.05$), social reciprocal interaction ($r=0.33$; $p<0.01$)), Conners' HI subscore ($r=0.25$; $p<0.05$), and the SAS ($r=0.25$; $p<0.05$). The LI also correlated with the Conners' IA subscore

(r=0.20; p=0.08), but this did not reach significance. A positive LI, indicating a stronger rightward bias in fixations also correlated significantly with more impaired ADOS emotion recognition subscore (r=0.29; p<0.05). This later finding may suggest rightward bias in the direction of fixations which is indicative of atypical neutral face processing could be associated with reduced spontaneous emotion recognition and understanding.

Overall, these correlations suggest that increased ASD symptom severity on the SCQ and increased hyperactive-impulsive symptoms are associated with a positive LI, indexing atypical face processing. Atypical face processing could therefore be important in comorbidity between ASD and ADHD.

5.3.3 HIERARCHICAL REGRESSION

In order to test if IQ / oppositional symptoms had significant contributions to the dependent variable, over and above ADHD and ASD factors, hierarchical linear regression was applied to the dependent variable as described in Section 3.2.2. In order to reduce the number of linear regression models, only significant variables presented in Section 5.3.1 and 5.3.2 were entered as the dependent variable for each analysis. For all eye tracking variables tested, neither IQ nor ODD symptoms explained a significant amount of the variance over and above ADHD or ASD factors. Hierarchical linear regression model results tables for each dependent variable were presented in the Appendix Section A.V.

5.4 DISCUSSION

Automatic orienting of visual attention to neutral faces in children with ADHD, ASD, ADHD+ASD and control children revealed differences among the groups using a 2x2 factorial approach. Those with ASD (ASD and ASD+ADHD) showed a stronger rightward bias in fixations (positive Laterality Index; LI) to neutral face stimuli compared to those without ASD (ADHD and controls). Furthermore, a stronger rightward bias in fixations is an indicator of atypical face processing (positive LI) was associated with both increased ASD symptom severity and ADHD HI symptoms. These findings suggest that a positive LI, indicative of atypical face processing could be important in comorbid ASD and ADHD.

Conversely, those with ADHD (ADHD and ASD+ADHD) showed reduced FCs to the right eye compared to those without ADHD (ASD and controls). As increased FCs to the right eye were associated with reduced ADHD hyperactive-impulsive symptoms, exploration of the right eye in neutral faces could be an important measure in differentiating ADHD from ASD. Taken together, this suggests differences in the neutral face processing between ADHD versus ASD and when considering comorbidity, direction of fixations to the face stimulus in addition to fixation to either eye is important.

5.4.1 COMPARISON WITH FINDINGS FROM OTHER STUDIES

Our findings regarding a stronger rightward bias in fixations, indexing atypical face processing of neutral faces in ASD are in keeping with chimeric face studies in children with ASD (Dundas et al. 2012; Dundas,

Gastgeb, and Strauss 2012; Guillon, Hadjikhani, Baduel, Kruck, et al. 2014). Chimeric face studies suggested reduced attention to the left of the face is indicative of reduced typical right hemisphere processing of faces in ASD. In our study, as children with ADHD (without ASD) and typically developing controls showed more leftward direction of fixations; this would be in keeping with typical right hemisphere face processing found in adults (Butler et al. 2005) and ADHD (Klimkeit et al. 2003; Blaskey, Harris, and Nigg 2008). However, we also found reduced right eye fixation in those with ADHD (ADHD and ASD+ADHD) compared to those without ADHD (ASD and controls), suggesting that visual attention to neutral faces is not typical in ADHD. One possible explanation for this finding of reduced fixation to the right eye in ADHD could be due to compensation of focus on the left of the face. As shown in Chapter 2, children with ADHD had more linear patterns of eye gaze (from left eye to mouth) with less triangulations between the eyes and the mouth. In order to 'preserve typical face processing' in relation to leftward fixations to the face, this could lead to reduced right eye looking in ADHD. As we also found increased fixation to the right eye was associated with reduced hyperactive-impulsive symptoms, the association of hyperactive-impulsive symptom severity and atypical visual attention to neutral faces in ADHD seems plausible. As reduced visual attention to the right eye, indexed by (DT; Dwell Time and FC: Fixation Count) was not associated with spontaneous emotion recognition on the ADOS, social skills severity on the SAS or ASD symptoms severity, this suggests that atypical visual attention to the right eye of neutral faces is not associated with social cognitive deficits or ASD

symptoms. Atypical processing of faces indexed by more rightward fixations over the face stimulus was however indicative of reduced spontaneous emotion recognition, social skills deficits on the SAS, ASD symptom severity and ADHD HI symptoms. This suggests that atypical face processing is primarily associated with ASD symptoms and social cognitive deficits, however the combination with ADHD HI symptoms may also play a role.

In this study we did not find an association of IQ and right eye fixation as was found in the sample presented in Chapter 3. Furthermore, children with ASD did not show reduced fixation to eyes and mouth in this study compared with the study presented in Chapter 3. In this study, children viewed black and white neutral faces without any prompt to name an emotion. However, in Chapter 3, children viewed colourful emotional faces with a prompt to name the emotion. Differing results between the studies could be related to the task type and potentially confined to the requirement to judge the emotional content of faces.

5.4.2 LIMITATIONS, STRENGTHS AND FUTURE DIRECTIONS

Due to study time limitations, participants were subject to fewer trials (n=3) in this sample. Although this allows for more bottom-up processing and increased saliency with less habituation, direct comparison with findings from Sample 1 are difficult as this contained 60 trials. Also, even though sample sizes from this sample (n=84) are larger than Sample 1 (n=43), different tasks were carried out in the two samples so direct comparison is somewhat hindered. Future studies looking at different tasks;

neutral and emotional, scrambled versus non-scrambled faces during free viewing and emotion recognition prompting tasks in the same sample are warranted to allow for direct comparison amongst the tasks, allowing for inferences to be strengthened.

5.4.3 IMPLICATIONS

Our findings in relation to neutral faces suggest that ADHD and ASD have differing face processing which could be related to differences in brain lateralisation between these disorders. Those with ADHD+ASD seem to have additive effects of both disorders suggesting pure comorbidity. Although atypical visual attention to the right eye was not associated with spontaneous emotion recognition or ASD symptom severity, atypical face processing indexed by increased rightward fixations was. Furthermore, fixations to the right eye and direction of fixations over the face stimulus seem to have different discriminatory patterns amongst the groups. This chapter has extended the work of the previous chapters by answering the thesis questions in relation to visual attention to neutral faces. Prediction of diagnoses from visual attention measures was tested directly using discriminant function analysis in the next chapter.

6 PREDICTION OF DIAGNOSES USING DISCRIMINANT FUNCTION ANALYSIS

6.1 OVERVIEW

The objective of this chapter was to test which eye tracking measures, indexing visual social-emotional attention best classified the groups and if this method could show potential as a diagnostic aid in clinical assessment. In this chapter, discriminant function analysis (DFA) was be used to predict the characterisation of diagnoses (ADHD, ASD, ASD+ADHD and controls) from significant quantitative eye tracking measures presented in the previous chapters. The results from each sample are presented separately. The last section includes a summary comparing results from DFA with machine learning approaches (as illustrated in Chapter 2). This chapter sought to extend the findings in this thesis in order to address the final question of the thesis on whether visual attention differentiates the groups on emotion recognition and social processing tasks.

6.2 STATISTICAL ANALYSIS

DFA was used to test predictability of diagnoses from significant eye tracking variables, indexing visual attention for each sample: Sample 1 from Chapter 3 (Sections 3.4.3.1, 3.4.3.2) and, Sample 2 from Chapter 4 (Sections 4.2.2 and 4.2.3) and Chapter 5 (Sections 5.3.1 and 5.3.2). Significant eye tracking variables were entered as the independent variables and diagnoses, with four levels (0=controls, 1=ADHD, 2=ASD, 3=ASD+ADHD) entered as the dependent grouping variable.

6.3 RESULTS 1: EMOTIONAL FACES IN SAMPLE 1

Significant eye tracking variables, indexing visual attention from Sample 1 in Chapter 3 were entered as the independent variables and diagnosis was entered as the grouping variable in the DFA. The independent variables and how they load onto the three functions are shown in Table 6.1.

Function 1 was significant (χ^2=30.00; $p<0.05$) and explained 81.3% of the variance. Function 2 (χ^2=7.10; $p>0.05$) and 3 (χ^2=1.70; $p>0.05$) were not significant explaining 14.5% and 4.2% of the variance respectively and are shown in the table for completeness. As shown in Table 6.1, DT to other areas of the face and mean fixation duration to the face stimuli were positively associated with the first discriminant function. However, DT to the mouth; total fixation number to the face; mean length between fixations; and fixation scanpath length over the face were negatively associated with the first discriminant function (Table 6.1). As the first function is positively associated with ASD and negatively associated with ADHD (see Table 6.2), these findings complement the findings from Chapter 3 which showed significantly reduced DT to other facial features in those with ADHD and a trend for increased DT to other facial features in those with ASD.

Table 6. 1: Loading of significant variables onto discriminant function (Sample 1)

Variable	Function		
	1	2	3
DT to other facial features	0.57*	0.12	0.09
DT to the mouth	−0.19	0.62*	−0.45
Mean FD to the face stimuli	0.31	0.39*	−0.38
Total FN to the face stimuli	−0.29	−0.31*	0.25
Mean LBF to face stimuli	−0.37	0.18	0.69*
Fixation SP length over face stimuli	−0.44	−0.15	0.55*

DT (Dwell Time); FD (Fixation Duration); FN (Fixation Number); LBF (Length between Fixations); SP (Scanpath); * Largest absolute correlation between each variable and any discriminant function. Significant function is shown in black.

As shown in Table 6.2, group mean scores for Function 1 differed the most for ASD (mean score=1.25) compared with ADHD (mean score=–1.44), with scores for controls and the ASD+ADHD group, mid-way on Function 1 (Table 6.2). This data is also shown graphically in Figure 6.1 with the group centroids for ASD and ADHD being most dispersed on the horizontal axis (Function 1; Figure 6.1).

Table 6. 2: Group mean scores on discriminant function (Sample 1)

Group	Function		
	1	2	3
Controls	0.21	0.52	0.05
ADHD	−1.44	−0.10	−0.26
ASD	1.25	−0.34	−0.14
ASD+ADHD	−0.49	−0.38	0.35

Significant function is shown in black.

Combining all these results suggests that ASD is positively associated with viewing time to other facial features and total fixation duration but, negatively associated with viewing time to the mouth; exploration of faces; mean length between fixations; and fixation scanpath length over face stimuli. The opposite pattern is found in those with ADHD on Function 1 (Tables 6.1 and 6.2). Those with ASD+ADHD have a mean group score midway between the ASD and the ADHD group although they are closer to the ADHD group than the ASD group on Function 1 (Table 6.2 and Figure 6.1).

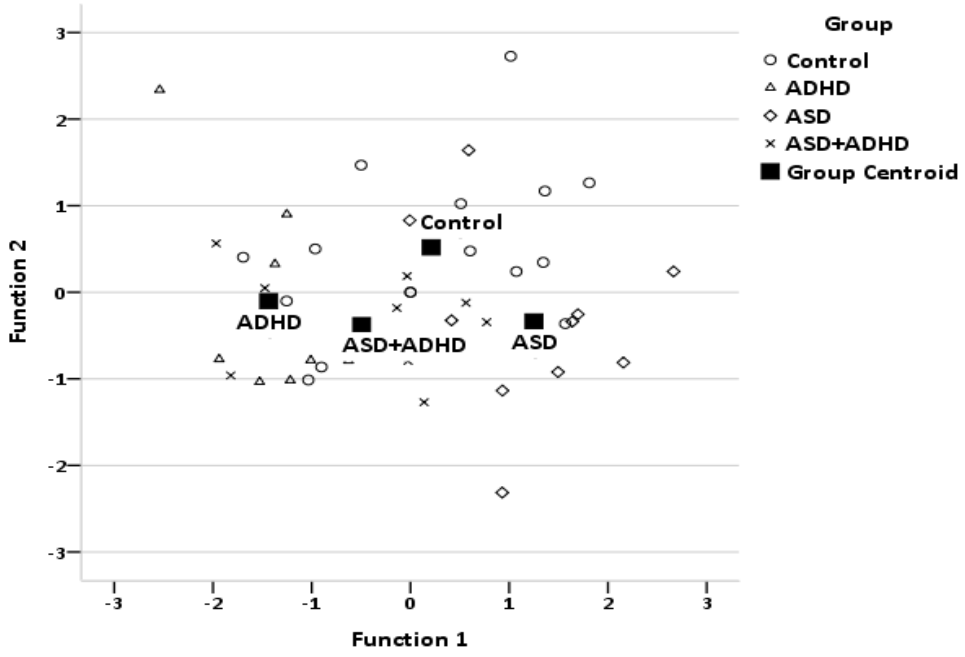


Figure 6. 1: Group centroids (mean group scores) and individual participant scores on discriminant function (Sample 1)

Prediction of diagnostic group based on the discriminant function are shown in Table 6.3. 58.1% of original grouped cases were correctly classified overall. Discrimination was particularly strong for ADHD which

were correctly classified in 87.50% of cases with 12.50% of cases being misclassified as ASD+ADHD. Classification for ASD was also effective with 80.00% of cases being correctly classified and 20.00% being misclassified as controls but none being misclassified as either ASD+ADHD or ADHD (Table 6.3).

Table 6. 3: Prediction of diagnostic group based on discriminant function

		Predicted Group Membership			
	Group	Control	ADHD	ASD	ASD+ADHD
Original	Control	**43.75**	18.75	25.00	12.50
	ADHD	0.00	**87.50**	0.00	12.50
	ASD	20.00	0.00	**80.00**	0.00
	ASD+ADHD	22.22	33.33	11.11	**33.33**

Classification rates are shown as percentage rates. Correct % classification per group is shown in bold.

Prediction of controls and ASD+ADHD was less efficient with 43.75% being correctly classified as controls and 33.33% being correctly classified as ASD+ADHD (Table 6.3). As scores for these groups were midway on Function 1 and the other Functions (2 and 3) were not significant, the ability to discriminate controls and ASD+ADHD is not as strong as ASD compared with ADHD which show the most discriminating pattern of visual attention to the emotional faces.

6.4 RESULTS 2: ADOS IMAGES AND NEUTRAL FACES IN SAMPLE 2

Significant eye tracking variables from Sample 2 in Chapters 4 and 5 were entered as the independent variables and diagnosis was entered as the

grouping variable in the DFA (as described in Section 6.2). The independent variables and how they load onto the three functions are shown in table 6.4.

Function 1 was significant (χ^2=56.50; p<0.01) and explained 44.2% of the variance. Function 2 was also significant (χ^2=32.32; p<0.05) and explained 29.9% of the variance. Function 3 approached significance (χ^2=15.12; p=0.09) and explained 25.9% of the variance (see Table 6.4).

Table 6. 4: Loading of variables onto discriminant functions (Sample 2)

Variable	Function		
	1	2	3
FC to right eye in neutral faces	0.56*	–0.11	–0.13
FC to faces in Holiday picture	0.44*	–0.43	0.21
FC to victim face in Monkeys cartoon	0.43*	–0.30	0.03
FC to man face in Cat cartoon	0.27*	–0.27	0.23
FFT to faces in Hollywood picture	–0.02	0.57*	–0.26
LI to neutral faces	–0.18	0.55*	0.30
DT to faces in Holiday picture	0.30	–0.53*	0.19
DT to faces in Meal picture	0.14	–0.47*	0.05
DT to non-social areas in Meal picture	0.29	–0.11	0.46
FC to non-social areas in Holiday picture	–0.09	–0.14	–0.34
DT to non-social areas in Holiday Picture	–0.18	–0.15	–0.23

FC (Fixation Count); DT (Dwell Time); FFT (First Fixation Time); LI (Laterality Index);
* Largest absolute correlation between each variable and any discriminant function. Significant Functions are shown in black.

As shown in Table 6.4, FC (exploration) to the right eye and faces in the ADOS images was associated with Function 1. Slower FFT (orientation) to faces and LI (more rightward fixations) was positively associated with Function 2 while DT (viewing time) to faces in the ADOS pictures was negatively associated with Function 2. Although just short of significance, DT (viewing time) and FC (exploration) of non-social areas in ADOS pictures was associated with Function 3.

As shown in Table 6.5, group mean scores differed the most for controls (mean score=0.83) compared with ADHD (mean score=–0.97) with scores for ASD and ASD+ADHD group midway on Function 1 (Table 6.5). This data is also shown graphically in Figure 6.2 with group centroids for Controls and ADHD being most far apart on the horizontal axis (Function 1; Figure 6.2).

Group mean scores differed the most for ASD (mean score=0.69) compared with ADHD (mean score=–0.61) with scores for controls and ASD+ADHD group midway on Function 2 (Table 6.5). This data is also shown graphically in Figure 6.2 with group centroids for ASD and ADHD being most far apart on the vertical axis (Function 2; Figure 6.2).

Table 6. 5: Group mean scores on discriminant functions (Sample 2)

Group	Function		
	1	2	3
Controls	0.83	–0.46	–0.02
ADHD	–0.97	–0.61	–0.31
ASD	0.09	0.69	–0.64
ASD+ADHD	–0.20	0.28	0.59

Significant Functions (1 and 2) are shown in black.

Combining these results for Function 1 suggests that controls are positively associated with exploring the right eye on neutral faces and exploring faces in the Holiday picture and victim faces in the cartoons. The opposite pattern is found in the ADHD group on Function 1 (Tables 6.4 and 6.5). Those in the ASD group appear to have a mean group score midway between the control group and the ADHD group on Function 1. The ASD+ADHD group appear midway between the ADHD group and the ASD group, albeit slightly closer to the ASD group on Function 1 (Table 6.5 and Figure 6.2).

Combining all these results for Function 2 suggests that the ASD group is positively associated slower orientation to faces in the ADOS picture and more rightward fixations on neutral face stimuli and negatively associated with viewing time to faces in the ADOS pictures. The opposite pattern is found in the ADHD group on Function 2 (Tables 6.4 and 6.5). Those in the ASD+ADHD group are closer to the ASD group than the ADHD group on Function 2. The control group are closer to the ADHD group than the ASD group on Function 2 (Table 6.5 and Figure 6.2).

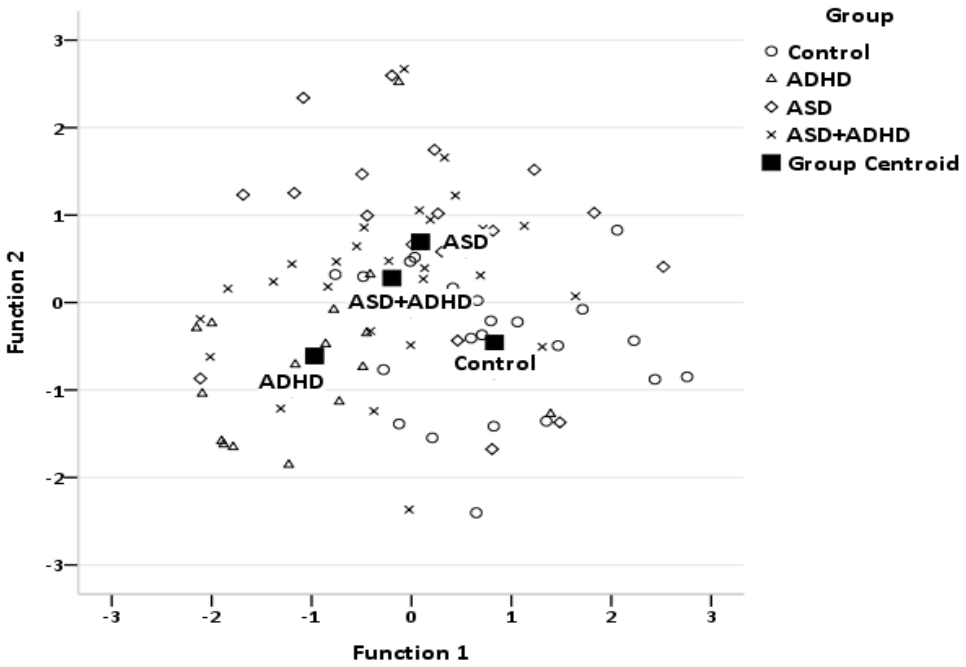


Figure 6. 2: Group centroids (mean group scores) and individual participant scores on discriminant functions (Sample 2)

Prediction of diagnostic group based on the discriminant functions are shown in Table 6.6. 64.3% of original grouped cases were correctly classified overall. Discrimination was strongest for ADHD which was correctly classified in 81.25% of cases with 12.50% of cases being misclassified as ASD and 6.25% as controls. None of the ADHD group were misclassified as ASD+ADHD (Table 6.6). Classification of the other clinical groups was reasonable with 61.11% of the ASD group being correctly classified and 60.71% of the ASD+ADHD group being correctly classified. 5.56% of the ASD group and 14.29% of the ASD+ADHD group were misclassified as ADHD. Correct classification for controls was 59.09% with 22.73% misclassified as ASD, 9.09% misclassified as ADHD and 9.09% misclassified as ASD+ADHD (Table 6.6).

Table 6. 6: Prediction of diagnostic group based on discriminant functions (Sample 2)

		Predicted Group Membership			
Original	Group	Controls	ADHD	ASD	ASD+ADHD
	Controls	**59.09**	9.09	22.73	9.09
	ADHD	6.25	**81.25**	12.50	0.00
	ASD	22.22	5.56	**61.11**	11.11
	ASD+ADHD	10.71	14.29	14.29	**60.71**

Classification rates are shown as percentage rates. Correct % classification per group is shown in bold.

6.5 SUMMARY AND DISCUSSION OF FINDINGS

6.5.1 SUMMARY OF MAIN FINDINGS

In summary, for Sample 1, the eye tracking measures, indexing visual attention that were loaded onto Function 1 and discriminated ADHD from ASD the most were related to extensive versus restrictive scanpaths respectively over emotional faces. In Sample 2, eye tracking measures, indexing visual attention that were loaded onto Function 1, discriminated ADHD from controls best and variables that loaded onto Function 2 discriminated ADHD from ASD the most. In Sample 2, the variables from Function 1 suggested reduced exploration (indexed by FC: Fixation Count) to social-emotional stimuli in ADHD compared to controls. The variables from Function 2 suggested quicker orientation (indexed by FFT: First Fixation Time), longer viewing time (indexed by DT: Dwell Time) and left visual field bias (indexed by a negative LI: Laterality Index with more leftward fixations) for faces in ADHD compared to ASD. Thus, the visual attention

profile for those with ADHD differs from those with ASD; with slower orientation and atypical processing of faces which could be related to local detailed focused processing in those with ASD.

Characterisation of diagnoses across both samples was good for ADHD (81–88%). Characterisation for ASD was between 61–80% across both samples. Characterisation for ASD+ADHD was more variable across both samples using DFA (33–61%). Findings should be interpreted with caution as the same variables should ideally be tested in a new sample using DFA.

Both samples had eye tracking variables loading onto significant discriminant functions which showed opposing patterns in the ADHD group versus ASD group. This finding is in line with one of the main arguments of the Thesis—that ADHD and ASD have differing visual social-emotional attention profiles (see Section 1.1.2).

On discriminant function analyses, the ASD+ADHD group appeared to be more similar to the ADHD group in Sample 1 but more like the ASD group in Sample 2, suggesting that both tasks could help to discriminate the ASD+ADHD group. As both tasks were not statistically tested in the same sample, caution should be taken when interpreting these results. Findings should therefore be considered preliminary until replication in future studies with larger sample sizes have been conducted, as discussed further in Section 7.3.

The ASD+ADHD group shows similar visual social-emotional attention profile to both pure groups, depending on task type and therefore

both visual social-emotional attention deficits across both samples. This is an important addition to the literature as few eye tracking studies have reported on combined ASD+ADHD diagnoses. Overall, these findings for the ASD+ADHD group suggested that this group have additive features of ADHD and ASD which is in line with a 'true' comorbidity model.

6.5.2 Comparison with findings from other studies

As few eye tracking studies have given both ADHD and ASD classification predictions based on visual social-emotional attention within the same sample, it is difficult to compare our findings directly. Our results are similar to eye tracking literature reporting either disorder for example, Frazer et al have shown accuracies of 86% for ASD compared with controls for visual social attention to dynamic stimuli (Frazier et al. 2018). Tseng et al have reported accuracies of 80% for ADHD (compared with controls and foetal alcohol syndrome) using eye tracking while viewing videos (Tseng et al. 2013). This suggests our predictions of ASD diagnosis and ADHD diagnosis from static stimuli are similar to those found in the eye tracking literature using dynamic stimuli.

6.5.3 Interpretation of findings

As shown in Chapter 2, detailed face processing sequencing using machine learning showed accuracies of up to 84% in the ASD+ADHD group. This supports the use of machine learning approaches for more complex co-occurring disorders compared to DFA. Additional use of clinical scales such as Conners' and SCQ are also likely to improve prediction of diagnoses

and be more akin to the use of eye tracking measures, indexing visual social-emotional attention as a diagnostic aid in clinical practice.

6.5.4 Limitations

Findings should be interpreted cautiously as the same variables should ideally be tested in a new sample using DFA. A major limitation is the small sample sizes especially for Sample 1 which only had 1 significant discriminant function. Replication in a larger sample across all social-emotional stimuli (ADOS images, emotional and neutral faces) and task type (direct emotion recognition request and free viewing) would be required before firm conclusions can be made.

6.5.5 Implications

Prediction of ASD and ADHD using eye tracking measures, indexing visual social-emotional attention could be helpful as a diagnostic aid during assessment of more complex cases such as Case 3 from the case vignettes (see Appendix I.). As eye tracking tasks can be completed in less than 5 minutes, these measures could help with assessment by improving efficiency, reducing the time to make comorbid diagnoses.

In the next chapter, synthesis of the overarching themes and use of eye tracking measures, indexing visual social-emotional attention in research and practice will be discussed. The discussion chapter will also contain a more detailed account of the limitations of the project.

7 DISCUSSION

The core problem that this project sought to address is a common clinical issue encountered in children, young people and families with ADHD. Children with ADHD presenting to clinical services often have observed impairing social cognitive difficulties including poor emotion recognition. The aim was to understand if these emotion recognition difficulties were a primary consequence of ADHD, linked to patterns of visual social-emotional attention or alternatively, social processing difficulties typically found in autism. The findings of this research have implications for the diagnosis and the management of ADHD and associated social impairments.

The proposal of this Thesis was that the study of visual social-emotional attention using eye tracking in ADHD would uncover important insights into social-emotional difficulties including emotion recognition and comorbidity with ASD. In particular, it was argued that visual social-emotional attention in children with ADHD could help to explain emotion recognition difficulties and could distinguish difficulties from ASD. The main hypothesis of this Thesis was that the visual social-emotional attention profile would differ between those with ADHD compared with those with ASD. Furthermore, it was hypothesised that those children with true comorbidity would show a combination of visual social-emotional attention problems from both pure disorders.

Through two novel empirical studies, this Thesis demonstrated that the measurement of visual social-emotional attention using eye-tracking in ADHD can:

1) identify emotion recognition deficits and social processing in children and young people with ADHD;
2) identify important similarities and differences compared with ASD and ASD+ADHD, shedding insights into comorbidity;
3) offer potential as a diagnostic aid characterising ADHD, ASD and ASD+ADHD groups.

Chapter 3 in particular presented results showing that visual social-emotional attention to emotional faces differed in those with ADHD (ADHD and ASD+ADHD) compared to those without ADHD (ASD and typically developing controls). Children with ADHD showed atypical 'hyper-extensive' scanning of emotional faces which was associated with reduced emotion recognition accuracy. Furthermore, reduced Dwell Time (DT, indexing viewing time) to other facial features was associated with poor social skills measured on the SAS and ADHD symptom severity but not ASD symptom severity. These findings are interesting as they suggest poor social skills are linked to atypical visual social-emotional attention primarily due to ADHD symptoms rather than ASD symptoms severity on a prompted emotion recognition task. This in part answers the main questions of thesis; that atypical visual social-emotional attention in ADHD in associated with ADHD symptoms severity, poor emotion recognition and, social skills deficits. Thus, suggesting that social skills difficulties in ADHD are secondary to ADHD symptoms rather than ASD. However, as emotion recognition was prompted on this task in Chapter 3, spontaneous emotion recognition on the ADOS was compared amongst the groups in Chapter 4.

Chapter 4 presented results from the second sample which showed many differences but some similarities in visual social-emotional attention to social scenes from ADOS images in those with ADHD compared with ASD in the context of spontaneous emotion recognition. Of note, results suggested slower orientation, indexed by FFT to faces in the ADOS images in those with ASD (ASD and ASD+ADHD) compared to those without ASD (ADHD and controls). Children with ADHD (without ASD) did not show slower orientation, indexed by FFT to faces in ADOS images, however suggesting that slower FFT to faces is primarily mediated by ASD. Furthermore, spontaneous emotion recognition on the ADOS was associated with atypical orienting and ASD. Findings relating to negative emotional valence cartoon however, showed that atypical visual social-emotional attention was associated with ASD and oppositional symptoms in those with ADHD. This suggest that spontaneous emotion recognition was associated with ASD and oppositional symptom severity rather than ADHD symptoms in ADHD which, contrasts with prompted emotion recognition in Chapter 3.

In Chapter 5, findings with a neutral face in children with ADHD (ADHD and ASD+ADHD) showed reduced viewing time (indexed by DT; Dwell Time) and exploration (indexed by FC; Fixation Count) to the right eye compared to those without ADHD (ASD and typically developing control children). Although atypical visual attention to the right eye was associated with ADHD symptom severity, there were no association with indices of social skills difficulties including spontaneous emotion recognition. Conversely, children with ASD (ASD and ASD+ADHD) showed increased

rightward direction of fixation (positive LI) which was associated with more difficulties on the ADOS emotion recognition subscore in the clinical groups. This suggests that the visual social-emotional attention indicative of atypical neutral face processing is related to performance on the ADOS. These findings provide some further preliminary evidence in favour of visual social attention measurement alongside the ADOS examination for the assessment of ASD in the context of comorbidity with ADHD.

Chapter 6 presented the results from discriminant function analysis including prediction of diagnoses from the visual social-emotional attention measures that yielded statistically significant effects in the factorial analyses presented in Chapters 3–5. Overall, those with comorbid ASD+ADHD showed a visual social-emotional attention profile in keeping with both pure groups suggesting true comorbidity although on some measures they were more similar to the ADHD group and on others were more similar to the ASD group; possible reasons for this will be discussed below. An overarching theme that emerged across the chapters was atypical laterality of visual attention to social-emotional stimuli and this showed reasonable discriminatory potential between the groups. Findings from discriminant function analysis gave the most accurate prediction for ADHD diagnosis, with classification rates in the region of 81–88% across both samples. These findings provided further evidence of discrimination of visual social-emotional attention in ADHD from typically developing children, ASD and comorbid children; addressing the final question of this thesis.

The purpose of this chapter was to bring together the main results from the previous chapters, presenting a visual social-emotional attention

profile that characterises ADHD and to place this in the context of existing literature. As highlighted in the literature review in Chapter 1, at the time of writing there was a lack of comparative studies of visual social-emotional attention using eye tracking in ADHD with ASD and comorbid ASD+ADHD. This chapter demonstrates how this Thesis addresses this gap, contributing to the study of visual social-emotional attention using eye tracking in neurodevelopmental disorders and enhancing scientific understanding of visual attention in relation to emotion recognition deficits in ADHD, ASD and ASD+ADHD.

As detailed in Chapter 1, the three main research questions of the Thesis are:

1) Is there an association between emotion recognition deficits in ADHD and visual attention to social-emotional stimuli?
2) Can visual attention to social-emotional stimuli clarify if emotion recognition deficits in ADHD are primary to ADHD or secondary to co-occurring ASD?
3) Does visual attention, indexed by eye tracking measures differentiate ADHD, ASD and ASD+ADHD on emotion recognition and social processing tasks?

The broad aim of the Thesis was to answer these three research questions. This chapter begins with a discussion of the main findings summarised in line with the main hypotheses and then the research questions with reference to the current literature. An evaluation of visual social-emotional

attention using eye tracking as a potential diagnostic aid in neurodevelopmental assessment and clinical relevance of the findings is then presented. The limitations of the project and future research avenues are also discussed. Final conclusions are drawn regarding visual social-emotional attention as a potential explanation for social-emotion difficulties in ADHD including the impact of ASD.

7.1 SUMMARY AND INTERPRETATION OF MAIN FINDINGS

Table 7.1 shows a summary of the main quantitative findings across Chapters 3–5 in terms of whether the main effects of ADHD, ASD and the ADHD*ASD interaction was significant on each measure. As a 2x2 factorial approach was used, a main effect of ADHD denotes a significant difference in children with ADHD (ADHD and ASD+ADHD) compared to children without ADHD (ASD and typically developing controls). Conversely, a main effect for ASD denotes a significant difference in children with ASD (ASD and ASD+ADHD) compared to children without ASD (ADHD and typically developing controls). Additionally, an ADHD*ASD interaction suggests the comorbid group differs from the pure group(s).

As shown in Table 7.1, a visual social-emotional attention profile in ADHD begins to emerge across the studies which differs from ASD. In the following sections, these findings are described and discussed. It is important to note that the visual social-emotional attention profile of those with ADHD and those with ASD showed links to their clinical

profile. Examples of how the visual social-emotional attention profile linked to the clinical profile are given throughout the discussion with reference to the Case Vignettes (detailed in the Appendix. I) and summarised in the clinical practice implications Section 7.4.3). This section provides an overview and interpretation of the main findings in the context of the literature. The findings are divided into two sections, the first presents interpretations from face stimuli and the second section presents findings from the ADOS images.

Table 7. 1: Summary of main findings

Task (Chapter; sample size)		**Measure**		**Main effect (fixed factors)†**		
Stimulus	**Measure name**	**Description of measure calculation**	**Interpretation of measure**	**ADHD**	**ASD**	**ASD* ADHD**
Emotional Faces (Chapter 3; n=41)	Emotion recognition (%)	Correct emotion selected (accuracy)	Explicit emotion recognition	↓	n/s	n/s
	DT to eyes+mouth	Sum of FD to eyes + mouth	Viewing time/saliency of eyes+mouth	n/s	↓	n/s
	DT to other areas of face	FD to face – (eyes + mouth)	Viewing time/saliency of facial creases	↓	↑ (trend)	n/s
	TFN	Sum of the number of fixations	Temporal face scanning	↑ (trend)	n/s	↓*
	MFD	Average FD		↓	n/s	n/s
	FSPL	Sum of total distances from fixation to fixation	Spatial face scanning	↑	n/s	n/s
	MLBF	Average distance between fixations		↑	n/s	n/s
ADOS (Chapter 4; n=59)	ADOS emotion recognition subscore**	< Comments on others emotions	< Spontaneous emotion recognition	n/s	n/s	-
Neutral Faces (Chapter 5; n=84)	DT to eyes+mouth	FD to eyes + mouth	Viewing time/saliency of eyes+mouth	n/s	n/s	n/s
	DT to other areas of face	FD to face – (eyes + mouth)	Viewing time/saliency of facial creases	n/s	n/s	n/s
	DT to right eye	FD to right eye	LHS bias for right eye viewing	↓	n/s	n/s
	LI	(Right fixations – left fixations)/total no	>Right fixations suggests LHS bias	n/s	↑	n/s
Faces in ADOS Pictures (Chapter 4; n=84)	DT	FD to faces	Viewing time/Saliency of faces	n/s	↓	n/s
	FC	Sum of fixation number in faces	Exploration of faces	n/s	↓ (trend)	n/s
	FFT	Time to first fixation to a face	Slower to orientate to faces	n/s	↑ (slower)	n/s
Faces in ADOS Cartoons (Chapter 4; n=84)	DT	FD to faces	Viewing time to –ve vs. +ve valence	↓ (trend)	n/s	n/s
	FC	Sum of fixation number in faces	Exploration of faces	n/s	n/s	↑
	FFT	Time to first fixation to a face	Slower to orientate to –ve bully face	n/s	↑ (slower)	n/s
	RC	No. of fixations in consecutive IA	Exploration between faces	n/s	n/s	↑

Legend for Table 7.1:

[†]2X2 factorial approach: ADHD (ADHD and ASD+ADHD) versus no ADHD (ASD and controls); ASD (ASD and ASD+ADHD) versus no ASD (ADHD and controls); ASD*ADHD (interaction of fixed factors; comorbid group differs from pure group(s)). DT (Dwell Time); FD (Fixation Duration); TFN (Total Fixation Number)*for disgust; MFD (Mean Fixation Duration); FSPL (Fixation Scanpath Length); MLBF (Mean Length Between Fixations); LI (Laterality Index); FC (Fixation Count); FFT (First Fixation Time- ↑ (slower)=increased time to fixate and slower to orientate); RC (Run Count); IA (Interest Area); ADOS (Autism Diagnostic Observation Schedule); ** ADOS emotion recognition subscore unavailable for typically developing controls; LHS (Left hemisphere); Direction of findings are significant ($p<0.05$) unless trend is shown in brackets ($p \geq 0.05$ and ≤ 0.06); n/s (non-significant; $p>0.06$)

7.1.1 DISCUSSION OF FINDINGS RELATING TO THE PROCESSING OF FACE STIMULI

In Chapter 2, children with ADHD showed a qualitative difference in the 'scatter' of fixations and a linear pattern of eye gaze (from eye to mouth) with fewer triangulations between eyes and mouth when viewing emotional faces compared to children without ADHD. From a symptom perspective this could be related to the core features of ADHD (hyperactivity, impulsivity and reduced concentration) suggesting a direct link to the clinical profile of ADHD (see Appendix I. Case 1).

This qualitative difference corresponded to an increased speed of fixations, verified quantitatively in Chapter 3 with increased number and shorter duration of fixations. Fixations were also more widely dispersed shown by a longer fixation scanpath length and mean length between fixations across the face stimulus. Interestingly, children with ADHD directed their attention towards the core features of the face (eyes and mouth, reflected in dwell time) but looked less at other facial features such as creases of the face. This could suggest that when not looking at the core features, those with ADHD could be distracted by other parts of the stimulus, for example hair and ears. The opposite pattern of findings was revealed in those with ASD, with reduced looking to core facial features and a tendency to look at the other facial features of the face. These findings are in line with those found in the literature on those with ASD viewing emotional faces (Chawarska and Shic 2009) and with the main hypothesis of the Thesis: that ADHD and ASD

would have different visual social attention profiles which would also differ from typically developing controls.

However, in Chapter 5 these findings were not replicated when a separate clinical sample viewed neutral faces without any prompt to name an emotion, suggesting that results in Chapters 2 and 3 could be related to the task type and potentially confined to the requirement to judge the emotional content of faces. An interesting pattern of results emerged to neutral faces which suggested that those with ADHD looked less at the eye in the right hemi-field (reflected in DT) while those with ASD made more rightward fixations over the neutral face stimuli (reflected in the LI, a measure of direction of fixation). Taken together, this suggests differences in brain lateralisation between ADHD versus ASD while processing emotionally neutral faces.

As ADHD has been consistently shown to have left hemi-neglect to non-face tasks (Manly et al. 2005), our results from neutral faces contrasts with previous findings and is somewhat intriguing. However, those with ADHD have previously been shown to have normal left hemi-face bias (Klimkeit et al. 2003), and so our results are in keeping with this. Thus, suggesting preservation of left hemi-face bias in those with ADHD, potentially at the expense of looking to the right eye. Conversely, those with ASD have a tendency for more rightward fixations suggesting more left brain lateralisation during neutral face processing. If these findings are related to the theory of brain lateralisation and personality; creativity and imagination in the right brain and logic and detail focussed in the left brain, remains to be elucidated (Mihov, Denzler, and Forster 2010). This would

be an interesting area of future research, as recognised strengths in neuro-developmental disorders such as entrepreneurism in those with ADHD and logic-detailed engineers and scientists on the autism spectrum have been documented in the literature (Lerner, Verheul, and Thurik 2019; Baron-Cohen et al. 1997).

7.1.1.1 **INTERIM SUMMARY**

Visual social attention findings from emotional and neutral face stimuli showed distinct findings between those with ADHD versus those with ASD. These findings could be in keeping with a double dissociation between the categorical disorders and the interpretation of this in the context of comorbidity is discussed in detail in Section 7.2.2 of this chapter. A potential caveat to these findings was that there was no expectation that the child had to orient their attention towards the face in these tasks as the child fixated on a central fixation cross for the face to then appear in the middle of the screen. In order to expand visual social attention measurement to include orienting, and to potentially enhance the ecological and clinical validity of the Thesis, social scenes from ADOS images were used as stimuli in Chapter 4, which is discussed next.

7.1.2 Discussion of ADOS images

The ADOS was originally designed as a research tool in the assessment of ASD and has become commonly adopted in clinical practice as a tool to standardise observed autistic behaviours as part of the diagnostic process (Feinstein 2010; NICE 2011). As the clinical phenotype of ASD has broadened there has been suggestion that the ADOS may not be sensitive enough to pick up all of these cases and can also be prone to assessor subjectivity (Fitzgerald 2017). Furthermore, the ADOS was not originally designed to be used in clinically complex cases with high levels of comorbidity. Our findings provide some preliminary support for the measurement of visual social attention alongside the ADOS examination; when children viewed ADOS pictures, visual attention to faces was reduced in those with ASD compared to those without. These findings are in line with findings in the literature using complex and dynamic scenes (Frazier et al. 2017). Those with ADHD (without ASD) did not show these atypicalities to ADOS pictures; in particular they did not show slower orienting to faces (measured as the latency of the first fixation to the face). The results from ADOS pictures therefore corroborate results from previous chapters suggesting that there are core visual social-emotional attention differences between ADHD and ASD.

In summary, the aspects of visual social attention that are thought to be more classical ASD deficits seem to be preserved in ADHD. For example, Chapters 2–4 revealed ADHD had 'preserved' visual social-emotional attention for core features (eyes and mouth) of emotional faces, preserved

left hemi-face bias to neutral faces and preserved visual social-emotional attention (including orienting) to faces in ADOS pictures compared to those with ASD. One interesting difference between the emotional and neutral face findings and ADOS pictures is that, in the latter, no costs to visual social-emotional attention were found in ADHD. For example, in the emotional faces task, children with ADHD had reduced viewing time to other areas of the face and in the neutral faces, reduced viewing time to the right eye. As no such cost to visual social-emotional attention was found for the ADOS pictures in ADHD, it could be postulated that the ADOS pictures were rewarding and motivating to look at as they were colourful with no explicit task requiring sustained attention. In contrast the neutral faces were black and white and the emotional faces consisted of 60 trials requiring sustained attention on a potentially more laborious explicit task. As motivation and reward have been shown to be as effective as stimulant medication for those with ADHD (Liddle et al. 2011), preserved visual social-emotional attention to ADOS pictures without expense to other areas of visual attention could be quite likely. This interpretation of findings seems particularly plausible in the context of results from the ADOS cartoons discussed next. Cartoons were black and white and contained more complex social interactions requiring potentially more sustained attention to the different characters in order to interpret the meaning. Furthermore, our findings could suggest that social impairments and atypical visual social-emotional attention in ADHD may not be pervasive but rather context dependent potentially influenced by intensity of stimulation, arousal, emotional valence and reward (Bellato et al. 2020).

In the ADOS cartoons, subtle differences and some similarities emerged between the groups. Those with ASD were slower to orient to the angry monkey face compared to those without ASD. Those with ADHD however showed a trend towards reduced viewing time to negative valence rather than positive valence cartoons; thus, ADHD could be showing this profile as they are finding positive valence more salient than negative. Furthermore atypical social-emotional attention to the negative emotional valence cartoon was associated with ASD and oppositional symptom severity. This is in keeping with findings of poor social communication skills and conduct problems including oppositional symptoms in a subset of children with severe ADHD and multiple comorbid symptoms, reported previously in the literature (Santosh and Mijovic 2004; Greene et al. 1996).

7.1.3 SUMMARY

The majority of the results presented in this Thesis showed findings in line with the hypothesis; that visual social-emotional attention profiles were different in those with ADHD versus those with ASD using a 2x2 factorial approach. In general, those with ASD+ADHD shared visual social-emotional deficits of both disorders, suggestive of true comorbidity. In the ADOS cartoons, there were two visual social-emotional attention measures that showed a similar profile in ADHD and ASD. These included a reduced exploration of faces (FC) and between faces (RC). There was an interaction between ADHD and ASD factor for both measures showing a trend for increased fixations in the ASD+ADHD group. Discriminant function analysis also showed that exploration of faces (FC) were reduced in those with ADHD compared with typically developing controls. The

findings have implications on comorbidity models in ADHD and ASD which were important research questions of the Thesis. In the next sections, the research questions of this Thesis will be addressed in turn below.

7.2 INTERPRETATION OF FINDINGS IN THE CONTEXT OF THESIS QUESTIONS

The main aim of this Thesis was to address the key research questions; the first regarding emotion recognition and ADHD, the second on comorbidity between ADHD and ASD and thirdly, the potential for visual social attention to differentiate between ADHD and ASD. Each of the research questions will be answered in turn below.

7.2.1 IS THERE AN ASSOCIATION BETWEEN EMOTION RECOGNITION AND VISUAL SOCIAL-EMOTIONAL ATTENTION IN ADHD?

In this Thesis, emotion recognition was tested in two different ways. In the first study, the participant was explicitly asked to name the emotion and so this was termed explicit emotion recognition and emotion accuracy was used as a measure of explicit emotion recognition. In the second sample, the task was free viewing of ADOS images and neutral faces and emotion recognition was tested separately on the ADOS. As detailed in the Appendix Section III, the ADOS emotion recognition subscore includes spontaneously commenting on others' emotions and making comments about others' feelings without prompting. For the purposes of the second study, emotion recognition was tested using the emotion recognition ADOS subscore. As the association between explicit emotion recognition and ADOS

emotion recognition varied in relation to visual social emotional attention in ADHD, they were addressed in turn.

7.2.1.1 EXPLICIT EMOTION RECOGNITION

As stated in Section 7.1, those with ADHD showed a visual social-emotional attention profile to emotional faces that was significantly distinct to those without ADHD. Those with ADHD also showed significantly reduced total emotional accuracy although the predicted emotion-specific deficits, for example reduced accuracy to anger or negative emotions, were not found. In addition, the visual attention profile was consistent across all emotions as opposed to specific emotions for all but one emotion, disgust (discussed in Section 7.2.2). Although the sample size was small compared with the projected estimated sample size calculated in section 2.2.1, the analytical 2x2 factorial approach increased the power of the study. A post hoc power calculation based on this 2x2 analytical approach showed there was sufficient power (87.7%) to find an interaction on with a medium effect size as described in section 3.2.2. Furthermore, an interaction for emotion type by ASD by ADHD on total fixation count was found with a medium effect size (ηp^2=0.07); substantiating sufficient power to detect an interaction of medium effect size. This suggests if other emotion specific findings exist in ADHD on this task, they would have a smaller than medium effect size.

With regards to the total emotional accuracy result, hierarchical linear regression revealed that ADHD significantly explained 15% of the variance, ASD explained 2% of the variance and when IQ was added into the

model it explained a significant further 11% of the variance over and above ADHD and ASD. Although those with ADHD had a lower IQ score than those without, those with ASD did not have a significantly different IQ score to controls. This could be why ASD did not show an overall explicit emotional deficit in Chapter 3 and in keeping with findings by Jones et al. (2011). Additionally, those with ASD could have been using effective alternate emotional processing strategies, as indexed by the machine learning results in Chapter 2 and in-line with the wider literature (Guillon et al. 2015).The type of stimuli used such graded emotions or dynamic stimuli, have been found to produce more of an effect (Frazier et al. 2018). As we used exaggerated still faces as stimuli in the first sample, this could also explain why those with ASD did not have a total emotional accuracy deficit and possibly why an emotion specific (anger) deficit was not seen in ADHD as hypothesised.

Children with ADHD had reduced Dwell Time (DT) to other facial features while viewing emotional faces which, negatively correlated with mean length between fixations which was increased in those with ADHD compared with those without. Mean length between fixations was also significantly associated with total emotional accuracy, suggesting widely dispersed fixations are associated with ADHD and poor emotion recognition. Marsh (2008) did not find this association; although their study contained fewer different emotions and trials. It is interesting to note that mean length between fixations did not correlate directly with ADHD symptoms in our study, suggesting that it could be additional factors within could be moderating the association. Within the hierarchical linear regression

model, ASD factor, IQ and ODD symptoms did not explain additional significant variance on mean length between fixations however, correlation between visual social-emotional measures could explain the findings. Reduced DT to other facial features correlated with increased mean length between fixations, ADHD IA and HI symptom severity and social skills difficulties on the SAS (see Figure 3.3). Overall, these findings are in keeping with atypical visual social-emotional attention, reduced total emotional accuracy and ADHD symptom severity. Furthermore, as these findings correlated with symptom severity on the SAS but not the SCQ, this suggests that ADHD is associated with reduced social skills deficits which are independent of ASD and, emotion recognition deficits which are also associated with low IQ on the prompted emotion recognition task.

7.2.1.2 **ADOS EMOTION RECOGNITION**

In the second sample, spontaneous emotion recognition was measured using the ADOS emotion recognition subscore. Children with ADHD had increased scores on the ADOS emotion recognition subscore which were not significantly different from those with ASD or ASD+ADHD. Although ADOS was not completed in typically developing children, if we consider that an ADOS emotion recognition score of 0 would be the expected score in typically developing children, then those with ADHD have raised scores. Thus, compared to explicit emotion recognition where only those with ADHD (ADHD and ASD+ADHD) were impaired, all clinical groups showed raised scores on the ADOS emotion recognition subscore.

Although the ASD group had a trend for a higher mean ADOS emotion recognition score (suggestive of more difficulties with spontaneous emotion recognition) amongst the clinical groups, this was not a statistically significant finding (Table 4.2).

The Laterality Index (LI) for neutral faces, suggestive of atypical face processing in those with ASD and ASD+ADHD was associated with more impairment on the ADOS emotion recognition subscore (presented in Chapter 5). The LI also correlated with ASD and ADHD hyperactive-impulsive symptom severity, suggesting that children with comorbidity have atypical visual social-emotional attention indexed by the LI. These findings suggest that spontaneous emotion recognition on the ADOS could be associated with true comorbidity at the symptom level. On discriminant function analysis however, LI was one of the variables which discriminated the ADHD group from the ASD group, suggesting that atypicalities in laterality of fixation in the pure ADHD group are 'subthreshold' with a trend for less impaired spontaneous emotion recognition subscores compared to those with ASD (ASD and ASD+ADHD).

An additional possibility is that shared comorbidity with oppositional symptoms amongst the ASD, ADHD and ASD+ADHD groups could also be contributing to impairments in spontaneous emotion recognition. In particular, atypical visual social-emotional attention to the negative emotional valence cartoon was associated with communication deficits on the SCQ and oppositional symptoms in Chapter 4. This suggests that comorbid communication and oppositional symptoms may relate to

atypical social-emotional attention in those with ADHD. We did not however find a direct link with spontaneous emotion recognition and atypical social-emotional attention to the negative valence cartoon; suggesting that atypical attention to negative valence does not necessarily translate to poor spontaneous emotion recognition on the ADOS. Overall, these findings support the hypothesis that spontaneous emotion recognition difficulties on the ADOS related are related to core ASD symptoms and ADHD HI symptoms.

7.2.1.3 **SUMMARY**

This Thesis presented evidence suggesting that visual social-emotional attention during explicit emotion recognition testing was associated with ADHD (ADHD and ASD+ADHD) whereas spontaneous emotion recognition on the ADOS was associated with ASD (ASD and ASD+ADHD). ADHD IA and HI symptom severity, was associated with reduced explicit emotion recognition, reduced DT to other facial features and social skills deficits on the SAS in the first sample. In contrast, atypical neutral face processing, indexed by the LI was associated with reduced spontaneous emotion recognition, ASD and ADHD HI symptom severity in the second sample. These findings suggest different mechanisms for explicit versus spontaneous emotion recognitions tasks in relation to ADHD and ASD. In particular findings suggest ADHD IA and HI symptoms are associated with explicit emotion recognition and, ASD and ADHD HI symptoms associated with spontaneous emotion recognition. Overall, these findings suggest that emotion recognition deficits are associated with atypical visual social-emotional attention in children with ADHD (ADHD and

ASD+ADHD); answering the first question of this Thesis. In the next section, the comorbidity between ADHD and ASD in light of the visual social attention profile is discussed further.

7.2.2 Can visual social-emotional attention clarify if emotion recognition deficits in ADHD are primary to ADHD or secondary to co-occurring ASD?

In Chapter 6, both samples had visual social-emotional attention variables loading onto significant discriminant functions which showed opposing patterns in the ADHD group versus ASD group. This finding is in-line with one of the main arguments of the Thesis; that ADHD and ASD have differing visual social-emotional attention (see Section 1.1.2).

In fact, some of the opposing patterns in Chapter 3 almost met criteria for a double dissociation. For example, those with ASD showed reduced viewing time, indexed by DT to core features of emotional faces with a trend towards increased viewing time to the other facial features. Conversely, those with ADHD showed the opposite pattern, with decreased viewing time to other facial features and preservation of viewing time to core features (eyes and mouth). This is quite striking as it could suggest that one mechanism could be responsible for visual social-emotional attention difficulties in viewing core features versus another mechanism for other facial features and that the former could be affected in ASD and the latter in ADHD. This was also confirmed at the symptom level with ASD symptom severity associated with dwell time to core features

and ADHD symptom severity and social skills deficits on the SAS associated with reduced dwell time to the other facial features. This later finding is particularly interesting, suggesting that atypical visual social-emotional attention in ADHD is associated with social skills deficits on the SAS a broader measure of social skills rather than the SCQ which is more specific to ASD. This supports the hypothesis that children with ADHD have social skills difficulties on the SAS which are primary to ADHD symptoms rather than ASD symptoms on the SCQ.

In Chapter 4, a dissociation was found with slower orienting to faces in those with ASD (ASD and ASD+ADHD) but not ADHD (without ASD); suggesting slower orienting to faces in the later stages of visual attention, is a specific finding in those with ASD. Furthermore, orienting to faces, indexed by the First Fixation Time (FFT) was significantly associated with repetitive stereotyped behaviour severity on the SCQ.

As the comorbid group showed visual attentional features of both disorders, this could imply a mechanistic view of each visual social attention deficit with the comorbid group potentially having both mechanisms affected leading to a double deficit (Pennington 2006). In terms of comorbidity, this would fit with true comorbidity as the comorbid group having additive effects indicates a true overlap of both disorders. As discussed in Chapter 1, there are some distinct but some shared genetic links between the disorders, in keeping with a correlated liabilities comorbidity model of Neale and Kendler (1995). Our findings are also in keeping with EEG studies investigating comorbidity in ASD and ADHD (Tye et al. 2014;

Groom et al. 2017), providing evidence that visual social-emotional attention measured using eye tracking has the capacity to provide similar results to the neural level, as discussed in Chapter 3.

An example of a true comorbidity was also shown in the findings from Chapter 5 which presented the heat maps for viewing time, indexed by DT of the ADHD participant concentrated over the left upper hemi-field; the viewing time of the ASD participant concentrated over the right hemi-field; and the ADHD+ASD participant viewing time concentrated in the centre of the stimulus (Figure 5.1b-d). It is important to note that the LI towards positive or more rightward fixations was correlated with ADHD HI scores, all SCQ subscores and the ADOS emotion recognition subscore. This implies atypical brain lateralisation associated with ASD, ADHD-HI and ADOS emotion recognition at a symptom level; suggesting a severity continuum which then reaches a diagnostic threshold liability in a subset of individuals.

In Chapter 5, the comorbid group shared both visual attention deficits while viewing faces. This could be conceptualised as the comorbid group viewing the left hemi-field and then making more rightward fixations to the mid-zone (nasal bridge) of the face, potentially avoiding eye contact. This could give a profile of variable eye contact as depicted in Case 3 (see Appendix I.). It could also have been possible that there were different subtypes of comorbidity as proposed by Van der Meer et al. (2012) with a predominant ADHD diagnosis but also meeting the threshold for ASD as described in Case 3 (see Appendix I.) and, alternatively predominant ASD but also meeting the threshold for ADHD as described in

Case 2 (see Appendix I.). As depicted, in the Case Vignettes in the Appendix, both Case 2 and 3 showing comorbidity had a delay in the less predominant diagnosis being diagnosed.

In the above examples, both viewing time (DT) and rightward fixations (LI) to the face can help to build the potential dynamic eye gaze patterns that were observed empirically in Chapter 2. These interesting findings suggest dynamic brain processing differences associated with alternate lateralised networks. Although this was a cross sectional study, alternate cortical networks have been proposed to be due to compensation of early pre- and perinatal insults in the brain (Johnson 2017). In this model, those with medium sized neuronal insults, for example neonatal hypoxic ischaemic encephalopathy, go onto have inhibitory and excitatory imbalances which lead to compensatory brain networks including both hypo- and hyper-connectivity in the brain in ASD (Johnson 2017). This would fit with findings in ASD in Chapter 3; children with ASD had atypical visual social attention to core features despite intact emotion recognition accuracy which has been suggestive of compensatory emotion recognition strategies in ASD by Harms et al. (2010). Johnsons' model (2017) also allows for the range of clinical phenotypes, including comorbid subtypes and the range of severity seen in complex neurodevelopmental disorders discussed in this section.

The literature reviewed in Chapter 1 documented that neurodevelopmental disorders are also highly heritable, with many genes to many phenotypes. This also explains our findings where gene environment interactions could allow for further compensatory changes during development in

a multiple liabilities to multiple cognitive deficit framework (Sonuga-Barke 2005; Pennington 2006). In Chapter 4, ADHD showed a trend towards reduced viewing time to negative valenced cartoons. However, hierarchical linear regression revealed that oppositional symptoms significantly explained 5% of the variance ($p<0.05$) for viewing time (indexed by Dwell Time; DT) to faces in the Monkeys Cartoon (negative valence) over and above ADHD and ASD factors. Although, there were some trends for oppositional symptoms to explain additional small amounts of variance to Fixation Count (FC; exploration to faces) and Run Count (RC; exploration between faces) in all cartoons this was not significant. Oppositional symptoms did however explain a significant additional variance to FC (5%) and RC (6%) over and above ADHD and ASD factors in negative emotional valence cartoons ($p<0.05$). Overall, these findings suggest an additional association for visual social-emotional attention to negative emotional valence with oppositional symptoms on Conners' parent rating scale, explaining a small but significant amount of the variance.

Developmental compensation over time (Johnson 2017; Pennington 2006) seems particularly plausible to explain our findings on shared visual social attention measures (FC and RCs) to ADOS cartoons in both ASD and ADHD. In Chapter 4, an interaction was found between ASD and ADHD on both FC and RC, showing reduced counts in the pure groups and a trend for increased counts in the comorbid group. There was a trend for higher counts to be associated with less impairment in communication on the SCQ suggesting the comorbid group doing better than the pure groups. In Chapter 3, a similar interaction was found between ASD and

ADHD for fixation number to disgust faces with a reduced number in the comorbid group and the ASD group but higher numbers in the ADHD group. A higher number of fixations in the prompted emotion task was signified by increased speed of fixations and a more dispersed scanning pattern associated with poor explicit emotion recognition. Thus, the comorbid group are showing a trend for an improved profile on three single measures which could be related to compensation in a subset of those with comorbidity.

Longitudinal studies will be required to verify the trajectory of the visual social-emotional attention profiles and the association with comorbidity over time. An optimal outcome study in ASD has shown emergence of ADHD symptoms in later development suggesting compensation can also occur at the symptom level (Fein et al. 2013). Thus, the reverse could conceivably be true whereby those with ADHD could show compensatory mechanisms leading to more clinical symptoms of ASD. Certainly, this could explain the delayed diagnosis for ASD in those with ADHD as illustrated in Case Vignette 3 where it was initially unclear if the clinical phenotype was severe ADHD versus a comorbid presentation. In Case 3, Callum was trying his hardest to make friends but continued to experience difficulties forming appropriate peer relations (see Appendix A.I). Case 3 could be in keeping with Lorna Wing's 'active but odd' subtype of ASD and this can be one of the hardest clinical presentations to disentangle in clinical practice (Wing 1996; Feinstein 2010). This could also be in keeping with an extreme multiformity model of comorbidity posited by Neale and Kendler (1995); whereby ADHD (above certain thresholds) generates symptoms of

ASD. Furthermore, it is still unclear if severe ADHD and the interaction with environmental experiences such as peer rejection lead to an emergence of subthreshold ASD symptoms, for example via a synergy model (Pennington 2006). The role of oppositional symptoms within a synergy model of comorbidity could also be important in the overall ADHD clinical phenotype. In this synergistic model, both ADHD and peer rejection would need to be present for subthreshold ASD symptoms to emerge. Additionally, clinical presentation could be more likely in those with oppositional symptoms and more impairment.

As described in Section 3.3.2, a 2x2 factorial design was used in the main analyses of the studies of this thesis in order to disentangle the influences of ASD versus ADHD in the case of comorbidity. The two factor design tests the main effect of ASD and ADHD factors on variables of interest in addition to an interaction between ASD and ADHD factors (Banaschewski et al. 2007; Groom et al. 2017). In particular, an interaction between ASD and ADHD factors could suggest a model compatible with the comorbid group belonging to a third separate nosology to either of the pure groups as described by Rutter and Taylor (2002). Alternatively, a main effect of ASD and ADHD factors, with a lack of interaction between ASD and ADHD factors could suggest an 'additive model' of comorbidity, especially if a double dissociation exists (Banaschewski et al. 2007). This additive model would be in keeping with the comorbid group sharing a profile with both the pure groups and potentially shared risk factors within the comorbid group. Although the majority of the results were in keeping with an additive model of comorbidity, as described above there were three

instances were an interaction was found which could suggest the comorbid group also has some unique elements to the pure groups.

Although sample sizes were smaller than projected in both studies, there was sufficient power to detect an interaction between ASD and ADHD factors with a medium effect size in both samples (sample 1, power = 87.7%; sample 2, power = 99.5%) (Section 3.3.2 and 4.1.6). This was supported by an interaction of medium effect size for emotion by ASD by ADHD on Total Fixation Number (ηp^2=0.07) in the first sample and, an interaction of medium effect size for ASD by ADHD on Fixation Count (ηp^2=0.08) and Run Count (ηp^2=0.05) in the second sample. This suggests that if further interactions exist, they are likely to be smaller than a medium effect size.

In addition to small sample sizes to detect an interaction, other methodological issues in relation to the 2x2 factorial statistical design to disentangle comorbidity in ADHD have been highlighted by Banaschewski et al (2007). These include the possibility of 'pretending an additive model' of comorbidity when the comorbid group is more severely impaired that both pure groups and, measurement issues affecting the results (Banaschewski et al. 2007). In this Thesis, both samples had a comorbid group that was more impaired than one of but not both of the pure groups so, it cannot be ruled out that the severity of the comorbid group had an additional impact on the additive model which was in keeping with our results. Furthermore, we found an interaction between ASD by ADHD on Total Fixation Number, Fixation Count and Run Count which are measured as counts and are smaller than measurements for fixation durations

measured in milliseconds. These measurement issues may also have influenced the pattern of results and interaction findings. Thus, although our results are in keeping with an additive model of comorbidity with some unique elements in the comorbid group, methodological issues discussed suggest that caution is required when interpreting results based on a statistically significant interaction or lack of interaction. Our results should therefore be viewed as preliminary, requiring replication in larger well defined samples as discussed further in Section 7.3.

In this Thesis, DFA presented in Chapter 5 complemented the main 2x2 factorial analysis by allowing for the four groups (ASD, ADHD, ASD+ASD and typically developing controls) to be compared directly. For the first study, the first function dissociated the ASD group from the ADHD group. Unfortunately, as only one function was significant in the first sample, this precluded the comorbid and the control group from adequately dissociated from each other. The second study had 2 significant functions and a third which was almost significant, which allowed for the control group to be more clearly dissociated from the comorbid group. Although this helps to differentiate groups at the categorical level, comorbidity at the dimensional level was more limited using these approaches and further suggestions to disentangle dimensional comorbidity over development are discussed in Section 7.3.

7.2.2.1 **SUMMARY**

Findings of visual social-emotional attention improve understanding of the relationship between emotion recognition and comorbidity. Across Chapters 2–6, many of the findings were in keeping with true comorbidity where visual social attention differs in ADHD versus ASD and the comorbid group had a profile that was additive with some unique elements, making the 'phenocopy' hypothesis of comorbidity unlikely. Overall, our findings were in keeping with a correlated liabilities model (Neale and Kendler 1995; Pennington 2006) with shared aetiology in the comorbid group. Although other models of comorbidity could also be likely for example, extreme multiformity and synergistic models; future studies discussed in Section 7.3 are needed to clarify the exact relationship between severity of ADHD and visual social-emotional attention over the developmental period.

In conclusion, atypical visual social-emotional attention indicative of reduced Dwell Time (DT) to other facial features and 'hyper-extensive' emotional face scanning suggest explicit emotion recognition deficits found in ADHD are mediated by ADHD IA and HI symptoms and, associated with social skills deficits on the SAS. Furthermore, comorbidity with ASD leads to additive spontaneous emotion recognition difficulties on the ADOS due to slower orienting to faces, associated with ASD symptom severity and, atypical face processing associated with ASD and ADHD HI symptom severity. As visual social-emotional attention showed these interesting profiles associated with comorbidity, the next section provides a

discussion of how well visual social-emotional attention, indexed by eye tracking measures differentiated the groups across the studies.

7.2.3 Does visual attention differentiate ADHD, ASD and ASD+ADHD on emotion recognition and social processing tasks?

Throughout this Thesis, it has been demonstrated that the visual social-emotional attention profile between ADHD versus ASD, is distinct. This was the case across two independent samples testing separate emotion recognition tasks. These visual social-emotional attention differences were initially revealed at the qualitative level and verified by machine learning in Chapter 2. Significant differences were also shown at the quantitative level in Chapters 3–5 using a 2x2 factor approach and verified at the group categorisation level using discriminant function analysis (DFA) in Chapter 6.

In Chapter 6, both samples had eye tracking variables, indexing visual social-emotional attention loading onto significant discriminant functions which showed opposing patterns in the ADHD group versus ASD group. This finding is in line with one of the main arguments of the Thesis which is that ADHD and ASD have differing visual social-emotional attention (see Section 1.1.2).

The observational coding framework protocol presented in Chapter 2 in a subsample from Sample 1, generated classification rates of 100%, 87.5% and 42.5% in the ADHD, ADHD+ASD and ASD group respectively ($\chi^2(9)=38.3$, $p<0.05$). As this was a very time-consuming approach and potentially subject to observer bias, validation using machine learning, an automatic data-driven approach was undertaken and is more likely to

be adopted in clinical practice in the future. On machine learning, accuracies of up to 84% were found in the combined group in the first sample which not only validated the empirical coding results but also provided additional algorithms on face processing in the ASD group, increasing the classification in ASD. On DFA in Chapter 6, characterisation of diagnoses across both samples was good for ADHD (81–88%). Characterisation for ASD was between 61–80% across both samples and characterisation for ASD+ADHD was more variable across both samples using DFA (33–61%). As stated above, however, accuracies using machine learning which categorised face processing patterns and 'scatter' of fixations in the groups gave better accuracies for the combined group.

In summary, using a combination of methodological approaches, it was demonstrated that eye tracking measures, indexing visual social-emotional attention differentiate ADHD, ASD and ASD+ADHD on emotion recognition tasks, although the accuracy of classification would require further optimisation prior to introduction as a diagnostic aid in clinical practice, alongside other clinical measures and tools. Before turning to clinical relevance, the limitations, strength and future work are discussed.

7.3 LIMITATIONS, STRENGTHS AND FURTHER WORK

As described in Section 7.2, the Thesis was successful in answering the three main research questions of the Thesis and providing evidence for the

main hypothesis on visual social-emotional attention and emotion recognition in ADHD. That being said, it is important to acknowledge the limitations of the methodologies used, the strength of the studies and suggestions for further work.

7.3.1 SAMPLE SIZE AND STUDY DESIGN

Despite two further rounds of recruitment, the sample size from Sample 1 in the emotional faces task was small, after which funding and time limitations ensued. Although the sample size was small compared with the projected estimated sample size calculated in section 2.2.1, the analytical 2x2 factorial approach increased the power of the study. A post hoc power calculation based on this 2x2 analytical approach showed there was sufficient power (87.7%) to find an interaction on with a medium effect size as described in section 3.2.2. Furthermore, an interaction for emotion type by ASD by ADHD on total fixation count was found with a medium effect size (ηp^2=0.07); substantiating sufficient power to detect an interaction of medium effect size. Despite the small sample size, the participants were well categorised and all children with ADHD were either stimulant naive or taken off stimulant medication minimising confound due to medication. In the second study, the number of geographical sites for recruitment were increased and the sample size was doubled. Further studies would benefit from taking this multisite approach so that analysis of subsamples such as within the comorbid group and in girls is more feasible. Additionally, children with an IQ less than 70 were excluded from both studies so, findings may not be generalizable to children with an IQ less than 70. As the free viewing tasks in the second sample could be conducted in children with an

IQ less than 70, future studies would benefit from inclusion of children with an IQ less than 70, making findings more generalizable to the whole of the autism spectrum including those with intellectual impairment.

As both studies were cross-sectional, it was not possible to make inferences about developmental changes and visual social-emotional attention in ADHD. As this was one of the first studies to compare visual social-emotional attention using eye tracking in ADHD and the impact of ASD; a cross-sectional study was needed in the first instance as longitudinal studies are costly and time consuming. It is difficult to establish causal pathways in cross-sectional designs so, the importance of establishing how genetic and environmental exposures affect the visual social-emotional attention profile in ADHD over time will be an exciting avenue for future direction.

In both samples, the DAWBA was used as opposed to more lengthy semi-structured interviews such as the ADI-R to aid the categorisation of ASD. The SCQ however relates closely to the ADI-R and the use of the SCQ in combination with the DAWBA has been used by the assessors (PK and CH) in a large longitudinal study previously (Johnson et al. 2010a, 2010b).

Due to study time limitations, the ADOS was only performed in a subset of children in the first study, although ADOS validated the diagnosis from the DAWBA in all cases. In the second study, it was possible to do the ADOS in most of the clinical cases as this was done on the initial testing day. However, as ADOS was not completed for the typically devel-

oping group, comparisons for ADOS scores including the emotion recognition subscore could only be made amongst the clinical groups. As an ADOS score of 0 is denoted as typically developing this can be substituted, allowing for a 'pseudo' comparison amongst the groups, but it is acknowledged that this was not explicitly tested and therefore was not carried out in the analysis.

The chosen tasks in Chapter 4 were based on tests used in clinical practice such as the ADOS and therefore, manipulation of the images was not undertaken. This means that differences between visual social-emotional attention to colourful ADOS pictures versus black and white cartoons could be influenced by colour contrast in addition to the characters' social interaction. Further studies that allowed for manipulation of the images such as making the cartoons colourful will help to elucidate the exact mechanism involved in the findings. Using a machine learning approach for the ADOS images including the transitions of fixations from faces to objects will allow further examination of shared findings on the cartoons such as fixation counts within and between faces. This would allow for a deeper understanding of social processing in relation to comorbidity models and potentially improve group categorisation accuracies.

In terms of study design, it is also important to consider the limitations of eye tracking. Firstly, there are technical issues with eye tracking. Head movements, eye blinking and participant fatigue can lead to artefact data which required data cleansing. Eye tracking measures are sensitive to luminance, image properties such as contrast and spatial properties. Although luminance was measured and kept constant in the second study, it

was not possible to control for some of the other stated factors as images were not manipulated. There are potential confounding factors when studying visual attention using eye tracking, for example lighting and cognitive loading of the task.

Visual social-emotional attention in the context of this Thesis explored overt attention in relation to active vision (Findlay and Gilchrist 2003). This design does not take covert attention into consideration thereby potentially missing the effects of early visual attentional processes that neural EEG techniques would detect.

Although the visual social-emotional attention profile between ADHD and ASD differed throughout the Thesis, one of the themes that emerged was that individual eye tracking measures, indexing visual social-emotional attention differed based on task type, task image, participant demographics and eye tracker type. As lack of replication of findings is a common finding in neuroscience of developmental disorders, it is important that future replication of findings and studies carefully controls for these subtle differences in task design.

7.3.2 Statistical analyses

A 2x2 factorial approach to examine the effects of ADHD and ASD as fixed factors on visual social-emotional attention variables was used as it is commonly used in studies of comorbidity (Banaschewski et al. 2007; Groom et al. 2017; Tye et al. 2014). The 2x2 factorial approach has the ability to differentiate the effect of ADHD, ASD and of comorbidity

through an interaction of fixed factors allowing for the research questions to be tested. Furthermore, it improves the power of the sample by the combination of 2 groups into one factor, essentially doubling the power of a more traditional group effect. Interpretation and comparison of findings (e.g. pure group versus controls) can be more difficult in the 2x2 factorial approach compared to the group approach. This was less of a problem for this Thesis as the main question was regarding ADHD versus ASD and comorbidity. Additionally, significant variables found on the 2x2 factorial approach were included in the discriminate function analyses (DFA) which used the group categorisation thereby validating the 2x2 factorial findings and allowing more ease in interpretation at the group level. It should be emphasised, however, that results from DFA should be interpreted cautiously as replication of findings in a separate independent sample are required.

Hierarchical linear regression was used to test for added variance of IQ and oppositional symptoms over and above ADHD and ASD on the significant eye tracking variables as clinical groups differed on IQ and oppositional symptoms have been shown to be important in social problems in ADHD (Santosh and Mijovic 2004). Although, it could have been argued that analysis of covariates (ANCOVA) could have been used, the use of ANCOVA has been shown to be a poor way of covarying for IQ in psychiatric and developmental disorders especially if IQ is tightly bound to the clinical profile of the disorder as is the case for both ASD and ADHD (Miller and Chapman 2001). Miller and Chapman (2001) highlighted that the covariate method removed too much of the variable of interest (in this

case ADHD), potentially leading to a false negative result. This would effectively wipe out an effect rather than explain the independent variance of ADHD and IQ on emotion recognition and visual attention as shown on hierarchical regression in Chapter 3. From a clinical perspective, regression is more meaningful as it provides information on the profile of ADHD with and without borderline IQ difficulties, potentially having more explicit emotion recognition accuracies due to additive atypical visual attention. It also points to the importance of clinical services providing intelligence testing to children with an IQ more than 70 and who do not meet criteria for Intellectual disabilities services in the National Health Service.

Miller and Chapman (2001) proposed that having a control group with a lower IQ would be the best way to examine the effects of IQ. Unfortunately, this was not possible in our studies due to recruitment difficulties and time limitations but future study designs will benefit from controls with lower IQ. Although our study did not have children with an IQ below 70, children with a better matched IQ in the control group compared with the clinical groups would be beneficial in future studies as we found an association with reduced emotion recognition and lower IQ. It would also be important to consider comparison of groups with other psychiatric disorders as studies have shown that visual attention can be affected in conduct and emotional disorders at the diagnostic level (Airdrie et al. 2018; Loughland, Williams, and Gordon 2002).

7.4 RESEARCH IN CONTEXT AND CLINICAL IMPLICATIONS

This Thesis was designed to address an important clinical problem; with the intention to clarify if social cognitive deficits such as emotion recognition difficulties that present in children with ADHD are a primary consequence of ADHD or secondary to a co-occurring disorder such as ASD. This section puts the findings from this Thesis into context.

7.4.1 ADDED VALUE OF THIS PROJECT

As this is one of the first eye tracking studies that has looked at visual social-emotional attention and compared it with ASD, this is an important contribution to the field. Three important research questions were answered in this Thesis:

1) There was an association between reduced explicit emotion recognition and atypical visual social-emotional attention, indexed by 'hyper-extensive' scanning of emotional faces in ADHD. Furthermore, reduced viewing time indexed by Dwell Time (DT) was significantly associated with 'hyper-extensive' scanning, ADHD IA and HI symptoms and social skills deficits on the SAS. Conversely, spontaneous emotion recognition on the ADOS was associated with ASD, and atypical processing of neutral faces, indexed by the Laterality Index (LI) and associated with ASD and ADHD HI symptom severity.
2) Visual social-emotional attention suggested that explicit emotion recognition deficits found in ADHD are primarily mediated by

ADHD and low IQ whilst, comorbidity with ASD leads to additive spontaneous emotion recognition deficits on the ADOS due to slower orienting to faces and atypical neutral face processing.

3) A combination of methodological approaches demonstrated that visual social-emotional attention measures differentiate ADHD, ASD and ASD+ADHD on emotion recognition tasks.

As this has implications for research and clinical practice, each will be addressed in turn.

7.4.2 Implication for research

Eye tracking is widely used in the field of ASD to measure visual social attention but much more rarely studied in ADHD. As there has been a vast number of studies documenting the comorbidity between ASD and ADHD, this study may be one of the first in an exponential rise in the field of eye tracking in ADHD and ASD. This study has extended the scope of study of visual social attention in neurodevelopmental disorders. As stated in Section 7.3, there are several research areas that would be useful to address further, including: the potential comorbidity subtypes with differing comorbidity models; the environment interactions including the impact of peer rejection on emotion recognition; and last but not least, the longitudinal mapping of visual social emotional attention in ADHD.

7.4.3 Clinical practice implications

This Thesis has demonstrated that the visual social-emotional attention profile found in the groups also relates to the clinical phenotype. In Chap-

ter 3, those with ADHD had reduced DT to other facial features of emotional faces, which associated with ADHD symptom severity and social skills deficits on the SAS. This suggests that atypical visual social-emotional attention in ADHD had effects on social skills which require assessment and treatment (as discussed further in section 7.4.5). As described in the Case 1 (see Appendix I.), Andy had some social-emotional difficulties however, these improved with stimulant medication but promptly returned on medication discontinuation.

It is interesting to note that there were more children in the ASD+ADHD group than the ADHD group in this Thesis. As these samples are from the clinic population, this is in keeping with comorbidity being common in child psychiatry (Gillberg 2010). As we found that those with ASD+ADHD had additional atypical visual social-emotional attention, associated with ADHD and ASD symptom severity, our findings support the early assessment of comorbid ASD in ADHD. Unfortunately, this is often not the case in current clinical practice; as exemplified by recent literature (Wei et al. 2018; Miodovnik et al. 2015) and in Case 3, who had delayed diagnosis of ASD in ADHD (see Appendix AI.). Prompt assessment of comorbidity would allow for timely treatment approaches for additional social cognitive difficulties in children with ASD+ADHD, with the potential to improve long term outcome (discussed further in section 7.4.5).

In this Thesis, reduced orienting to faces and reduced looking to core features (eyes and mouth) was found in those with ASD (ASD and ASD+ADHD), which was associated with ASD symptoms severity on the

SCQ. As poor eye contact during social interactions is one of the hallmarks of ASD and frequently encountered during the clinical interview (see Appendix I.; Case 4), this relationship between the clinical profiles and the visual social-emotional attention profile are intrinsically appealing. Furthermore, those with ASD (ASD and ASD+ADHD) show greater atypical hemispheric lateralisation during neutral face processing as indexed by the positive LI, which was associated with reduced spontaneous emotion recognition on the ADOS, ASD and ADHD HI symptom severity. As the left brain is associated with being logical, analytical and detail focused (Friedman and Forster 2005; Mihov, Denzler, and Forster 2010; Schmeck 1988; Happe and Frith 2006), this can help to explain to patients with ASD where their strengths can lie. As depicted in Case 4 (see Appendix I.), Daniel was very good at computing and programming. Thus, eye tracking can not only be indicative of the clinical profile but it can also act as a window to the brain providing further evidence of its use as a behavioural biomarker in ASD (Bradshaw et al. 2019; Murias et al. 2018; Del Valle Rubido et al. 2018; Shic 2016).

A relationship between the visual social-emotional attention profile and clinical ADHD phenotype was also found. Increased speed of fixations to the emotional face stimulus was present both qualitatively and quantitatively which could be related to the hyperactivity and restlessness, one of the core features of ADHD. Also, there was preservation of orienting to the face and viewing eyes and mouth of emotional faces compared to those with ASD. As detailed in the Case 1 (see Appendix I.), young people with ADHD often have reasonable eye contact when they are engaged

in the interview. Additionally the link between right brain lateralisation for neutral faces in our study and right brain dominance for creativity, holistic processing and intuition associated with entrepreneurism in the literature, helps to provide evidence of strengths to those with ADHD who may have been struggling academically (Mihov, Denzler, and Forster 2010; Moore, McIntyre, and Lanivich, 2019; Gonzalez-Carpio, Serrano, and Nieto López 2017).

It is accepted that hemispheric bias is an over simplistic generalisation on the neural basis of personality traits and cognitive style (Happe and Frith 2006) however, our findings on laterality can support a strengths based as well as needs based approach to therapeutic assessment and engagement in clinical practice. This is important as the addition of strengths based approaches to assessment and treatment has been advocated by neurodevelopmental participation literature (Zener 2019).

The links between clinical profile, visual social attention and brain networks is not only intuitively appealing to families and clinicians but also provides further support of the clinical utility of eye tracking. This could be helpful as routine diagnostic assessment in clinical practice is based on semi-structured interview which includes informant bias including recall bias and interviewer bias. Although the ADOS is an observer-based tool by a trained clinician, it can still be prone to subjective bias by the administrator. In Chapter 6, discriminant function analysis showed that atypical visual social-emotional attention to ADOS images showed good discrimination between the groups in the second sample. Having measures of eye

tracking, indexing visual social-emotional attention while the child completes the ADOS could also provide additional validity to complex assessment in the clinic setting. The next section detailed the feasibility of eye tracking as a diagnostic aid.

7.4.4 EYE TRACKING AS A DIAGNOSTIC AID

As described in Section 7.2.3, visual social-emotional attention discriminated the groups suggesting potential clinical utility as a diagnostic aid. Head-to-head comparison of studies by diagnosis showed that the visual social-emotional attention on the explicit emotion recognition task was better at differentiating ADHD versus ASD than the spontaneous emotion recognition task. Visual social-emotional attention during the spontaneous emotion recognition tasks however, had more accurate rates for classification of ASD+ADHD. Observation coding results from Chapter 2 and discriminant function analysis in Chapter 6 reveal lower classification accuracies in the control group compared with the clinical groups, providing evidence that eye tracking would be better placed as a diagnostic aid alongside other assessment measures in clinic rather than as a screening tool. Machine learning for the eye gaze patterns yielded best accuracies at the diagnostic level in the first study and it is likely that a combination of variables found in both studies via a machine learning approach will yield the best accuracy in aiding diagnoses. Further studies are needed to replicate and incorporate the findings into a single model to include a combination of the social-emotional stimuli and eye tracking measures used in one study sample.

If findings were replicated and a suitable model and algorithm tested in clinical trials, it could still take many years to get relevant approvals and for the technology to be adapted into clinical practice (Bansal et al 2012). With the advent of improving technology and the current wave of digital mental health, policy makers may be more likely to incorporate this form of diagnostic aid but it is still likely to be lengthier than clinicians and families would like.

Although a brain based (Jung et al. 2018) and/or a genetic test would be the gold standard, the time to translate this to the clinic takes several years. Also, imaging is expensive and blood tests are painful; both often require sedation prior to the test in children with neurodevelopmental difficulties. The use of saliva samples for genetic testing for polygenic risk scores holds promise as an alternative to blood tests in children and adolescents (Krapohl et al. 2017).

As current diagnostic assessment methods are subjective, diagnostic aids can bring objectivity into the diagnostic process and could also create efficiency by leading to quicker (Hollis et al. 2018) and potentially more accurate diagnosis. This has many benefits for the family and young person including a more robust and timely assessment which can lead to better mental health outcomes in the short, medium and long term. Diagnostic aids may also have a positive effect on services by helping to get the diagnoses correct from the outset, reduction in waiting times and less demand overall due to prevention of secondary mental health problems. A caveat to this is that with any diagnostic aid, it is important to be upfront that this is

not a test and cannot be used in isolation in assessment or for screening in the community.

As eye tracking on portable machines (e.g. smartphones or tablets) is non-invasive and accessible, measures can be completed in the child's home or school and the usability of this non-invasive technology is high. The tasks can be quick and the monetary costs are relatively cheap compared to imaging techniques. The added advantage of incorporation of emotion recognition and training such as teaching emotions or cognitive control using eye tracking is also important to consider in future (see Section 7.4.5 for further work).

The future of assessment of neuropsychiatric conditions will hopefully hold a range of options (e.g. eye tracking, imaging and genetic tests) so that the families can choose how they proceed with their assessment with the clinician on an individual basis, depending on the needs of the child and young person.

7.4.5 Future direction for clinical application

In addition to the potential for eye tracking as a diagnostic aid, as stated in the previous section, it is also important to consider therapeutic applications. Designing studies both on and off stimulant medication could allow for further understanding of the impact of core symptoms in ADHD on visual social-emotional attention. A key test of the hypothesis that there is a primary visual social-emotional attention deficit in ADHD would be normalisation with stimulant medication. Studies investigating the potential

therapeutic role of non-stimulant ADHD medication on visual social-emotional attention and emotion recognition could also be fruitful. Furthermore, non-stimulant alpha adrenergic agonist, Guanfacine, has been documented as having promising effects on social function (McClure et al. 2019) and treating addition comorbid symptoms including ASD and ODD in ADHD (de Groof, De La Marche, and Danckaerts 2019). Findings on Guanfacine suggest that additional mechanisms could also be involved in social function and visual social-emotional attention, which may benefit from direct testing. For example, it could be conceived that Guanfacine may improve atypical visual social-emotional attention to the negative emotional valence cartoon as this was associated with ASD and oppositional symptom severity in ADHD. Conversely, stimulant medication may have a direct effect on viewing time (indexed by DT) to other facial features of emotional faces which was associated with ADHD IA and HI symptom severity, in addition to social skills deficits on the SAS. Therefore, some visual social-emotional attention profiles could respond differently to medication classes and this would allow for individualised medication suggestions depending on the visual social-emotional attention profile and clinical symptom severity subscales.

In addition to medication, our findings on atypical visual social-emotional attention in ADHD and ASD may also have implications for other therapeutic avenues. The explicit emotion recognition task was an adapted version of the Frankfurt test and training of social affect (FEFA) which also teaches emotions (Bolte et al. 2002). The incorporation of eye tracking to aid learning for example, orienting to the face and fixating on

the eyes for a certain amount of time in ASD, or teaching children with ADHD to look at the subtle facial features such as the brow during emotion recognition could be important therapeutic interventions. A recent study found that children with social skills training improved emotion recognition more in children with ADHD compared to children with ASD, whom required additional training (Lee et al. 2018). This could be due to additional difficulties in viewing time to social areas and orientating visual social-emotional attention in children with ASD compared with ADHD without ASD found in our study.

Group social skills training has been shown to improve social cognition and communication with, improved peer interactions in adolescents with ASD and, this group programme had also shown improvements in social skills in adolescents with ADHD (Laugeson et al. 2012; Gardner, Gerdes, and Weinberger 2019). An interesting avenue of future study could consider if improved outcomes in group social skills training relates to normalisation of visual social-emotional attention to ADOS cartoons, which was atypical in children in the ASD group and the ADHD group in this Thesis.

Additionally, there could be an impact of parenting programmes on emotion recognition and visual social-emotional attention in ADHD. Although parenting programmes improve parent-child interactions, there have been inconsistent findings on core ADHD symptoms (Sonuga-Barke et al. 2018). Visual social-emotional attention could potentially reveal the impact of parenting on emotion recognition in the ADHD phenotype. Finally, it

could be conceived that a combination of medication, social skills and family interventions may improve visual social-emotional attention in those children with most impairment including those with ASD+ADHD. This suggests that multimodal treatment studies are warranted, in order to provide an evidence base for management of combined social-emotional attention difficulties in children with ASD+ADHD.

In summary a visual social-emotional attention profile at the outset of treatment could help to tailor the individual treatment package, be included in the social skills training package and, also aid with therapeutic monitoring alongside clinical symptom severity rating scales. This is important as, providing appropriate intervention(s) for social-emotional difficulties has the potential to improve poor long term outcomes in children with ADHD, ASD and ASD+ADHD and therefore merits further study.

7.5 FINAL CONCLUSIONS

This Thesis demonstrated that the study of visual social-emotional attention in ADHD would uncover important insights into social cognitive difficulties including emotion recognition and comorbidity with ASD. In particular, the hypothesis that ADHD would have a primary problem with visual social-emotional attention which could explain emotion recognition and social skills difficulties and, that this would differentiate from visual attention in ASD, was supported for explicit emotion recognition. Findings also suggested that comorbidity with ASD leads to additive spontaneous emotion recognition deficits on the ADOS due to atypical orienting and,

atypical neutral face processing which was associated with ASD and ADHD hyperactive-impulsive symptom severity. Visual social-emotional attention differentiated the groups in two samples with highest classification accuracies for the ADHD group. Overall, the research questions for this Thesis were answered and the aims were met.

As this is one of the first eye tracking studies that has reported visual social-emotional attention in ADHD, ASD, ASD+ADHD and typically developing control children this is an important contribution to the field. As this research has direct clinical relevance and application, replication of the work in experimental study and progressing to clinical trials is warranted in order to provide further evidence, prior to the use of eye tracking as a diagnostic aid. This Thesis has answered important questions regarding the association of ADHD and emotion recognition by studying visual social-emotional attention using eye tracking. The research has also narrowed the gap in the search of diagnostic aids differentiating ADHD, autism and comorbidity.

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APPENDICES

I. CASE VIGNETTES

Case examples are given for illustrative purposes so they have been generalised to include scenarios from several children that may have presented in clinical practice with similar difficulties. The names are fictitious and circumstances such as age and family circumstances have been changed for anonymity.

Case 1: ADHD

Andy was referred to the community CAMHS when he was 13 years old. He was struggling academically and getting told off for poor concentration and disruption in the class. He found it difficult to line up to go to lunch at school and would but into conversations at school and at home. Andy also found it difficult to take turns and follow the rules of sports games during physical education and would get easily frustrated if he lost the game. Andy would get into arguments with peers in some situations and was starting to fall out with friends. It was reported that Andy would misinterpret social situations, found it difficult to express his emotions and found it difficult to say sorry after doing something wrong.

After some family therapy in CAMHS Andy was referred to the consultant for an assessment of ADHD due to ongoing concerns regarding impulsivity and poor concentration. During the ADHD assessment, Andy had reasonable eye contact and rapport but he was fidgeting towards the end of

the interview. He also corroborated struggling with concentration for as long as he could remember and his mother confirmed he had been a very active pre-schooler. School reports showed poor concentration in primary school and he would get into fights with his peers. Parent, self and teacher Conners' rating scale were suggestive of ADHD combined type.

There was no significant medical history and early developmental milestones were reported as achieved at the expected time. There were no difficulties with the pregnancy and Andy was born on time weighing 3.5kg. There was no family history of ADHD or other neurodevelopmental disorders. Parents are divorced and Andy does not get on with his father.

In terms of social history, Andy has a few close friends and liked to go to the park with them but struggled to go to the cinema with them as he could not stay to watch the film throughout. Andy did not have any particular hobbies. Andy tried cannabis which helped to calm him down but he does not take this regularly. He does not take other illicit drugs or drink alcohol. There is no forensic history.

A diagnosis of ADHD was made and Andy was titrated onto a long acting stimulant medication. Stimulant medication had a good effect when he remembered to take it and he went on to sit his GCSE exams and passed them. He is now doing an apprenticeship in construction and he is enjoying this. He continues to take stimulant medication regularly as he feels this helps him focus and stops him from feeling angry and getting into trouble.

Case 2: ASD+ADHD

Barry was referred at 15 years of age to the CAMHS for a second opinion for management of his ADHD medication. Barry was born preterm at 28 weeks gestation weighing 1.5kg and required assisted ventilation for 1 week on the special care baby unit. Barry was sent home from the special care baby unit after 4 weeks with no further medical problems. Barry achieved all of his motor milestones on time but there were some concerns regarding social interaction, imaginative play and making friends. He also found it very difficult to concentrate and sit still in the mainstream classroom environment.

Barry was diagnosed with ASD when he was in primary school and with ADHD when he entered secondary school. He was given an educational healthcare plan to support his needs and was put on long acting stimulant medication to help with ADHD symptoms. Unfortunately, although the long acting stimulants helped with concentration this was counteracted by very poor sleep. Barry was therefore put on short acting stimulant medication twice a day for ADHD and long acting melatonin at night to help with sleep. Barry did well on this medication regime and sat his GCSESs and passed them all. He continues to need lots of prompting from his parents to get organised, has poor eye contact, difficulties with reciprocal social interaction and limited friendships. He enjoys computer games, spending much of his time doing this and he also has a keen interest in animals. His parents initially struggled to come to terms with the diagnosis

and with some of the limitations of treatment for symptoms but now feel more empowered to help Barry.

Case 3: ASD+ADHD or severe ADHD?

Callum was referred to CAMHS by the GP at the age of 13 years as his grandfather was struggling to manage his behaviour. Callum had been living with his grandfather for 2 years and his parents do not have regular contact with him.

Callum presented as a boy with intermittent eye contact and rapport, occasional fidgeting during the interview and mild restlessness. Callum's self-report included poor concentration and difficulty completing work in class. He reported getting into trouble at school for 'messing around'. School reported Callum had difficulties with listening, talking back to teachers and not achieving his potential. Callum had been put in 'isolation' as punishment at school several times which he disliked. Callum said he wanted to make friends but was not sure how. He would often dominate conversations with peers and talk at length about his preferred topics of conversation, potentially suggestive of difficulties with to and fro conversation and reciprocal social interaction. It was reported that despite Callum's efforts he did not have any close friendships.

According to Callum's grandfather, Callum was like him and he did not think there was a family history of any neurodevelopmental disorders in the family. As far as Callum's grandfather was aware, there had been no

problems with Callum's birth or early milestones. Callum's grandfather reported that Callum's mother's care can be erratic but he was unsure about post-natal depression or illicit drugs during the pregnancy. It was difficult for Callum's grandfather to complete the ASD screening questionnaires and obtain an accurate early developmental history. Callum also had a QBtest for ADHD and an ADOS for ASD, both of which were positive for ADHD and ASD respectively. Conners' parent, self and teacher questionnaires were also suggestive of ADHD combined type. A sensory assessment was completed which indicated difficulties with sensory processing including increased sensitivity to noise and touch.

Due to Callum's clinical presentation being strongly suggestive of ADHD, a diagnosis of ADHD was given in the first instance and long acting stimulant medication was initiated. Unfortunately, Callum proved to be very sensitive to ADHD longer acting stimulant medication but did reasonably well on short acting Methylphenidate. Callum did not receive recommended extra support at school for ADHD despite an Education Health Care Plan. As he continued to struggle in interactions with peers, an ADOS was repeated while on stimulant medication and this was just above threshold for a diagnosis of ASD. In particular, Callum had reduced observed gestures, reduced reciprocal social communication, less comments on others' emotions, reduced quality of social overtures and social responses on the ADOS. A diagnosis of ASD was given in addition to ADHD and a revised support plan for Callum attending to sensory sensitivities and a structured environment was advised. Callum's grandfather was given support to help him put boundaries in place at home.

Case 4: ASD

Daniel was referred to CAMHS by the GP at the age of 12 for an assessment of ASD. He was struggling with his new secondary school and the school had suggested that it would be helpful for Daniel to be referred as he was struggling in the new school environment. Daniel has gone to a small primary school and his mum reported that she had always suspected that Daniel had ASD but because the educational environment and home environment could support his need for a structured quiet environment, they did not need to seek a diagnosis until now.

Daniel had an older brother at university and there was a family history of ASD in the extended family. Daniel was born by normal delivery weighing 3.8kg. When he was born the umbilical cord was wrapped around his neck although he cried shortly after some stimulation. He did not need to spend time on the special care baby unit and there are no known medical problems. Mum reports that that major milestones were on time but Daniel was shy and quiet, finding it difficult to make friends.

Mum reports Daniel has some sensory sensitivities and had an intense interest in dinosaurs when he was younger. Mum reported that he did not imitate or take part in imaginative play with others his age when he was younger. Daniel is currently interested in information technology and programming although he reports that he finds it hard to learn at the college as it is loud. He also finds it hard to ask for help and feels that he is behind in his course. He doesn't find it difficult to concentrate on the work. Although he was bullied briefly at primary school, Daniel says that this is not the

case in secondary school although he reports that he has not made any friends. There is no forensic history or use of illicit drugs or substances.

In clinic, he had poor eye contact and his speech was quiet and he spoke in the same tone throughout. He did not have any abnormal movements during the interview. There were limited non-verbal gestures and display of facial emotion. An ADOS and ADI-R were completed which showed that Daniel was above the threshold for ASD. Daniel was diagnosed with ASD and the parents were offered techniques to help with sensory sensitivities. The diagnosis and sensory interventions suggested were shared with the school by the family. Daniel obtained an educational health care plan and was given a mentor, extra support and extra time in course work and exams. He was also given a quiet place to eat his lunch and do his work when out of structured lessons. Daniel progressed in mainstream school and passed all his exams and was very good at computer programming. His parents were pleased with his progress although he continued to find it difficult to articulate his emotions in clinic without support from his parents.

II. TRANSCRIPTS FROM OBSERVATIONAL CODING

Table A.1: Showing example notes for 4 participants and designation into groups during observation and coding (Chapter 2)

Proposed Group	First Stage (control versus clinical status)		Second Stage (specific clinical group status)		
	Control	Clinical	ADHD	ASD+ADHD	ASD
Notes on participant video fixation patterns over 60 face trials (Blind to actual group)	Tends to triangulate (fixation circles moving from left eye area to mouth to right eye area: does not go back to left eye so more v shaped rather than upside down triangle) No scattered fixation pattern (fixation spots are not fast or dispersed on video) Does not tend to have scatter unless very easy emotion e.g. happy. Does not tend to be focused on other features (non- eyes/mouth/ midline features unless there is an obvious feature e.g. ears that stick out. Did focus on nasal bridge/ bottom of forehead a lot in face 22 – disgust as this contained salient information for this emotion.	This eye tracking pattern is very different to the previous participant. Very fast appearance of fixation circles and fixation circles are very sparse covering a larger volume and was difficult to keep up with. Did go to left eye and mouth but only a few fixation circles here and seemed to go off face and back again a lot more. Also spent some time (though quite brief) on distractors such as beard and hairline. Does not tend to cover upper portion of the face. By face 16 seems to be able to focus on some areas more with slightly less scattered pattern. Due to very fast fixation pattern I would say this child has and severe ADHD. Tends to focus on irrelevant things like nose and cheek when in frame this would suggest possibly also ASD. Much less looking at eyes.	Fixation circles all over the place- ? Distracted a lot, scatter present. Goes 'off screen' early. Looked at a core feature. Towards the end started looking at cheek/mouth e.g. for happy. Only did this in the last block.	Severe ADHD due to 'scatter' with some ASD features e.g. looking at irrelevant areas - cheeks and nose proportionally more. No 'triangulation' and does not look at eyes much so have chosen comorbid group.	Mainly looked at lower half of face and focused on non-salient features: nose, chin. Not much scatter- fixation circles close together). No 'triangulations' or 'V shape', occasional linear patterns of fixation between core features.

III. ADOS EMOTION RECOGNITION SUB-SCORE

The ADOS emotion recognition score refers to the subscore B4 and B5 in ADOS modules 3 and 4 respectively. This subscore is termed comments on others' emotions/empathy. The scoring details and wording of this item are taken directly out of the ADOS-2 module 3 and 4 booklet and can also be found in the ADOS-2 manual (2014).

"The focus of this item is on the participants' communication of his or her recognition, understanding, and/or response to the feelings of other people or characters, real or conveyed in stories or other tasks.

"0=Spontaneously communicates clear understanding or labelling of and/or appropriate response to several different emotions in other people/characters. Labelling several emotions in others is sufficient but not necessary if there are other clear indications of understanding and/or appropriate response.

"1=Communicates some understanding, labelling, or response to an emotion in others (e.g. spontaneously and correctly identifies at least one emotion in another person/character).

"2=No or minimal identification/communication of understanding of emotion in others."

IV. ADOS CARTOON SERIES'

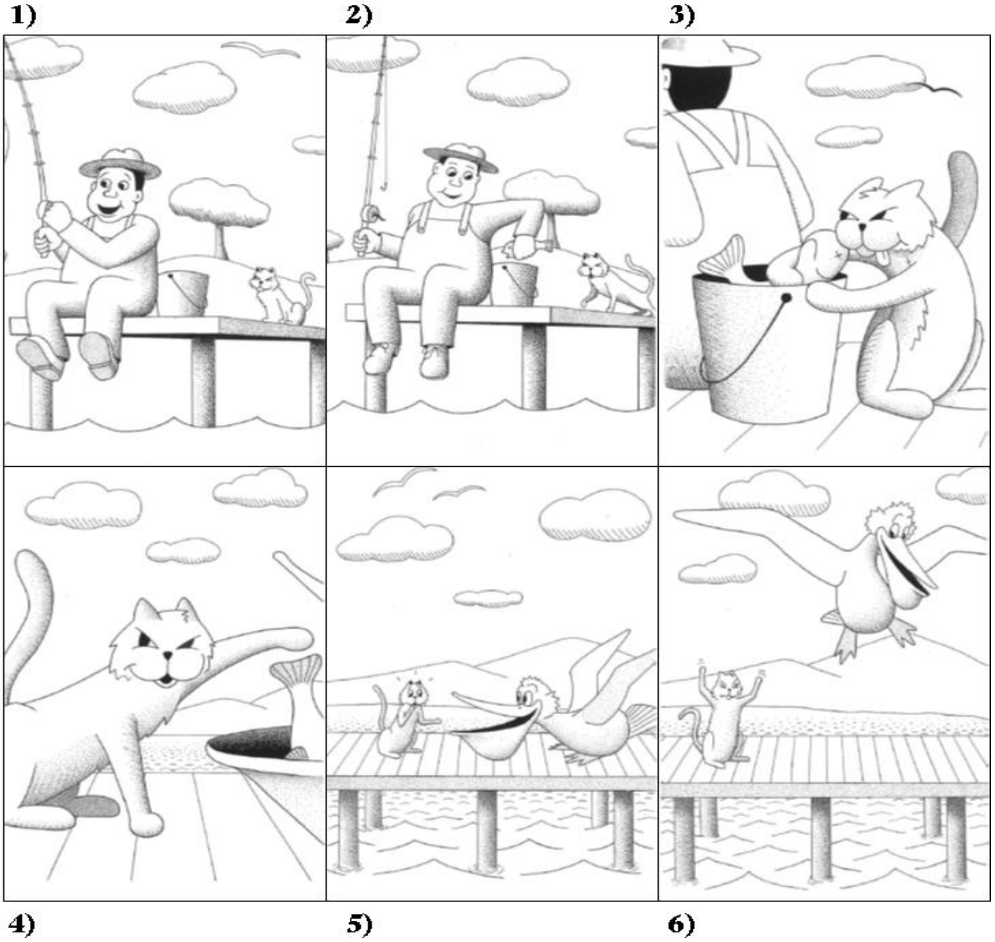


Figure A1: ADOS Cat cartoon series A

Cards are numbered 1) through 6) with card 1) being the first in the series and card 6) the final card of the series. Card 1) depicts a man fishing who is unaware of the cat behind him who wants to steal the fish. Card 2) the man puts the fish in the bucket. Card 3) the cat steals the fish. Card 4) the cat then places the fish in another bucket. Card 5) the other bucket turns to be the beak of a pelican. Card 6) the pelican flies off with the fish and the cat is angry. Only card 1) was used in the eye tracking procedure described in Chapter 4.

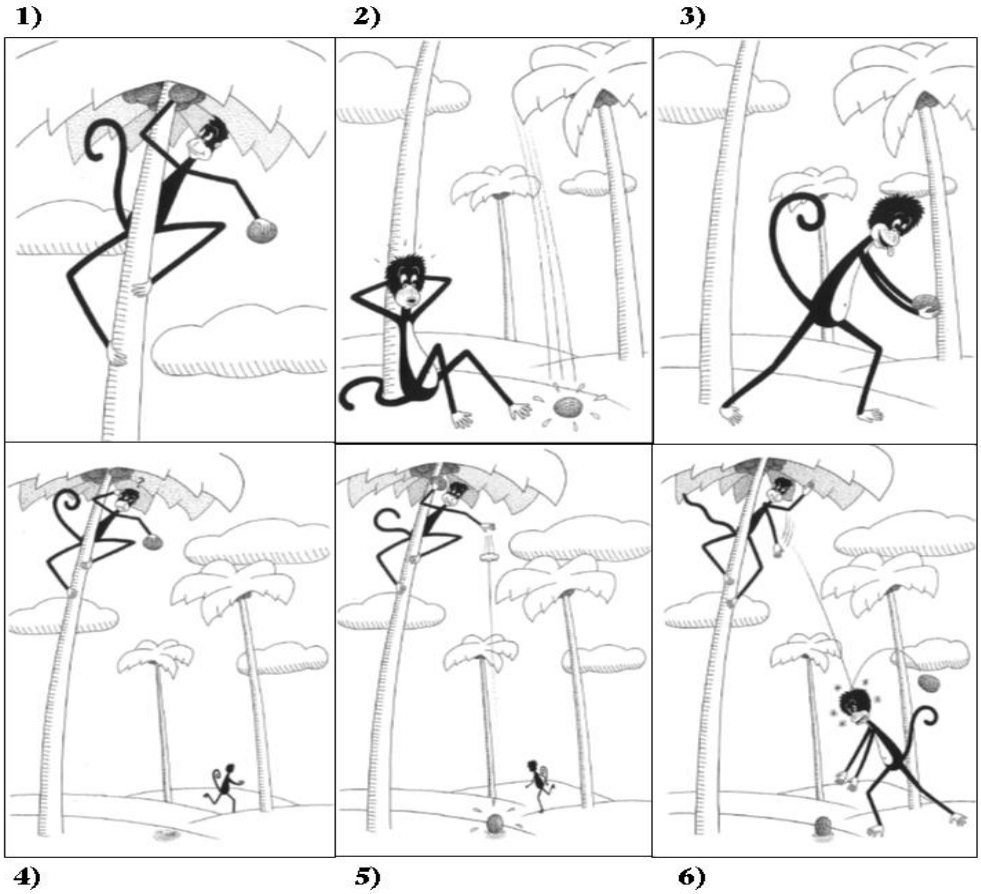


Figure A2: ADOS Monkeys cartoon series B

Cards are numbered 1) through 6) with card 1) being the first in the series and card 6) the final card of the series. Card 1) the first monkey in the tree is collecting coconuts. Card 2) the second monkey is at the bottom of the tree and sees a coconut fall. Card 3) the second monkey picks up the coconut and takes it away. Card 4) the first monkey wonders where his coconut has gone. Card 5) the first monkey then realises his coconut has been taken and starts throwing the other coconuts on the ground. Card 6) the first monkey hits the second monkey on the head with one of the coconuts. Only card 6) was used in the eye tracking procedure described in Chapter 4.

V. SUPPLEMENTARY DATA FROM HIERARCHICAL REGRESSION FOR CHAPTERS 3–5

Chapter 3

Hierarchical linear regression model tables described in results section 3.4.3.3 were presented in this part of the appendix. For each model the p-value was denoted as significant if $p<0.05$. If the p-value for a model was between 0.05–0.10, this value was shown in the table to allow for trends in the data to be presented. Significant R^2 change within each model was denoted as $p<0.05$.

Table A.2: Hierarchical linear regression models for emotional accuracy

Model (predictors)	R^2	R^2 **change**	F	**p-value**
1 (ADHD factor)	0.15	0.15*	6.71	<0.05
2 (ADHD factor, ASD factor)	0.17	0.02	3.87	<0.05
3 (ADHD factor, ASD factor, FSIQ)	0.28	0.11*	4.88	<0.01
4 (ADHD factor, ASD factor, FSIQ, Conners' OD T score)	0.30	0.02	3.83	<0.05

FSIQ (Full Scale Intelligence Quotient); OD (Oppositional); *(significant R^2 change; $p<0.05$)

Table A.3: Hierarchical linear regression models for DT to mouth

Model (predictors)	R^2	R^2 **change**	*F*	**p-value**
1 (ASD factor)	0.10	0.10	4.08	=0.05
2 (ASD factor, ADHD factor)	0.10	0.00	2.02	n/s
3 (ASD factor, ADHD factor, FSIQ)	0.13	0.03	1.71	n/s
4 (ASD factor, ADHD factor, FSIQ Conners' OD T score)	0.13	0.00	1.28	n/s

FSIQ (Full Scale Intelligence Quotient); OD (Oppositional); *(significant R^2 change; p<0.05); n/s (non-significant)

Table A.4: Hierarchical linear regression models for DT left eye

Model (predictors)	R^2	R^2 **change**	*F*	**p-value**
1 (ASD factor)	0.00	0.00	0.01	n/s
2 (ASD factor, ADHD factor)	0.01	0.01	0.14	n/s
3 (ASD factor, ADHD factor, FSIQ)	0.05	0.04	0.61	n/s
4 (ASD factor, ADHD factor, FSIQ Conners' OD T score)	0.08	0.03	0.72	n/s

FSIQ (Full Scale Intelligence Quotient); OD (Oppositional); *(significant R^2 change; p<0.05); n/s (non-significant)

Table A.5: Hierarchical linear regression models for DT right eye

Model (predictors)	R^2	R^2 **change**	*F*	**p-value**
1 (ASD factor)	0.03	0.03	0.01	n/s
2 (ASD factor, ADHD factor)	0.08	0.06	0.14	n/s
3 (ASD factor, ADHD factor, FSIQ)	0.30	0.22**	0.61	<0.01
4 (ASD factor, ADHD factor, FSIQ Conners' OD T score)	0.31	0.01	0.72	<0.05

FSIQ (Full Scale Intelligence Quotient); OD (Oppositional); **(significant R^2 change; p<0.01); n/s (non-significant)

Table A.6: Hierarchical linear regression models for DT to other facial features

Model (predictors)	R^2	R^2 **change**	*F*	**p-value**
1 (ADHD factor)	0.22	0.22**	10.35	<0.01
2 (ADHD factor, ASD factor)	0.26	0.04	6.19	<0.01
3 (ADHD factor, ASD factor, FSIQ)	0.30	0.03	4.73	<0.01
4 (ADHD factor, ASD factor, FSIQ, Conners' OD T score)	0.34	0.04	4.15	<0.01

FSIQ (Full Scale Intelligence Quotient); OD (Oppositional); ** (significant R^2 change; p<0.01); n/s (non-significant)

Table A.7: Hierarchical linear regression models for Mean Fixation Duration

Model (predictors)	R^2	R^2 **change**	*F*	**p-value**
1 (ADHD factor)	0.08	0.08	10.35	=0.08
2 (ADHD factor, ASD factor)	0.12	0.03	6.19	n/s
3 (ADHD factor, ASD factor, FSIQ)	0.12	0.00	4.73	n/s
4 (ADHD factor, ASD factor, FSIQ, Conners' OD T score)	0.18	0.06	4.15	n/s

FSIQ (Full Scale Intelligence Quotient); OD (Oppositional); n/s (non-significant)

Table A.8: Hierarchical linear regression models for Total Fixation Number

Model (predictors)	R^2	R^2 **change**	*F*	**p-value**
1 (ADHD factor)	0.06	0.06	2.33	n/s
2 (ADHD factor, ASD factor)	0.08	0.03	1.65	n/s
3 (ADHD factor, ASD factor, FSIQ)	0.09	0.00	1.11	n/s
4 (ADHD factor, ASD factor, FSIQ, Conners' OD T score)	0.13	0.05	1.29	n/s

FSIQ (Full Scale Intelligence Quotient); OD (Oppositional); n/s (non-significant)

Table A.9: Hierarchical linear regression models for Mean Length between Fixations

Model (predictors)	R^2	R^2 **change**	*F*	p-value
1 (ADHD factor)	0.09	0.09	3.68	=0.06
2 (ADHD factor, ASD factor)	0.12	0.03	2.38	n/s
3 (ADHD factor, ASD factor, FSIQ)	0.13	0.01	1.70	n/s
4 (ADHD factor, ASD factor, FSIQ, Conners' OD T score)	0.13	0.00	1.24	n/s

FSIQ (Full Scale Intelligence Quotient); OD (Oppositional); n/s (non-significant)

Table A.10: Hierarchical linear regression models for Fixation Scanpath Length

Model (predictors)	R^2	R^2 **change**	*F*	p-value
1 (ADHD factor)	0.12	0.12*	5.05	<0.05
2 (ADHD factor, ASD factor)	0.16	0.04	3.38	<0.05
3 (ADHD factor, ASD factor, FSIQ)	0.16	0.00	2.27	n/s
4 (ADHD factor, ASD factor, FSIQ, Conners' OD T score)	0.18	0.02	1.85	n/s

FSIQ (Full Scale Intelligence Quotient); OD (Oppositional); *(significant R^2 change; $p<0.05$); n/s (non-significant)

Chapter 4

Hierarchical linear regression model tables described in results Section 4.2.4 were presented in this part of the appendix. For each model the p-value was denoted as significant if $p<0.05$. If the p-value for a model was between 0.05–0.10, this value was shown in the table to allow for trends in the data to be presented. Significant R^2 change within each model was denoted as $p<0.05$.

Table A.11: Hierarchical linear regression models for ADOS emotion recognition score†

Model (predictors)	R^2	R^2 **change**	F	**p-value**
1 (ASD factor)	0.06	0.06	3.70	=0.06
2 (ASD factor, ADHD factor)	0.06	0.00	1.90	n/s
3 (ASD factor, ADHD factor, FSIQ)	0.06	0.00	1.22	n/s
4 (ASD factor, ADHD factor, FSIQ Conners' OD T score)	0.07	0.00	0.93	n/s

†ADOS score only available for clinical cases. FSIQ (Full Scale Intelligence Quotient); OD (Oppositional); *(significant R^2 change; $p<0.05$); n/s (non-significant)

Table A.12: Hierarchical linear regression models for DT to ADOS pictures

Model (predictors)	R^2	R^2 **change**	*F*	**p-value**
1 (ASD factor)	0.06	0.06*	4.70	<0.05
2 (ASD factor, ADHD factor)	0.06	0.00	2.33	n/s
3 (ASD factor, ADHD factor, FSIQ)	0.06	0.00	1.59	n/s
4 (ASD factor, ADHD factor, FSIQ Conners' OD T score)	0.06	0.00	1.18	n/s

FSIQ (Full Scale Intelligence Quotient); OD (Oppositional); *(significant R^2 change; p<0.05); n/s (non-significant)

Table A.13 Hierarchical linear regression models for FC to faces in ADOS pictures

Model (predictors)	R^2	R^2 **change**	*F*	**p-value**
1 (ASD factor)	0.04	0.04	3.52	=0.06
2 (ASD factor, ADHD factor)	0.05	0.00	1.90	n/s
3 (ASD factor, ADHD factor, FSIQ)	0.05	0.00	1.30	n/s
4 (ASD factor, ADHD factor, FSIQ Conners' OD T score)	0.05	0.00	0.96	n/s

FSIQ (Full Scale Intelligence Quotient); OD (Oppositional); *(significant R^2 change; p<0.05); n/s (non-significant)

Table A.14: Hierarchical linear regression models for FFT to faces in ADOS pictures

Model (predictors)	R^2	R^2 **change**	*F*	**p-value**
1 (ASD factor)	0.08	0.08*	6.32	<0.05
2 (ASD factor, ADHD factor)	0.08	0.00	3.31	<0.05
3 (ASD factor, ADHD factor, FSIQ)	0.09	0.02	2.64	=0.06
4 (ASD factor, ADHD factor, FSIQ Conners' OD T score)	0.10	0.00	2.07	=0.09

FSIQ (Full Scale Intelligence Quotient); OD (Oppositional); *(significant R^2 change; p<0.05); n/s (non-significant)

Table A.15: Hierarchical linear regression models for DT to faces in Monkeys Cartoon (negative valence)

Model (predictors)	R^2	R^2 **change**	*F*	**p-value**
1 (ADHD factor)	0.02	0.02	1.62	n/s
2 (ADHD factor, ASD factor)	0.03	0.01	1.32	n/s
3 (ADHD factor, ASD factor, FSIQ)	0.05	0.01	1.24	n/s
4 (ADHD factor, ASD factor, FSIQ, Conners' OD T score)	0.10	0.05*	2.01	=0.09

FSIQ (Full Scale Intelligence Quotient); OD (Oppositional); *(significant R^2 change; p<0.05); n/s (non-significant)

Table A.16: Hierarchical linear regression models for FCs to faces in cartoons

Model (predictors)	R^2	R^2 **change**	*F*	**p-value**
1 (ADHD factor)	0.01	0.01	1.10	n/s
2 (ADHD factor, ASD factor)	0.02	0.01	0.79	n/s
3 (ADHD factor, ASD factor, FSIQ)	0.03	0.01	0.76	n/s
34 (ADHD factor, ASD factor, FSIQ, Conners' OD T score)	0.07	0.04	1.38	n/s

FSIQ (Full Scale Intelligence Quotient); OD (Oppositional); *(significant R^2 change; p<0.05); n/s (non-significant)

Table A.17: Hierarchical linear regression models for FCs to faces in negative emotional valence (Monkeys) cartoon

Model (predictors)	R^2	R^2 **change**	*F*	**p-value**
1 (ADHD factor)	0.03	0.03	2.85	n/s
2 (ADHD factor, ASD factor)	0.05	0.02	2.03	n/s
3 (ADHD factor, ASD factor, FSIQ)	0.06	0.01	1.67	n/s
4 (ADHD factor, ASD factor, FSIQ, Conners' OD T score)	0.11	0.05*	2.31	=0.07

FSIQ (Full Scale Intelligence Quotient); OD (Oppositional); *(significant R^2 change; p<0.05); n/s (non-significant)

Table A.18: Hierarchical linear regression models for FFT to perpetrator Monkey face in negative emotional valence (Monkeys) Cartoon

Model (predictors)	R^2	R^2 **change**	*F*	**p-value**
1 (ASD factor)	0.06	0.06*	4.92	<0.05
2 (ASD factor, ADHD factor)	0.07	0.01	2.74	=0.07
3 (ASD factor, ADHD factor, FSIQ)	0.07	0.00	1.82	n/s
4 (ASD factor, ADHD factor, FSIQ, Conners' OD T score)	0.08	0.02	1.69	n/s

FSIQ (Full Scale Intelligence Quotient); OD (Oppositional); *(significant R^2 change; p<0.05); n/s (non-significant)

Table A.19: Hierarchical linear regression models for RCs between faces in cartoons

Model (predictors)	R^2	R^2 **change**	*F*	**p-value**
1 (ADHD factor)	0.02	0.02	1.40	n/s
2 (ADHD factor, ASD factor)	0.02	0.00	0.78	n/s
3 (ADHD factor, ASD factor, FSIQ)	0.04	0.02	1.00	n/s
4 (ADHD factor, ASD factor, FSIQ, Conners' OD T score)	0.07	0.04	1.48	n/s

FSIQ (Full Scale Intelligence Quotient); OD (Oppositional); *(significant R^2 change; p<0.05); n/s (non-significant)

Table A.20: Hierarchical linear regression models for RCs between faces in negative emotional valence (Monkeys) cartoon

Model (predictors)	R^2	R^2 **change**	*F*	**p-value**
1 (ADHD factor)	0.04	0.04	3.00	=0.09
2 (ADHD factor, ASD factor)	0.06	0.02	2.50	=0.09
3 (ADHD factor, ASD factor, FSIQ)	0.08	0.02	2.00	n/s
4 (ADHD factor, ASD factor, FSIQ, Conners' OD T score)	0.13	0.06*	2.90	<0.05

FSIQ (Full Scale Intelligence Quotient); OD (Oppositional); *(significant R^2 change; $p<0.05$); n/s (non-significant)

Chapter 5

Hierarchical linear regression model tables described in results Section 5.3.3 were presented in this part of the appendix. For each model the p-value was denoted as significant if $p<0.05$. If the p-value for a model was between 0.05–0.10, this value was shown in the table to allow for trends in the data to be presented. Significant R^2 change within each model was denoted as $p<0.05$.

Table A.21: Hierarchical linear regression models for DT to right eye in neutral faces

Model (predictors)	R^2	R^2 **change**	F	**p-value**
1 (ADHD factor)	0.04	0.04	3.72	=0.06
2 (ADHD factor, ASD factor)	0.05	0.00	1.99	n/s
3 (ADHD factor, ASD factor, FSIQ)	0.05	0.00	1.32	n/s
4 (ADHD factor, ASD factor, FSIQ, Conners' OD T score)	0.05	0.00	1.07	n/s

FSIQ (Full Scale Intelligence Quotient); OD (Oppositional); *(significant R^2 change; $p<0.05$); n/s (non-significant)

Table A.22: Hierarchical linear regression models for FCs to right eye in neutral faces

Model (predictors)	R^2	R^2 **change**	F	**p-value**
1 (ADHD factor)	0.09	0.09**	7.54	<0.01
2 (ADHD factor, ASD factor)	0.09	0.01	4.05	<0.05
3 (ADHD factor, ASD factor, FSIQ)	0.09	0.00	2.67	=0.05
4 (ADHD factor, ASD factor, FSIQ, Conners' OD T score)	0.09	0.00	1.98	n/s

FSIQ (Full Scale Intelligence Quotient); OD (Oppositional); ** (significant R^2 change; p<0.01); n/s (non-significant)

Table A.23: Hierarchical linear regression models for LI to neutral faces

Model (predictors)	R^2	R^2 **change**	F	**p-value**
1 (ASD factor)	0.10	0.10**	8.36	<0.01
2 (ASD factor, ADHD factor)	0.10	0.00	4.34	<0.05
3 (ASD factor, ADHD factor, FSIQ)	0.10	0.00	2.89	<0.05
4 (ASD factor, ADHD factor, FSIQ Conners' OD T score)	0.12	0.02	2.55	<0.05

FSIQ (Full Scale Intelligence Quotient); OD (Oppositional); ** (significant R^2 change; p<0.01); n/s (non-significant)

VI. RAW DATA FROM CHAPTERS 3-5

Chapter 3 – Emotional faces

Raw behavioural and eye tracking data in the groups from the sample described in Chapter 3 are presented in Table A.24.

Table A.24: Raw data in the groups from Chapter 3 – Emotional faces

	Group			
Mean	**ADHD** (n=8)	**ASD** (n=10)	**ASD+ADHD** (n=9)	**Controls** (n=16)*
Emotion recognition (SD; range)	**0.71**(0.14; 0.43-0.85)	**0.76**(0.08; 0.60-0.88)	**0.67**(0.13; 0.52-0.82)	**0.77**(0.08; 0.53-0.90)
DT right eye (SD; range)	**375.78**(381.83; 17.31-1056.88)	**469.94**(262.36; 131.41-863.59)	**458.67**(344.58; 101.68-1161.20)	**664.97**(452.45; (19.19-1595.25)
DT left eye (SD; range)	**746.05**(627.65; 22.87-1816.14)	**655.83**(277.17; 229.41-1149.13)	**603.57**(446.25; 179.56-1575.27)	**540.47**(516.73; 22.37-1999.10)
DT mouth (SD; range)	**1189.20**(603.27; 548.00-2450.40)	**867.38**(300.60; 400.55-1362.40)	**905.19**(376.68; 250.48-1650.07)	**1158.69**(472.24; 253.66-2121.42)
DT other facial features (SD; range)	**852.46**(162.65; 629.43-1065.93)	**1298.31**(287.22; 741.41-1749.96)	**1017.22**(238.52; 573.24-1359.20)	**1159.28**(368.78; 531.47-1742.85)
TFN (SD; range)	**7.68**(1.41; 5.95-9.85)	**6.68**(1.51; 3.64-8.62)	**7.61**(0.54; 6.92-8.53	**6.80**(1.79; 3.61-9.61)
TFD (SD; range)	**4141.55**(245.16; 3663.09-4381.71)	**4111.24**(223.00; 3708.28-4449.66)	**4048.67**(197.57; 3716.75-4256.60	**4146.12**(339.41; 3294.78-4450.59)
MFD (SD; range)	**619.09**(142.07; 424.29-839.49)	**786.29**(263.94; 513.90-1431.50)	**609.97**(51.85; 519.76-685.20)	**772.68**(322.24; 427.47-1446.66)
FSPL (SD; range)	**175.97**(48.57; 129.69-275.63)	**130.35**(37.62; 65.46-188.69)	**172.70**(21.63; 136.06-200.02)	**148.45**(46.09; 65.46-219.97)
MLBF (SD; range)	**22.36**(2.94; 19.75-28.21)	**18.80**(4.08; 10.15-24.04)	**22.49**(3.00; 17.55-27.27)	**21.31**(4.14; 10.15-27.38)
SDLBF (SD; range)	**17.57**(3.30; 12.22-21.44)	**16.89**(4.64; 10.25-24.27)	**19.37**(3.87; 13.39-26.53)	**18.56**(5.49; 10.25-30.28)
Trials excluded** (SD; range)	**5.75** (6.16; 0.00-18.00)	**5.20**(5.16; 0.00-17.00)	**9.22**(8.41; 0.00-30.00)	**2.43**(2.79; 0.00-9.00)

DT (Dwell Time); TFN (Total Fixation Number); TFD (Fixation Duration); MFD (Mean Fixation Duration); FSPL (Fixation Scanpath Length); MLBF (Mean Length Between Fixations); SDLBF (Standard Deviation Length Between Fixations). *2 control children were not included in the eye tracking analysis due to inadequate data acquisition (as described in Section 3.3). 1 child in the ADHD group could not complete the calibration so could not complete the task (as described in Section 2.2.4). **Mean number of face trials excluded in the eye tracking data per group (total number of face trials = 60).

Chapter 4 – ADOS images

Raw eye tracking data in the groups from Chapter 4 are presented in Table A.25.

Table A.25: Raw eye tracking data in the groups from Chapter 4 - ADOS images

	Group			
Mean	**ADHD** (n=16)	**ASD** (n=18)	**ASD+ADHD** (n=28)	**Controls** (n=22)
DT to faces in ADOS pictures (SD; range)	**2614.63** (1159.19; 565.33-4207.33)	**1983.69** (1154.96; 568.00-4486.00)	**2425.38** (1582.36; 683.33-6926.00)	**3225.91** (1331.61; 1094.00-5944.67)
FC to faces in ADOS pictures (SD; range)	**8.42** (4.54; 1.67-16.67)	**7.08** (4.72; 1.00-18.67)	**8.17** (4.88; 2.00-22.67)	**11.02** (4.48; 3.67-21.67)
FFT to faces in ADOS pictures (SD; range)	**3105.42** (3583.92; 38.67-13871.33)	**5415.84** (3615.02; 918.00-10568.67)	**3900.94** (3097.32; 38.67-11026.12)	**2264.27** (1227.13; 807.33-5193.33)
DT to faces in ADOS cartoons (SD; range)	**3894.44** (2240.10; 411.00-9230.00)	**3502.94** (1898.39; 257.00-6391.00)	**4138.46** (1916.40; 153.00-7378.00)	**4611.95** (1460.76; 1314.00-6646.00)
FC to faces in ADOS cartoons (SD; range)	**7.68** (1.41; 5.95-9.85)	**6.68** (1.51; 3.64-8.62)	**7.61** (0.54; 6.92-8.53	**6.80** (1.79; 3.61-9.61)
FFT to faces in ADOS cartoons (SD; range)	**2171.69** (3070.87; 2.00-11849.00)	**1666.72** (1466.17; 429.00-6334.00)	**1357.04** (1841.59; 2.00-10366.00)	**840.18** (250.78; 354.00-1303.00)
RC to faces in ADOS cartoons (SD; range)	**7.00** (3.22; 1.00-13.50)	**7.47** (3.70; 1.00-13.50)	**8.07** (2.86; 1.00-12.50)	**9.39** (2.42; 3.00-13.50)
Trials excluded* (SD; range)	**0.00** (0.00; 0.00-0.00)	**0.06** (0.24; 0.00-1.00)	**0.04** (0.19; 0.00-1.00)	**0.00** (0.00; 0.00-0.00)

DT (Dwell Time); FC (Fixation Count); FFT (First Fixation Time); RC (Run Count).
*Mean number of trials excluded in the eye tracking data per group (total number of trials = 5). 2 control children and 1 child in the ASD+ADHD group were excluded due to inadequate data acquisition (as described in Section 4.1.4).

Chapter 5 - Neutral faces

Raw eye tracking data in the groups from the neutral faces in Chapter 5 are presented in Table A.26.

Table A.26: Raw eye tracking data in the groups from Chapter 5 – neutral faces

	Group			
Mean	**ADHD** (n=16)	**ASD** (n=18)	**ASD+ADHD** (n=28)	**Controls** (n=22)
DT right eye (SD; range)	**547.27** (542.68; 00.00-1802.67)	**822.44** (764.24; 0.00-2259.33)	**748.52** (652.93; 0.00-2409.33)	**1144.79** (793.67; 61.33-2826.00)
DT left eye (SD; range)	**787.85** (730.32; 0.00-2187.33)	**483.06** (582.50; 0.00-1772.00)	**791.94** (753.10; 0.00-3092.67)	**671.03** (463.80; 0.00-1469.33)
DT mouth (SD; range)	**514.54** (410.01; 0.00-1362.00)	**512.33** (777.29; 0.00-3442.67)	**425.98** (518.30; 0.00-2536.57)	**530.24** (379.25; 0.00-1365.33)
DT other facial features (SD; range)	**1163.69** (399.69; 539.00-1821.33)	**1290.94** (533.04; 304.67-2642.00)	**1304.15** (606.28; 393.00-2458.67)	**1189.28** (596.85; 196.67-2336.67)
FC right eye (SD; range)	**1.31** (1.09; 0.00-3.33)	**2.19** (1.97; 0.00-7.33)	**1.68** (1.21; 0.00-5.33	**2.92** (1.98; 0.33-9.67)
FC left eye (SD; range)	**1.84** (1.62; 0.00-5.00)	**1.61** (1.96; 0.00-6.00)	**1.87** (1.37; 0.00-5.67)	**1.73** (1.00; 0.00-4.00)
FC mouth (SD; range)	**1.57** (1.29; 0.00-4.00)	**1.33** (1.40; 0.00-6.33)	**1.28** (1.46; 0.00-7.00)	**1.48** (1.00; 0.00-3.67)
FC other facial features (SD; range)	**4.01** (1.52; 2.00-7.33)	**3.78** (1.75; 1.67-9.33)	**3.60** (1.48; 1.00-7.00)	**3.59** (1.95; 0.67-9.33)
LI (SD; range)	**-0.15** (0.29; -1.00-0.18)	**0.00** (0.39; -1.00-1.00)	**0.03** (0.25; -0.78-0.50)	**-0.21** (0.28; -1.00-0.20)
Trials excluded* (SD; range)	**0.13** (0.34; 0.00-1.00)	**0.06** (0.24; 0.00-1.00)	**0.24** (0.52; 0.00-2.00)	**0.00** (0.00; 0.00-0.00)

DT (Dwell Time); FC (Fixation Count); LI (Laterality Index). *Mean number of face trials excluded in the eye tracking data per group (total number of face trials = 3). 2 control children and 1 child in the ASD+ADHD group were excluded due to inadequate data acquisition (as described in Section 4.1.4).