Reasons for the Sex Difference in the Prevalence and Age of Autism Spectrum Disorder Diagnosis

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Abstract

In the absence of intellectual impairment, girls are diagnosed with Autism Spectrum Disorder (ASD) both substantially less and later than boys. In this thesis I explored potential reasons for the sex difference in the prevalence and age of the diagnosis of ASD. Two theories were explored. First, girls may genuinely develop ASD less than boys, due to an advantage in the typical development of cognitive and environmental factors associated with social development. Alternatively, girls may be better able to hide their underlying impairments and present with different overt behaviours, resulting in the under-detection of the disorder. While little evidence was found for the first theory, across two studies I found evidence to support the theory that ASD presents differently girls, and is thus potentially more difficult to detect. Findings indicate that the current estimate of the rate of ASD in girls likely underestimates the true prevalence of the disorder in this population.

To investigate whether girls may genuinely develop ASD at a lesser rate to boys, I explored sex differences in the cognitive and social profiles of typically-developing pre-schoolers. In particular, I focussed on cognitive factors (theory of mind and executive function), communication style with parents (mental state talk), and play style, all of which are linked to social development. Results from 68 pre-school aged children (27 girls) failed to show robust evidence of girls being protected by better developed cognitive or social skills. While girls were more readily exposed to complex social environments, through parent-interaction and through a preference for pretend-play, this was not related to more advanced social competence.

However, robust evidence was found for the second theory, that girls may be diagnosed less with ASD due to the under-detection of the disorder. This theory was investigated over two studies. In the first, I explored the pre-diagnosis concerns of 152

caregivers (60 of girls) whose cognitively able children were late-diagnosed with ASD. In the second, I explored sex differences in a sample of 69 boys and 69 girls all diagnosed with ASD, based on clinician and teacher ratings. Evidence across both studies showed girls were reportedly better able to imitate, and use this in a social environment in an attempt to copy social interactions. Further, while girls were equally impaired as boys in some key underlying social impairments, this manifested in quite different overt behaviours. It is likely many of these overt behaviours (e.g., better use of nonverbal gestures) further camouflages girls' underlying impairments. This ability to camouflage seemed most notable when in school, with teachers reporting far fewer concerns for girls than for boys, including the majority of girls being rated by teachers as having quite typical social skills. Outside of the social domain, girls were also found to present with different types of restricted interests to boys, which were potentially more difficult to detect as atypical, or indeed as a sign of ASD. Results provided insight into why the disorder may be more difficult to detect in girls, particularly in the younger years and by professionals not specifically trained in the diagnosis of ASD. Further, results provide a framework for how we can better identify the disorder in girls.

Declaration

I certify that this thesis does not incorporate, without acknowledgement, any material previously submitted for a degree or diploma in any university; and that to the best of my knowledge and belief it does not contain any material previously published or written by another person, except where due reference is made in the text.

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Rachel M. Hiller

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Chapter 1: Introduction

Overview

Autism Spectrum Disorder is a pervasive developmental disorder, characterised by developmental delays in social-communication abilities and restricted/repetitive behaviours (American Psychiatric Association, 2013). The disorder is usually diagnosed in childhood and may or may not present with comorbid intellectual disability and severe language impairment. When severe language impairment and intellectual impairment are absent, the label Asperger's Disorder has traditionally been used (American Psychiatric Association, 2000). In 2013, the fifth edition of the diagnostic statistical manual was released (DSM-5; American Psychiatric Association, 2013). The DSM-5 combines previous diagnostic labels of Autistic Disorder, Asperger's Disorder, Childhood Disintegrative Disorder and Pervasive Developmental Disorder, not otherwise specified (PDD-NOS) under the umbrella term of Autism Spectrum Disorder. On the release of the DSM-5, the diagnostic criteria changed from a triad of impairments to a dual diagnostic system. This includes social-communication impairments (e.g., deficits in social-emotional reciprocity, difficulty initiating friendships, deficits in non-verbal behaviour) as well as the presence of restricted and repetitive interests (including fixated interests, routine adherence, and sensory sensitivity). In line with recommendations made by the DSM-5, I will use the term Autism Spectrum Disorder (ASD) to encompass Autistic Disorder, Asperger's Disorder, and PDD-NOS, with high-functioning ASD or cognitively-able referring to the disorder when present without comorbid intellectual impairment or severe language delay.[1]

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[1] While the term ASD also encompasses Childhood Disintegrative Disorder, this sample was not targeted in this thesis.

One of the most consistent yet under-researched areas in the literature on ASD is the large sex difference in the diagnostic rates. Prevalence studies estimate boys are diagnosed at a rate four times more than girls. Moreover, when ASD is not comorbid with intellectual impairment or severe language delay, this diagnostic ratio increases to around ten boys diagnosed to every one girl (Fombonne, 2009; Rivet & Matson, 2011). In the absence of intellectual impairment, there is also evidence that girls with ASD are diagnosed up to 1.5 years later than their male counterparts (Begeer et al., 2012; Siklos & Kerns, 2007). Consequently, it is rare for a cognitively-able girl to be diagnosed before school age, meaning many miss early intervention, or potentially crucial support for the child and their family (Dworzynski, Ronald, Bolton, & Happé, 2012; Warren et al., 2011).

It is currently unclear why these sex differences exist. Potential explanations include that girls are somehow biologically protected from developing ASD as readily as boys (Baron-Cohen, 2002; Szatmari et al., 2012; Werling & Geschwind, 2013), that the disorder is inherently different in boys and girls, or that ASD, as it is currently know, occurs more equally in girls, but that the deficits are somehow less apparent in this population (Dworzynski, et al., 2012; Kothari, Skuse, Wakefield, & Micali, 2013). Indeed, the sex discrepancy at the cognitively-able end of the spectrum may be a combination of these explanations. In this thesis I explored two potential reasons for the sex discrepancy in the prevalence and age of ASD diagnoses. First, the disorder may genuinely occur less in females because the abilities that allow children to develop typical social skills may develop better in girls. Alternatively, the disorder may occur more equally across the sexes, but may be detected less in females, because the underlying impairments at the core of ASD manifest in a different behaviour presentation in girls, resulting in the under-detection of the disorder.

In this thesis, I have explored three distinct samples to provide a comprehensive exploration of why ASD is diagnosed less and later in girls. First, I investigated sex differences in typically developing children to explore whether a true prevalence difference may result from girls having protective factors that reduce the likelihood that they will develop ASD. Second, over two studies, I explored whether the prevalence difference may not be genuine, at least of the current magnitude, and rather an artefact of the difficulty identifying the disorder in girls. This included an examination of sex differences in pre-diagnosis concerns; to explore what concerns led parents to seek professional opinion on their child's development and the responses of health care professionals to these concerns. Further, I examined sex differences in the behavioural presentation of children and adolescents with a current ASD diagnosis. This involved a larger sample of girls and moved beyond the broad diagnostic criteria to explore whether underlying impairments may manifest in different overt behaviour presentations for boys and girls.

Theory 1: Are Girls Less Likely to Meet ASD Criteria Due to a Typical Advantage in Social Development?

One explanation for the sex difference in the prevalence rates of ASD, is that girls are genuinely less likely to meet criteria due to an advantage in the development of abilities associated with social functioning, a key impairment in ASD (American Psychiatric Association, 2013). To explore this, I was interested in whether an early female advantage in typical cognitive, language, and resulting social development, may protect girls from meeting some or all criteria for ASD. The rationale for this line of research originates from the *extreme male brain theory* (Baron-Cohen, 2002; Baron-Cohen & Hammer, 1997; Baron-Cohen, Jolliffe, Mortimore, & Robertson, 1997). The extreme male brain theory has proposed that girls are biologically protected from

meeting criteria for ASD due to a gender advantage in processes commonly impaired in the disorder (e.g., empathy; Baron-Cohen, 2002; Baron-Cohen & Hammer, 1997). This theory was an extension of the systemising-empathising theory and suggests females are biologically advantaged in their empathising (the desire to identify and respond to another's emotions), while the male brain shows a propensity for systemising (focussing on detail, and the deterministic rules that govern behaviour). Baron-Cohen and Hammer (1997) suggested this systemising brain, in the extreme, is demonstrated in people with ASD (e.g., the fixation to detail, preference for rules, and collecting behaviour).

Some support has been found for this hypothesis, with higher levels of autistic traits found in general-populations of boys compared to girls (Constantino & Todd, 2003). Moreover, recent evidence suggests girls may require a higher genetic liability to express restricted interests, a key criterion for ASD (Szatmari, et al., 2012). Likewise, in support for the extreme male brain theory, there is also evidence of a female advantage in empathy from the pre-school years to adulthood (Baron-Cohen & Wheelwright, 2004; Roberts & Strayer, 1996; Tilburg, Unterberg, & Vingerhoets, 2002). However, in a review on sex differences in children's social and emotional development, it was noted that findings on sex differences in regards to empathy, were largely dependent on how the variable was operationalised (Rose & Rudolph, 2006), with evidence of no sex difference in children's empathy, based on teacher- and peer-report (Roberts & Strayer, 1996). Consequently, it is not yet understood whether girls have genuinely better developed empathy, or are simply better at reporting how one should act in a social situation. It is also not yet clear whether sex differences reflect biological differences or differences in the early social environments of boys and girls (Constantino & Todd, 2003). Further, while empathy has received much attention in the literature, and support

for the extreme male brain theory remains inconsistent, there are numerous other potentially important mechanisms, related to social development, which may play a role in protecting girls from developing social deficits as readily as boys.

One cognitive ability of importance to social development, and often implicated in the development of ASD, is theory of mind. Theory of mind refers to a person's ability to interpret the perspective of others, how it may differ from the self, and how this perspective may shape their behaviour (C. Hughes & Leekam, 2004) (Premack & Woodruff, 1978). This includes understanding that others may want, know, or think differently from oneself, meaning the ability to impute the mental states of both others and oneself. Underpinning this cognitive process are such mechanisms as metarepresentation and pretence (Charman & Baron-Cohen, 1992; Leslie, 1987). Metarepresentation, as an example, is defined as the child's ability to represent another's beliefs, thoughts or knowledge towards something (Charman & Baron-Cohen, 1992; Leslie & Happe, 1989). Theory of mind is of interest to the field of autism research given its link to social functioning (C. Hughes & Leekam; Lillard, 1993; Watson, Nixon, Wilson, & Capage, 1999). Typically developing children with greater theory of mind understanding have shown superior social functioning both in longitudinal (Watson, et al., 1999) and cross-sectional (Bosacki & Wilde Astington, 1999) research. Further, while children with autism will most often fail theory of mind tasks (Frith, 1994; Happé, 1995), those who do pass have demonstrated more advanced social insight, compared to those who fail such tasks (Frith, 1994, Wellman et al. 2001).

Research already shows some evidence that females may develop more advanced theory of mind ability, with evidence of a female advantage in the pre-school years (Carlson & Moses, 2001; Charman, Ruffman, & Clements, 2002; Walker, 2005), school years (Bosacki & Wilde Astington, 1999; Calero, Alejo Salles, & Sigman, 2013),

and adulthood (Baron-Cohen, et al., 1997). However, the strength of the association between theory of mind and sex differs substantially. For example, Charman and colleagues (2002) showed evidence of only a weak female advantage in theory of mind in a sample of over 1000 two to six year old children, while Walker (2005) found evidence of a strong (Cohen's d = 1.23 – 3.05) female advantage in a sample of 112 three to five year olds. Further, evidence also points to no significant sex difference in theory of mind abilities (Devine & Hughes, 2013; C Hughes & Dunn, 1998; Mathieson & Banerjee, 2011), including a large-scale longitudinal study, which found no evidence of a significant sex difference in theory of mind ability at five-, six-, or seven-years of age (Caputi, Lecce, Pagnin, & Banerjee, 2012). One potential reason for these inconsistencies was that Caputi and colleagues (2012) controlled for receptive vocabulary, while the previously discussed studies either included no vocabulary measure (Walker, 2005) or had vocabulary information on a small number of participants (Charman, et al., 2002). Vocabulary is a strong predictor of theory of mind performance, and is particularly important to control for given the verbal nature of most theory of mind tasks (Cutting & Dunn, 1999; Happé, 1995). However, even when language is controlled for, evidence shows both a female advantage in theory of mind (Carlson & Moses, 2001) and no sex differences (e.g., Caputi, et al., 2012). Potentially, differences in findings may reflect a developmentally sensitive period for a female advantage in theory of mind. That is, as suggested by Caputi and colleagues, girls may be advantaged in their earlier development of theory of mind, shown during the pre-school years, but typically developing boys are largely able to 'catch-up' by school age. Alternatively, as suggested by Charman and colleagues (2002), mixed evidence of the presence or absence of sex differences in theory of mind may be the result of the difference only being a weak effect.

Our ability to draw conclusions on the role of a potential female advantage in theory of mind has thus far been limited by two major methodological limitations. The primary methodological limitation has been the sole focus on false belief ability as a single measure of theory of mind. Given false belief ability does not develop until approximately three and a half to four years of age, this focus on false belief particularly impedes our understanding of potential sex differences in the toddler and early pre-school years (i.e., under 3.5 years old; Wellmann, Cross, & Watson, 2001). Despite false-belief ability not developing until the later pre-school years, studies using younger samples (e.g., 2 year olds; Charman, et al., 2002; and 3 year olds; Walker, 2005) have used continued to use false belief as their primary measure of theory of mind. Moreover, the extensive focus on false-belief is in contrast to knowledge that theory of mind encompasses a range of processes that develop well before the age one would expect to see false belief emerge. Consequently, there is little evidence of theory of mind ability (and whether a sex difference exists) under four years of age (C. Hughes & Leekam, 2004). If a female advantage in theory of mind did exist in toddlerhood and the early pre-school years, it may have important implications for why ASD is less likely to occur in girls.

A second issue affecting our ability to draw conclusions on the role of theory of mind development is the concerning lack of well-validated and reliable measures for theory of mind as a construct. Even for the most commonly used theory of mind task (false belief), there is debate about its psychometric properties, with evidence of strong (A. Hughes, Happe, Jackson, Taylor, & Caspi, 2000), moderate (Charman & Campbell, 1997), and poor (L. Mayes, Klin, Tercyak, Cicchetti, & Cohen, 1996) reliability. Indeed, this issue in itself may explain the inconsistency in findings between studies, as it is not yet clear if the task commonly used to assess theory of mind accurately tap the

construct of interest. Unsurprisingly, the little information on theory of mind, pre false belief, means there is a particular lack of well-validated measures for testing theory of mind in the toddler and early pre-school years.

These two methodological issues are targeted in Chapters 2 and 3 of the thesis, where I have investigated the usability of a theory of mind scale (Peterson, Wellman, & Lui, 2005; Wellman & Liu, 2004) proposed to measure a range of theory of mind abilities that emerge prior to false belief ability. While this scale has been proposed to provide an accurate measure of early theory of mind ability, even prior to false belief, thus far the scale's use has focussed on age ranges of children where one would expect false belief ability to have emerged (i.e., 3.5 year olds to 12 year olds; Shahaeian, Peterson, Slaughter, & Wellman, 2011; Wellman, Fang, & Peterson, 2011). Consequently, I was particularly interested in the scale's usability with children from toddlerhood and thus its ability to detect sex differences in the pre false belief skills of typically developing children.

Could sex differences in executive function explain a female advantage in theory of mind? I was also interested in whether certain cognitive or language processes, linked to theory of mind, could provide insight into why girls may present with the hypothesised better developed theory of mind skills. The first construct of interest was executive function ability. Executive function is a cognitive construct comprised of three related abilities; (i) shifting, (ii) updating, and (iii) inhibition (Miyake et al., 2000). Shifting (also referred to as attention-shifting) is the ability to shift between different tasks, including the ability to disengage in irrelevant tasks and engage in relevant tasks. Updating is closely linked to working memory and is proposed to be the ability to manage, monitor and update information. Finally, inhibition is the ability to inhibit certain responses, including the inhibition of inappropriate behaviours

(Miyake, et al., 2000). A recent review of the executive function of pre-schoolers found all three of these executive function abilities appeared to develop early in the pre-school years (Garon, Bryson, & Smith, 2008). As such, like for theory of mind, the pre-school years represent a dynamic period of development for executive function. Further, executive function ability also has implications for social development, including associations with better ratings of social skills and lower ratings of disruptive behaviour and attention problems (Olson, Sameroff, Kerr, Lopez, & Wellman, 2005; Rhoades, Greenberg, & Domitrovich, 2009)**.**

Executive function was of most interest to this thesis due to its early association with theory of mind (Carlson & Moses, 2001; C. Hughes & Ensor, 2007; Pellicano, 2010). There are a number of potential theoretical explanations for the association between these two cognitive constructs, including that some executive function ability is required, although not solely, for the emergence of theory of mind (emergence theory), that theory of mind ability cannot be expressed until some executive function ability has development (expression account), that executive function development is dependent on earlier theory of mind development, or that the tasks used to assess each construct require the same reasoning skills (e.g., see Moses & Tahirogulu, 2009; Sabbagh, Moses & Shiverick, 2006).Indeed, much research has demonstrated an association between executive function and theory of mind, including Carlson and Moses (2001) who found significant positive associations between the inhibitory control ability and false belief theory of mind ability of 3-4 year old children. Moreover, evidence suggests this association also holds true for atypical samples, including children with ASD (Pellicano, 2010) and in cross cultural samples (Sabbagh, et al., 2006). Longitudinal studies have also explored whether executive function may precede theory of mind, or visa-versa. Based on the current literature, the explanation

garnering most support is that theory of mind emerges following the development of executive control (Hughes, 1998; Hughes & Ensor, 2007; Moses & Tahirogulu, 2009; Pellicano, 2010). That is, longitudinal research suggests executive function development may be necessary for the development of theory of mind, rather than visa-versa (Pellicano, 2010). Consequently, results from these longitudinal studies have suggested that executive function ability is a necessary, although likely not the sole component necessary, for theory of mind development (Moses & Tahirogular, 2010; Pellicano, 2010). Based on the association between these variables, I was interested in whether the proposed sex differences in early theory of mind may be due to sex differences in executive function performance. That is, could there be evidence of an overall female advantage in cognitive abilities related to social development?

There is some evidence of a female advantage in the executive function abilities of pre-school aged children (Carlson & Moses, 2001). This is particularly true for the ability to inhibit behavioural responses (i.e., inhibitory control; Carlson & Moses, 2001). In this thesis I was particularly interested in the further exploration of sex differences in various early executive function abilities and their association with a broader range of early theory of mind abilities. In particular, I was interested in furthering understanding on what specific theory of mind tasks, particularly pre false belief development, may be associated with executive function ability.

Could sex differences in environmental influences explain a female advantage in theory of mind? Research shows theory of mind development is also influenced by environmental factors, including number of siblings, type of parent interactions, and imagination (for review see, C. Hughes & Leekam, 2004). Indeed, research by Charman and colleagues (2002) on sex differences in pre-school theory of mind development hypothesised that the slight female advantage in theory of mind may

be due to girls being more readily exposed to environments that promote its development. This supports findings that, in the general population, higher autistic traits in young males than females, may be the result of females being more sensitive to early environments that promote social competency rather than biological differences (Constantino & Todd, 2002).

The use of mental state talk by parents, when interacting with their child, is one such environment that may promote social competence, through its association with theory of mind development (C Hughes & Dunn, 1998; Ruffman, Perner, & Parkin, 1999; Ruffman, Slade, & Crowe, 2002). These mental state utterances may include making reference to emotions (e.g., "happy", "sad", "worried"), thought processes (e.g., "I thought", "Did you know"), or desires (e.g., "wish", "want", "like"). Longitudinally, early mental state talk, when engaged in interactions with parents, has been positively associated with children's later theory of mind development (Ruffman, et al., 2002). However, again, we know little about associations between mental state talk and theory of mind, outside of false belief ability.

Research shows that compared to boys, girls are more readily exposed to mental state talk during interactions. Specifically, parents of girls, compared to parents of boys, have been found to make significantly more references to mental state talk during interactions with their child (Cervantes & Callanan, 1998; Fivush, Brotman, Buckner, & Goodman, 2000). For example, Fivush and colleagues (2000), with a sample of 21 children aged 2 to 4 years old, found girls were exposed to significantly more utterances about emotions, than were boys. This was particularly the case when discussing emotional events during the parent-child interaction. Based on this evidence, girls may develop more advanced theory of mind during the pre-school years because they are more readily exposed to situations where they are able to practice perspective taking.

However, research has also shown that girls make more frequent references to mental states (Cervantes & Callanan, 1998; C Hughes & Dunn, 1998). For example, Hughes and Dunn (1998) examined the mental state use in 25 pairs of friends (i.e., 50 children) aged between 3 and 6 years old and found young girls used both more frequent and more advanced mental state utterances compared to boys. This difference was most pronounced at the final time point measured, when the children were around five years of age. As such, parents more frequent use of mental state talk with daughters, may actually reflect parents simply matching their daughters more advanced use of mental state talk, rather than parents 'causing' the more advanced language in girls. The longitudinal impact of parents' use of mental state talk was explored by Taumoepeau and Ruffman (2008) when children were 15, 24 and 33 months of age. They found early parental mental state talk did uniquely predict children's later mental state use and emotion understanding, suggesting parents' use of these utterances promotes children's social learning. In this thesis I will further explore the role of sex differences in parent and child use of mental state talk, and in particular how it may be associated with a female advantage in early theory of mind ability.

Summary for theory 1: Are girls protected from meeting criteria for ASD?
In sum, the first study in this thesis was designed to explore whether girls may develop better skills related to social development (a key impairment in ASD). The primary focus of this investigation was whether young girls would present with more advanced theory of mind abilities compared to boys. Factors that may explain why girls are advantaged in early theory of mind were also explored. This included executive function and mental state talk, both said to precede the development of theory of mind. Given theory of mind, or lack thereof, is linked to ASD, it is possible a female advantage in the ability may protect girls from developing ASD as readily as boys.

Theory 2: Could ASD Occur More Frequently in Girls but be Under-Detected?

A second potential reason for the sex difference in the diagnostic rates of ASD is that, despite the disorder being present, it is under diagnosed in girls. That is, ASD may occur more equally in the sexes (or at least not of a magnitude of 10:1) but be under detected in girls, due to differences in how the overt behaviours manifest. Research has shown that the time lapse between when a parent first expresses concern and when a child first receives a diagnosis of ASD is more pronounced for females, suggesting that the female presentation of the disorder is indeed more difficult to identify (Begeer, et al., 2012; Siklos & Kerns, 2007). For example, Silkos and Kerns (2007) examined the diagnostic process from first concern to diagnosis, in a sample of 56 children and teens with ASD. They found girls waited, on average, 1.5 years longer to receive a diagnosis, than what it took for boys. This was despite there being no difference in the number of medical professionals visited during the process, with parents accessing an average of 4.5 professionals. More recently, Begeer and colleagues (2012) investigated the timing of ASD diagnoses in a survey of over 2000 individuals with ASD. Results showed that for individuals less than 18 years of age, girls with Asperger's Disorder (where no intellectual or language impairment is evident) were diagnosed significantly later than their male counterparts. This was despite there being no difference in the timing of the age of the child when concern was first expressed. These findings particularly highlight the difficulty identifying the disorder in girls when intellectual disability is not present, potentially explaining why the diagnostic discrepancy is most pronounced at the cognitively-able end of the spectrum (i.e., in the absence of intellectual impairment). In particular, it suggests diagnosing the disorder in girls in the younger years is especially problematic. Why this may be the case will be explored in this thesis.

The impact of the diagnostic process on the diagnosis of girls. To understand how an autism diagnosis may be under detected in girls, the complexity of the diagnostic process must be acknowledged. Given the higher prevalence of boys diagnosed with ASD, much of our knowledge of ASD currently reflects the male presentation of the disorder. However, it has now been acknowledged in the DSM-5 that the disorder may present differently in girls (American Psychiatric Association, 2013). What we do not yet know is how these differences manifest. Broadly, there are three key factors that may be considered when deciding whether an impairment may be a sign of ASD, and thus may impact the diagnosis of girls. These are (1) the overt behaviours demonstrated by the child (e.g., obsessional interests, reduced eye contact, atypical motor movements), (2) the child's underlying understanding of social situations, and (3) the presence of impairments commonly associated with the disorder, such as impaired imitation. In various combinations, impairments in all of these areas potentially lead to the behaviour presentation of a child on the autism spectrum.

There are also a range of professionals who may be involved in deciding whether or not a child may be presenting with signs of ASD. The first professionals, to whom a parent would most likely express concern, are the family doctor or the child's teacher. These professionals are often not trained in the diagnosis of ASD, and thus may not have an understanding of the full spectrum of the disorder, let alone how it may present differently in girls. Consequently, these professionals may rely more on what they view as the 'typical' presentation of ASD, which may include the misconception that ASD is a 'boy disorder.' In the absence of a full diagnostic assessment, they would also likely rely more heavily on the overt behavioural presentation of the child, to judge whether an impairment may fit an ASD diagnosis. If these overt behaviours are different in girls, it may explain why the disorder is more difficult to detect. Because the

disorder is diagnosed so much less in girls, and given the behaviour presentation may be different, diagnostic clinicians and other professionals are likely to be far less experienced in how to identify the disorder in girls. Consequently, the diagnosis may be missed in girls, or, in those whose impairments do eventually becomes more salient, the diagnosis is delayed.

Do sex differences in the core symptoms of ASD explain why girls are diagnosed less? One reason ASD may be more difficult to identify in girls is that the core presentation of the disorder differs. Current knowledge on sex differences in the core symptoms of ASD provides inconsistent evidence on the potential role of explaining sex differences in the diagnostic rates. From the research, perhaps the more consistent finding regarding the core diagnostic criteria, is that fewer girls with ASD present with restricted interests, with this difference evident across toddlerhood, childhood, and adolescence (Hartley & Sikora, 2009; Lord, Schopler, & Revicki, 1982; Mandy et al., 2012; Szatmari, et al., 2012). Szatmari and colleagues (2012) found evidence to suggest females have a higher genetic liability to develop restricted and repetitive behaviours, explaining why girls may meet criterion for restricted interests less frequently than boys. However, clinical anecdote has suggested restricted interests are present in girls, but are different, thus potentially under-detected (Attwood, et al., 2006). However, the latter explanation is yet to be empirically explored.

Results for differences between the sexes are less consistent across the social and communication domains of ASD. When controlling for IQ, some studies show evidence of no sex differences in the social profiles of individuals with ASD, from toddlerhood to adulthood (Andersson, Gillberg, & Miniscalco, 2013; Dworzynski, et al., 2012; Holtmann, Bolte, & Poustka, 2007; Pilowsky, Yirmiya, Shulman, & Dover, 1998; Volkmar, 1993). These studies all included individuals with and without

comorbid intellectual impairment. When only cognitively-able individuals with ASD are included, some evidence still points to no sex differences in social impairment (Holtmann, et al., 2007). This includes a recent, larger scale study (n = 52 females, n = 273 males) that found no significant sex difference in social functioning of children and teens with ASD, based on a number of diagnostic assessments, including the Autism Diagnostic Observation Schedule (Mandy, et al., 2012). However, the literature also shows evidence of females with ASD having more severe communication and social deficits in childhood (Hartley & Sikora, 2009) and adulthood (McLennan, Lord, & Schopler, 1993). In further contrast, there is also evidence of less severe social and communication deficits in female adults diagnosed with high-functioning ASD (Lai et al., 2011). Our ability to draw conclusions across these studies has thus far been impacted by methodological issues including small samples of females (e.g., Andersson, et al., 2013; Pilowsky, et al., 1998) and the reliance on retrospective reporting after large time lapses (in some cases up to 40 years; Lai, et al., 2011). In Chapters 4 and 5, I have overcome these limitations, in particular with studies that engage larger samples of girls with high-functioning ASD, than what is currently seen in the literature. Further, when retrospective reporting was used (Chapter 4), I engaged a more restrictive age range to minimise the time lapse.

Given samples commonly focus on boys and girls who have already met criteria for ASD, it is perhaps not surprising that the research often fails to find evidence of significant sex differences in the core symptoms of the disorder. I argue that this information provides only limited insight into why girls are diagnosed both less and later at the cognitively-able end of the spectrum. For example, focussing on the core symptoms of ASD, for those already diagnosed in the pre-school years (Andersson, et al., 2013; Hartley & Sikora, 2009), can potentially only provide limited information on

how we may be missing girls during the pre-school years, as these early 'missed' girls would not be captured in the sample of early diagnosed children. Of interest to this thesis was moving away from exploring the core diagnostic criteria of ASD, to instead investigate the pre-diagnosis period, as well as how boys and girls come to meet the criteria. That is, what specific behaviours within each criterion led a clinician to provide that child with a positive diagnosis, and how may these more subtle differences make the diagnosis of girls more difficult? This provides more in-depth analysis of sex differences in the overt behaviours which may have been difficult for a medical professional or clinicians to identify. These studies also primarily focussed on those girls who, despite early concerns, were not diagnosed until school age, and thus also provides a more comprehensive insight in to potential reasons for why the diagnosis was not made earlier.

How girls with ASD present differently to boys: The role of behavioural presentation. The camouflage hypothesis provides an overview of how and why girls with ASD may present differently to boys (Attwood et al., 2006; Kopp & Gillberg, 1992; Wing, 1981). However, the hypothesis has largely remained embedded in clinical case studies (Kopp & Gillberg, 1992). The cornerstone of the hypothesis is the prediction that ASD is more difficult to identify in girls due to their ability to camouflage underlying impairments, primarily through imitating social interactions. This idea, proposed by Kopp and Gillberg (1992) more than two decades ago, was based on case studies of six girls with ASD, none of whom had an ASD diagnosis even considered until after six years of age, despite concern expressed to numerous medical professionals. Kopp and Gillberg noted that the girls tended to engage in imitation of speech and movement. Consequently, their social presentation seemed more typical than one would expect for ASD, despite the fact the girls were unable to understand

social rules. Further, the girls tended to be more clingy to people, rather than presenting as socially aloof. Drawing on these case studies and their own clinical experience, Attwood and colleagues (2006) further proposed ASD was more difficult to detect in girls primarily due their ability to mimic social interactions. This mimicking behaviour would mean underlying impairments often go unnoticed, at least until socialising becomes more complex in later childhood or adolescence. Importantly, the theory suggests girls with ASD experience comparable levels of underlying social impairments to boys with ASD, but behaviourally present differently.

Two recent studies have provided some empirical evidence for girls potentially engaging in strategies to hide their social impairments. Kothari and colleagues (2013) engaged a general population study and focussed on sex differences in children who were considered to have high autistic traits. The authors found girls high in autistic traits were better than their male counterparts at identifying facial emotions. In contrast to this, girls were just as impaired as boys in accurately identifying emotions from a novel social emotion recognition task. The authors suggested these findings may mean girls high in autistic traits are able to perform better on tasks where they could have learnt the behaviour (i.e., facial emotion recognition) but were equally impaired in their underlying social-emotion understanding (a task that could not be learnt). Similarly, Dworzynski and colleagues (2012) also engaged a general population sample, and drew on the Childhood Autism Spectrum Test (CAST) to explore the profiles of girls and boys who met criteria for ASD, compared to those who were just below the cut-off for meeting criteria. For those children who met criteria for ASD, the authors found that girls, compared to boy, were more likely to present with additional problems (e.g., lower intelligence and behaviour problems). Further, having these additional problems distinguished those children with ASD, from those just below the cut-off, for girls, but

not for boys. The authors suggested these findings may reflect girls' ability to engage in strategies that, in the absence of other significant behaviour and intellectual problems, hide the disorder. However, outside of these two population studies, there remains little evidence for if, how, and why, girls with ASD are able to hide their impairments.

The role of imitation. A female advantage in the imitation abilities of girls with ASD is the cornerstone of the camouflage hypothesis (Attwood, et al., 2006). That is, girls are said to be better at mimicking social interactions, which consequently may allow them to superficially camouflage their true social impairments (Kopp & Gillberg, 1992). Compared to typically developing children and those with other developmental delays, young children with ASD have consistently shown impairment in their ability to imitate the actions of others (Rogers, Hepburn, Stackhouse, & Wehner, 2003; G. S. Young et al., 2011). Indeed, whilst it is not considered a key diagnostic requirement, most early screening and diagnostic tools include information on imitation impairment (e.g., the Autism Diagnostic Observation Schedule; ADOS; Lord et al., 1989). Further, imitation training is also the focus of many early interventions, given its association with social competence in children with ASD and its role in early social learning (Rogers, et al., 2003; Sallows & Graupner, 2005). Case studies and anecdotal evidence suggest that girls with ASD present with better imitation skills (Kopp & Gillberg, 1992). However, as yet there is no empirical evidence regarding both sex differences in the imitation skills of children with ASD, as well as in the specific strategies (mimicking or otherwise) that girls with ASD use to navigate social situations. In chapters 4 and 5 of this thesis, using larger samples reporting on girls with ASD, I investigated whether girls were indeed more likely to engage in mimicking behaviour, compared to boys. This included information on parent report of imitation and information gathered from diagnostic clinicians' reports on children's and adolescents'

abilities to imitate for social gain. That is, I was not just interested in whether the child could or could not imitate, but rather whether the child showed evidence of generalising that imitation ability to a social context (e.g., copying others' interactions).

Differences in restricted interests. The camouflage hypothesis also proposed differences in restricted interests would further compound the difficulty in identifying ASD in girls (Attwood, et al., 2006). Attwood and colleagues (2006) suggested girls with ASD would typically present with different restricted interests that would be more difficult to determine as atypical. For example, a young girl with ASD may obsessively collect dolls, a behaviour which may be difficult to determine as atypical, and not considered a 'classic' presentation in ASD. This hypothesis suggests current evidence that females present with fewer restricted interests (e.g., Mandy, et al., 2012; Szatmari, et al., 2012) may be exaggerated due to the under-identification of restricted interests in girls. I have targeted this issue in the final two studies of this thesis, providing the first empirical exploration of sex differences in the types of restricted interests shown by girls and boys.

Sex differences in school presentation. Finally, the camouflage hypothesis also proposed girls would be particularly skilled in camouflaging their underlying lack of social understanding, when outside the home environment (Attwood, et al., 2006). Based on clinical experience, Attwood and colleagues (2006) suggested teachers would be less inclined to notice impairments in girls with ASD, as they would be less likely to cause behavioural disruptions in a classroom setting compared to boys with ASD. Specifically, Attwood and colleagues suggested girls would present in a school environment as introverted or withdrawn, and thus be less likely to draw attention to themselves and their difficulties, compared to boys who display more disruptive behaviours.

Until recently, this hypothesis also remained untested. However, two recent studies suggest teachers do indeed report fewer problematic behaviours for girls versus boys (Dworzynski, et al., 2012; Mandy, et al., 2012). To date, Mandy and colleagues (2012) have provided the most comprehensive investigation of sex differences in the home versus school presentation of children with ASD. Based on teacher responses on the Strengths and Difficulties Questionnaire, vast differences were found in the presentation of girls and boys with ASD when in the school environment. That is, teachers of girls were far less likely to report concerns than teachers of boys, including concerns with hyperactivity and peer relationships. This was in direct contrast to parent report, where more concern was reported for the emotional symptoms of girls compared to boys. That is, concern for girls did not appear consistent across settings. Girls presenting as less disruptive and with fewer peer problems, when at school, likely further compounds the difficulty of making an ASD diagnosis, given the impairments would not present consistently across settings. In this thesis I provide a further comprehensive exploration of the role of sex differences in the school presentation of girls and boys with ASD.

Summary

At the cognitively-able end of the autism spectrum, boys are diagnosed with ASD up to ten times more often than girls (Rivet & Matson, 2011). Evidence suggests this may not be a true estimate of prevalence, given the diagnosis of girls appears more problematic (Begeer, et al., 2012; Siklos & Kerns, 2007). However, as yet, we know little about why a sex discrepancy exists in both the prevalence and age of ASD diagnosis. This thesis explored two potential explanations for why ASD is diagnosed less and later in girls; (1) that girls may genuinely develop ASD less frequently than boys due to a typical advantage in the early development of factors associated with

social development and (2) that ASD may occur in girls more frequently than what is reflected in the diagnostic rates, but is under-detected in this population.

Contributions of the Thesis

Across this thesis I have made a number of contributions to the currently limited research on reasons for the sex difference in the prevalence and age of ASD diagnoses. First, I explored whether girls are protected from meeting ASD criteria as frequently as boys. This involved a more comprehensive exploration of the potential role of theory of mind development, with a particular focus on theory of mind abilities proposed to emerge prior to false belief understanding. Within this, I also provided an evaluation of a scale of theory of mind tasks that has the potential to provide a longitudinal assessment tool for early theory of mind ability as a construct (Peterson, et al., 2005). However, perhaps the largest contribution of this thesis is the exploration of reasons for why ASD may be more difficult to identify in girls. This included an exploration of sex differences in the specific factors that led parents to seek advice on their child's development, and an investigation into what specific strategies boys and girls reportedly used to manage social situations, prior to them receiving a diagnosis of ASD. Across the final two studies presented in this thesis I have also provided the first exploration of sex difference in the specific types of restricted interests displayed by children with ASD, to explore whether the restricted interests of girls may be more difficult to identify as atypical, thus further compounding the difficulty identifying the disorder. Finally, I provided the first exploration of how the newly proposed DSM-5 criteria impacts the diagnosis of ASD in girls, along with only the second comprehensive investigation of the role of teacher versus home presentation as a potential reason for the under-identification of the disorder in girls.

Structure of the Thesis

This thesis is arranged over 6 chapters, with the first having provided an introduction and overview of current knowledge on reasons for the sex difference in the rate and timing of ASD diagnoses. Chapter 2 of this thesis provides a brief overview of the current state of measures used to assess theory of mind, along with the validation of a five-item theory of mind scale (Peterson, et al., 2005; Wellman & Liu, 2004). Using this scale, Chapter 3 presents an empirical study of sex differences in typically developing children aged 2-5 years old. In this chapter I investigated whether there may be a female advantage in cognitive abilities which would result in greater early social competence, meaning girls would potentially be less likely to develop ASD. Chapters 4 and 5 present empirical studies of atypical populations. In chapter 4, I examined sex differences in the pre-diagnostic concerns for cognitively able children later diagnosed with ASD. Here the investigation was two-fold: First, I explored whether sex differences in pre-diagnosis concerns may provide insight into why it appears more difficult for girls to receive a diagnosis of ASD. Second, I was interested in whether girls and boys later-diagnosed with ASD engaged in different strategies to manage social settings. In my final empirical study, presented in Chapter 5, I explored sex differences in a population of children and adolescents with a current ASD diagnosis. Here, I explored numerous behaviours, based on DSM-5 criteria, that may (or may not) lead a medical professional to determine whether a developmental delay is indeed ASD. This chapter also includes a discussion on the impact of the new DSM-5 on the diagnosis of girls. Chapter 6 provides on overall discussion of the thesis findings, including how results can assist in developing a framework around improving the identification of ASD in females.