Gender Comparisons in Children with ASD Entering Early Intervention

Abstract

Background: Males are diagnosed with Autism Spectrum Disorder (ASD) approximately four times as often as females. This has led to interest in recent years of potential under-diagnosis of females, as well as negative consequences for females with ASD due to under-identification. A number of potential explanations for gender bias in diagnosis are discussed including that females and male may present differently despite showing the same core symptoms. Previous research has shown inconsistent findings in comparisons between genders in young children with ASD for whom early intervention is vital. Thus, the aim of the present study was to investigate the social, communication, and cognitive functioning, as well as level of ASD symptoms, in a cohort of children who presented for early intervention to inform understanding of gender differences in this population, as well as to inform understanding of the mechanisms by which gender bias may occur.

Method: Participants included 254 children (42 females) aged 29-74 months who completed measures of cognition, communication skills, adaptive behaviour, and ASD symptoms on entry to early intervention.

Results: Consistent with hypotheses, no significant gender differences were found both overall, and when split by functioning level. However, a similar ratio of males and females was found in both high- and low-functioning groups contrary to predictions.

Conclusions: These results are consistent with some of the previous research that suggests gender differences may not be apparent in clinical samples at this young age. We highlight a need for further research that may use universal screening or longitudinal methods to understand the trajectory of development for females with ASD specifically. Such research could better inform timely and tailored intervention from the preschool years onwards.

Keywords: Autism; gender: ASD; preschool; early intervention

What this paper adds
Recent research has investigated potential gender differences in symptom expression in males and females diagnosed with Autism Spectrum Disorder. However, there is a paucity of research in real-world clinical settings, particularly for those in the preschool years where mixed results in the existing research is found, and for whom early intervention is critical. Thus, this paper adds an investigation of cognitive, adaptive, and communication skills, and ASD symptoms between males and females on intake to a community-based early intervention service. This provides new information into the similarity of males and females in this population.

Introduction

Autism Spectrum Disorder (ASD) is diagnosed approximately four times more commonly in males than in females (e.g., Centers for Disease Control and Prevention [CDC], 2014). This raises concerns that females with ASD may be under-identified and subsequently miss opportunities for essential supports and services including early diagnosis and intervention. These concerns are based on the hypothesis that an equal proportion of males and females in the population truly have the constellation of core pervasive social-communication and behavioural impairments outlined in diagnostic criteria (e.g., American Psychiatric Association, 2013; World Health Organisation, 1992), but that females are less likely to receive a diagnosis. In this article, we examine evidence for and against diagnostic gender bias in a sample of preschool (2 ½ to 5 years) children receiving community-based early intervention services in Australia. Understanding similarities or differences in social, communication, and cognitive functioning, as well as ASD symptom levels, in females and males with ASD in early intervention is vital to ensure females, as well as males, with ASD receive appropriate and timely intervention services.

Effects of Under-identification of Females

The apparent under-identification of females has a number of knock-on effects which may be conceptualised as developmental cascades whereby cumulative effects are seen across a variety of domains and systems as a consequence of under-identification (see Masten & Cicchetti, 2010). First, as females with ASD are more difficult to identify, historically they have been virtually absent from studies investigating ASD (Constantino & Charman, 2012; Fountain, King, & Bearman, 2011). Second, and as a consequence of the former, diagnostic criteria for ASD have been developed almost entirely using the male behavioural and symptomatic presentation of ASD (Goldman, 2013; Svenny Kopp & Gillberg, 2011; S. Kopp, Kelly, & Gillberg, 2010). Third, females with ASD often experience difficulties obtaining

diagnosis, and therefore appropriate treatment and services. This delay is frequently reported to negatively impact on areas of life and development (Svenny Kopp & Gillberg, 1992, 2011; Kopp et al., 2010; Lai, Lombardo, & Baron-Cohen, 2014; Werling & Geschwind, 2013a) thus showing the impact of a developmental cascade. While the issue of diagnostic gender bias has been raised within the ASD research and clinical community in the past five years, a clear understanding of the developmental trajectory and symptomatic presentation of females with ASD that may help to explain any such bias is lacking.

Potential Explanations for Gender Bias

There are four main mechanisms by which gender bias in diagnosis may occur. First, in general, females may have less contact with diagnostic pathways as males demonstrate more externalising behaviours than females (Kreiser & White, 2014), which may bring them to the attention of health professionals or therapists. Second, it has been suggested that diagnostic criteria may over-emphasise behavioural manifestations of core symptoms more commonly seen in males than females, meaning that females are less likely than males to demonstrate behaviours consistent with the descriptions presented in the criteria (Baron-Cohen et al., 2011). Consistent with this explanation, Wing (1981) first described the "camouflage hypothesis" as an explanation for gender ratio in Autism. This hypothesis suggests that females with ASD develop an ability to conceal their ASD symptoms after they learn the rules of social situations, allowing them to navigate social situations with a certain level of prowess compared to males with ASD (Wing, 1981). Wing noted that females with normal to high IQ and a diagnosis of ASD demonstrate empathic and nurturing behaviours, which were incongruent with typical diagnostic criteria of ASD. Importantly however, this hypothesis is primarily drawn from observations of older children without comorbid ID. Additionally, many of the female children Wing describes under her camouflage hypothesis, were referred for diagnosis later than the males in the cohort, and later than is expected for a

traditional diagnosis of ASD, as such, it is difficult to apply this hypothesis to children entering early intervention.

A third mechanism is that practitioners may be interpreting and/or applying the diagnostic criteria in different ways for males and females, leading to different rates of diagnosis. For instance, practitioners may place undue emphasis on repetitive behaviours commonly observed in typically developing males (e.g., lining up toy cars), but less frequently observed in typically developing females (Shefcyk, 2015), leading to more frequent diagnosis of males (Lai et al., 2014). Fourth, it is possible that despite both females and males displaying the same core symptoms, females may present with more subtle or differing manifestations that may not appear to constitute the "clinically significant impairment in social, occupational, or other important areas of current functioning" (American Psychiatric Association, 2013, p. 50) necessary for diagnosis.

Previous Research

To date, research examining sex differences in prevalence has focused on the fourth proposed mechanism: that females with ASD are identified less often and later in age than males because they may show qualitative (e.g., type of repetitive behaviour or restricted interest) or quantitative (i.e. degree) differences in their manifestation of symptoms. This proposed mechanism implies two key hypotheses. First, if females are only identified when their symptoms present similarly and reach a threshold similar to that of males, we should expect to see few differences in the presentation of males and females who ultimately receive a diagnosis. Second, if it is true that only females who present with more significant development needs (e.g., ID) are likely to receive a diagnosis, we should see a higher proportion of females who have a diagnosis of ASD presenting with intellectual disability (i.e., delayed cognition and adaptive behaviour) than males. There is some evidence to support both hypotheses.

A systematic review conducted by Rivet and Matson (2011) revealed few consistent differences between genders on measures of social, communication, language, and adaptive behaviour. There is evidence that the ratio of males to females is indeed more similar in children with a diagnosis of ASD and intellectual disability (ID). The authors report that females and males with higher cognitive functioning demonstrated ratios as high as 9:1, but that that the average ratio is closer to 4.3:1. Looking at preschool aged children specifically (aged 2.5-4 years), Postorino et al (2015) found no gender differences in 30 age-matched male and 30 female children on a range of social and cognitive measures including the Vineland Adaptive Behaviour Scale, the Griffiths Mental Development Scale-Extend Revised, and the Child Behaviour Checklist. However, this study included only children within lower ranges of functioning so the findings cannot be generalised to higher functioning preschool aged children with ASD (aged between 2 and 5.4 years).

Consistent with Rivet and Matson (2011), Reinhardt et al (2015) reported no significant differences in 511 males and females without intellectual disability aged between two and three years on measures of social, verbal, non-verbal, and adaptive skills. However, the literature is equivocal, with other studies with young children (2-5 years) such as Andersson et al., (2013); Carter et al., (2007); and Hartley and Sikora (2009) reporting gender-based differences, possibly due to differing sample methods resulting in less comparable groups across studies with respect to age, proportion of females and males recruited, and diagnostic criteria used. Thus, it appears the first hypothesis that females who receive a diagnosis present similarly to males has some support in the existing literature, although there are exceptions that do find gender-based differences in young children.

Similarly, the Autism and Developmental Disabilities Monitoring Network (2009) reported higher incidence of females with intellectual disability and a male to female ratio of as low as 2.7:1 for this cohort. However, more recent epidemiological studies (e.g., CDC,

2014) have shown mixed results, with some states showing similar gender ratios with lower IQs, but other states failing to demonstrate this effect. Thus, although there is some support that females with intellectual disability are more likely to be diagnosed, the findings are inconsistent, even across different states within a single country, suggesting that multiple factors impact on diagnostic practices.

An important study by Hiller, Young and Weber (2016) explored the underlying triggers for parents and carers seeking an ASD diagnosis in 92 males and 60 females without ID. Specifically, the authors reported that the early warning signs that eventually led to diagnosis, differed between the male and female children, including seemingly high social drives to be liked and toward imaginative play, limited interest in mechanical or systems based play, and slightly below average vocabulary skills. In addition, Siklos and Kerns (2007) found no difference in the number of visits to health care professionals in the process of obtaining a diagnosis, a finding that was echoed by Hiller, Young and Weber (2016). Taken together, these findings suggest that while they may be present at preschool age, females are less likely to be identified during this time.

Present Study

Although previous research sheds light on the possible mechanism by which gender bias may occur, few studies have examined evidence for its effect in clinical services, particularly those for preschool aged children for whom early intervention is critical. Presumably, if females with ASD are identified less often and later in age than males because their symptoms are more subtle or qualitatively different, in a community sample of children accessing early intervention, we should see (a) similarities in assessments of core ASD symptoms (e.g., SCQ) because they have been assessed using the same ASD criteria, (b) similar scores on assessments of language (e.g., PLS) because they will have required a sufficient level of symptoms in order to reach threshold for clinical impairment, but (c) more

similar gender ratios in low-functioning subgroups, as evidenced by assessments of adaptive behaviour (e.g., VABS) below clinical cut-offs (70) because females with more pronounced disability will have been more likely to have been diagnosed. Our aim was to test these hypotheses, by examining social, communication, and cognitive functioning, as well as ASD symptom level, in a cohort of children with ASD receiving community based early intervention services.

Method

Ethics

Ethics approval was granted by Griffith University (Protocol Number AHS/47/14/HREC). Signed informed consent was obtained from parents of participating children.

Participants

Participants included 254 children (81.5% male) who completed their first assessment at an average age of 45.18 months ($SD = 9.50$, range 29-74 months). All children had an existing DSM-IV or DSM-5 diagnosis of an Autism Spectrum Disorder made by a paediatrician or psychiatrist as per eligibility criteria for the early intervention program. Most children ($n = 226$) had an SCQ at or above 11 (as per Eaves, Wingert, Ho, & Mickelson, 2006 suggested cut-off for preschool aged children), however as exclusion of those with an SCQ below 11 ($n = 18$) or missing an SCQ ($n = 10$) did not substantively alter the results the full sample was retained.

Measures and Procedure

Standardised assessments of cognitive, adaptive behaviour, and communication skills, along with ASD symptoms were conducted as part of a larger evaluation of the intervention program and are outlined in brief below. For further details on measures see Paynter et al (2015).

Cognition. The *Mullen Scales of Early Learning* (MSEL: Mullen, 1995) is a standardised child assessment of early devlelopmental skills and was used to assess cognitive functioning. A total composite developmental quotient was calculated by summing age equivalent scores across the four subscales for composite scores (Visual Reception, Fine Motor, Receptive Language, and Expressive Language) and dividing this by each child's chronological age as per previous research with young children with ASD (e.g., Eapen *et al.* 2013, Paynter *et al.* 2015). This developmental quotient was used due to many children not scoring high enough for calculation of meaningful standard scores (i.e. floor effects).

Communication Skills. The *Preschool Language Scale – 4th Edition* (PLS: Zimmerman, Steiner, & Pond, 2003) was used to assess communication (updated to 5th Edition when it became available, $n = 43$). Similar to the Mullen, many children scored too low for calculation of meaningful standard scores, thus an overall developmental quotient was calculated to standardise overall communication scores to child age for comparison of overall levels of communication skills.

Adaptive Behaviour. The *Vineland Adaptive Behaviour Scales- 2nd Edition* (VABS: Sparrow, Dominic, Cicchetti, & Balla, 2005) parent-caregiver version was used to assess adaptive behaviour. An average overall age equivalent score of subdomain age equivalent scores was calculated and used for comparison based on recommended use of age equivalents, rather than standard scores, as a more sensitive measure of analysis in recent research with young children with ASD (Yang, Paynter, & Gilmore,2016).

ASD Symptoms. The *Social Communication Questionnaire* (SCQ: Berument *et al.* 1999), a short 40-item questionnaire derived from the *Autism Diagnostic Interview-Revised* (Lord *et al.* 1994) was used to assess levels of ASD symptomatology and to verify diagnosis as per previous research (e.g., Eapen et al., 2013; Paynter, Riley, Beamish, Davies, & Milford, 2013). Total scores were used to compare levels of symptoms.

Results

The sample included 42 females and 177 males with a gender ratio thus of 1:4.21. Means and standard deviations for each of the four areas of interest are shown in Table 1. Four one-way ANOVAs were conducted to examine differences between gender and functioning level for the four outcome measures. No main effect for gender was found across outcome measures including cognition, adaptive behaviour, communication, and ASD symptoms. To explore the potential impact of functioning level, participants were divided into a high functioning group (males: $n = 94$, females: $n = 22$) that had a Vineland Adaptive Behaviour Composite (ABC) score of 70 or higher ($M = 79.22$, $SD = 8.61$, range 70-115); and a low functioning group (males: $n = 101$, females: $n = 23$) that had a score below 70 ($M = 61.36$, $SD = 6.02$, range 44-69). There was no significant difference in the proportion of each gender in each functioning group χ^2 (1, N = 240) = .007, $p = .93$. No significant interaction effects were found. A main effect of functioning level was found with children in the low functioning group performed significantly worse on all outcome measures than high functioning children. ANOVAs for all outcome measures are presented in Table 2.

[Insert Table 1 about here]

[Insert Table 2 about here]

Discussion

Our aim was to examine evidence for and against diagnostic gender bias in a cohort of children with ASD receiving community based early intervention services, based on analyses of measures of their social, communication, and behavioural functioning and ASD symptoms. We found no significant differences in our sample between preschool females and males in terms of overall levels of adaptive functioning, cognition, language, or ASD symptoms. Furthermore, we found no difference in gender ratio between males and females with low adaptive functioning and those with average or above adaptive functioning. These findings

are discussed herein with reference to previous literature and the clinical and research implications.

The fact that we found no gender-based differences in overall levels of adaptive functioning, cognition, or ASD symptoms is consistent with our hypotheses and some (Andersson, Gillberg, & Miniscalco, 2013; Postorino et al., 2015), but not all (Carter et al., 2007; Hartley & Sikora, 2009; Sipes, Matson, Worley, & Kozlowski, 2011), previous research involving preschool aged children. As noted in the introduction, differences in findings across studies may be due to different sampling methods, such as the recruitment of cohort of children already enrolled in an early intervention program in the current study. That said, irrespective of whether differences are found in a particular preschool population, there is some evidence from studies of older children and adults for gender-based differences in cognition, adaptive behaviour (e.g., social skills, see Head, McGillivray, & Stokes, 2014; Svenny Kopp & Gillberg, 1992; Kopp et al., 2010; Mandy et al., 2012), and communication (e.g., see review by Rivet & Matson, 2011). It may be that gender differences emerge with development, or it may be that females who present with a differing phenotype have not yet been diagnosed and are thus not presenting for early intervention, as was seen in Hiller et al. (2016). These explanations are not mutually exclusive and it may be a combination of both of these factors. For example, females who are diagnosed at a younger age may show the traditionally male phenotype early in their development, but this may change over the course of their development.

Consistent with previous epidemiological data (e.g., Centers for Disease Control and Prevention, 2014; Lai et al., 2014; Mandy et al., 2012; Postorino et al., 2015), we found a ratio of approximately 4:1 (males:females) in our sample of children commencing early intervention. Furthermore, consistent with previous research (Autism and Developmental Disabilities Monitoring Network Principal Investigators, 2009), children differed across areas

by functioning level with those with lower adaptive functioning showing greater levels of impairment across all measures. However, in contrast to previous research (Abrahams & Geschwind, 2008; Baron-Cohen et al., 2014; Baron-Cohen et al., 2011; Fombonne, 2001; Fombonne, 2003; Kim et al., 2011), as well as our hypothesis, this gender ratio of approximately 4:1 was found in both the low- and high-functioning subgroups. Thus, in our sample, we did not find evidence to support the notion that females who present with more significant developmental needs (e.g., intellectual disability) are more likely to receive an ASD diagnosis than females with average or above average intelligence. This may be due to improvements in diagnostic practices over time, including greater awareness of ASD in females and males amongst general practitioners, paediatricians, and other early childhood healthcare providers, thus leading to higher rates of referrals for assessment.

A further possible explanation for these findings is the Female Protective Effect (FPE). FPE suggests that females require a greater abnormal genetic load in order to achieve diagnosis for ASD (Robinson, Lichtenstein, Anckarsäter, Happé, & Ronald, 2013). In other words, females with ASD may have a genetic safeguard that reduces their likelihood of developing and therefore being diagnosed with ASD (Jacquemont et al., 2014; Werling & Geschwind, 2013a; Werling & Geschwind, 2013b). The extreme argument of our findings is that there is no undiagnosed female phenotype of ASD, but rather the hetereogeneity of ASD regardless of gender. Alternatively, differences in the phenotypic presentation of very young females with ASD may not differ to that of very young males with ASD, and that any differences seen later in development, are the result of systematic socialisation over time that are not yet apparent in early development.

Limitations

Our sample included 42 females; while this is comparable to those in other recent studies into this age group (Andersson et al., 2013; Postorino et al., 2015) even when split

into subgroups of 19 in each, was limited by the number of females presenting to the early intervention service. The sample size precluded fine-grained analyses and may not have been sufficiently sensitive to more subtle gender differences in adaptive behaviour, ASD behavioural characteristics, cognitive profiles, or communication. Furthermore, in considering gender-based differences in autism symptoms and adaptive behaviour, it is important to note that the group in this study cannot be assumed to be representative of the broader preschool population of females with ASD. These females may be qualitatively or quantitatively (e.g., severity) different to females not diagnosed at this point or engaged in early intervention. Our aim however, was to look for evidence for a gender-bias in children receiving an early intervention program, not to ascertain the proportion of females who may have not received a diagnosis and hence been referred for early intervention. Consistent with the alternative proposed mechanisms by which gender bias may occur presented in the introduction (e.g., diagnostic criteria over-emphasises behavioural manifestations of core symptoms more commonly seen in males than females), our sample may not represent those diagnosed later or who seek services in less intensive avenues and may present with milder symptoms which may be an important avenue for future research. Evidence against this possibility is the finding of a similar gender ratio in this study, as in studies of 8-year-old children which would include some children diagnosed that continued to fine a 4;1 ratio (e.g., CDC, 2014). However, such studies are impacted by use of the similar diagnostic tools which may likewise under-detect females at older ages and there is a need to develop and utilise tools that are sensitive enough to identify potential gender differences (Lai et al., 2014).

There is some evidence that the diagnostic tools and measures used in this study are not optimal for detecting gender differences in young children with ASD, or those without ID. For example, while the ADOS shows high specificity and sensitivity for children with an

associated ID, the ADOS becomes increasingly less sensitive and specific for higher functioning individuals, particularly females (Van Wijngaarden-Cremers et al., 2014). In light of this, it is possible that some females in our study will demonstrate significant social and behavioural differences compared to the males as their development continues, particularly if they show development into the higher functioning range.

Conclusion

This study adds to the growing literature examining the issue of gender differences in children with ASD, focusing on those entering early intervention, and provides evidence for a lack of gender differences in pre-schoolers who attend early intervention. However, there is a need for further research including population-based or universal screening or developmental surveillance (e.g., see Barbaro & Dissanayake, 2010, for a possible approach to developmental surveillance). Such an approach could evaluate deviance in development more broadly and be more sensitive to differences and establish whether the clinical phenotype of ASD differs in unselected samples between genders in preschoolers in the general population, whether females showing a different phenotype are diagnosed later in development, or indeed if differences exist later in development or are part of the broader heterogeneity and an artefact of small sample sizes in research to date. In addition, future research that tracks the developmental trajectory of females may provide important information on the course and prognosis for females with ASD. In particular, there is a need to compare trajectories (and the possible emergence of gender based differences over time) of children with differing degrees of intellectual ability/disability. These comparisons should be conducted both longitudinally and cross-culturally, with the view to identifying possible time points at which the skills and needs of males and females with ASD may diverge, particularly in response to socialisation over time. It will also be important to re-evaluate retrospective diagnostic and developmental histories of females diagnosed later in development (as per Hiller, Young,

&Weber, 2016) to further elucidate potentially different developmental trajectories between males and females. This information would have clear implications for clarifying potential gender differences to inform and improve early accurate diagnosis and the provision of timely and tailored early intervention programs aimed at meeting children's changing needs during the preschool and school-years.

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Tables

Table 1

Means and Standard Deviations by Functioning Level, Gender, and Total for Cognition, Adaptive Behaviour, Communication and ASD Symptoms

		Group		
Cognition (MSEL)		*Male*	*Female*	*Total*
High Functioning	*M (SD)*	64.37 (19.06)	62.70 (13.72)	64.05 (18.12)
	n	93	22	115
Low Functioning	*M (SD)*	39.60 (15.19)	42.29 (16.09)	40.11 (15.33)
	n	100	23	123
Total	*M (SD)*	51.54 (21.14)	52.27 (18.04)	51.14 (20.65)
	n	204	47	251
Adaptive Behaviour (VABS)				
High Functioning	*M (SD)*	30.94 (10.38)	31.87 (12.73)	31.12 (10.98)
	n	92	22	114
Low Functioning	*M (SD)*	17.56 (5.84)	15.84 (4.60)	17.24 (5.65)
	n	101	23	124
Total	*M (SD)*	23.94 (10.66)	23.68 (12.39)	23.89 (10.98)
	n	193	45	238
Communication (PLS)				
High Functioning	*M (SD)*	60.45 (20.12)	60.78 (32.20)	60.52 (20.56)
		78	19	97
Low Functioning	*M (SD)*	36.00 (19.19)	41.59 (37.61)	36.94 (23.18)
	n	94	19	113
Total	*M (SD)*	47.09 (23.06)	51.18 (32.20)	47.83 (24.92)
	n	172	38	210
ASD Symptoms (SCQ)				
High Functioning	*M (SD)*	15.83 (5.22)	16.38 (4.81)	15.93 (5.13)
	n	93	21	114
Low Functioning	*M (SD)*	20.41 (5.36)	21.74 (5.21)	20.65 (5.33)
	n	101	23	124
Total	*M (SD)*	18.21 (5.76)	19.18 (5.65)	18.39 (5.74)
	n	194	44	238

Table 2

ANOVAs for Outcome Measures by Gender and Functioning Level

Outcome	df	F	p	$\eta^2_{partial}$
Adaptive Behaviour				
Functioning Level	1, 238	107.93	.000	.361
Gender	1, 238	.078	.781	.000
Interaction Effect	1, 238	.878	.350	.004
Cognition				
Functioning Level	1, 238	66.03	.000	.220
Gender	1, 238	.033	.855	.000
Interaction Effect	1, 238	.616	.433	.003
Communication				
Functioning Level	1, 210	30.40	.000	.129
Gender	1, 210	.559	.455	.003
Interaction Effect	1, 210	.441	.507	.002
Autism Symptoms				
Functioning Level	1, 238	32.05	.000	.120
Gender	1, 238	1.155	.284	.005
Interaction Effect	1, 238	.198	.657	.001