Current Developmental Disorders Reports (2019) 6:57–66
https://doi.org/10.1007/s40474-019-00164-y

AUTISM SPECTRUM (A RICHDALE AND L LAWSON, SECTION EDITORS)

Sex Differences in Autism Spectrum Disorders Across the Lifespan

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Published online: 18 April 2019
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Abstract

Purpose of Review This review aimed to examine contemporary findings on sex-related differences in autism spectrum disorder from pre-school to adulthood. By exploring the literature within developmental time points, it is possible to consider emerging lifespan patterns and determine consistency of results without the impact of developmental change.

Recent Findings Findings continue to be varied due to numerous methodological differences across studies. However, some results are more consistent than others. For instance, while there is no evidence for a sex difference in cognition in early childhood, there may be executive functioning differences in adolescence/adulthood. Further males exhibit more and different restricted repetitive behaviours, while females have more motivation toward friendships and compensatory behaviours.

Summary The results reviewed provide emerging evidence for a female behaviour phenotype of ASD. However, future research should include a non-autistic comparison sample and consider the impact of sample characterisation (e.g. age range and genotype).

Keywords Autism spectrum disorder · Sex differences · Lifespan · Behaviour · Cognition · Psychopathology

Introduction

Autism spectrum disorder (ASD) is a set of developmental conditions that are defined by impairments in social communication and the presence of restricted and repetitive behaviours (RRBs) [1]. Early epidemiological studies identified a disparate sex ratio of 2.3–2.6:1 males to females [2–4], with lower ratios found among individuals with an associated intellectual disability 1.3–2.1:1 [3, 4]. A review of prevalence rates between 1986 and 2007 found that the sex ratio is increasing over time, with males becoming increasingly overrepresented [5], and the most recent meta-analysis of 54 studies identified a current sex ratio of 3.5:1 [6•]. Further, recent findings show a higher sex ratio in childhood/adolescence (3.5:1) compared with adulthood (1.8:1) [7•], suggesting that more females may be receiving diagnoses later in life.

It has been proposed that ASD may be under-identified in females without co-occurring cognitive impairments or behavioural difficulties [8]. Biases in existing diagnostic tools—mainly developed from data on males with ASD—may be contributing to the under-identification of females. For instance, several items in the Autism Diagnostic Interview-Revised (ADI-R) [9] differ between males and females, indicating a possible bias in the tool [10••]. Females also tend to be referred for comorbid conditions rather than primary concerns related to an ASD diagnosis [11]. Therefore, research into sex-related behavioural differences is crucial to be able to accurately identify all individuals with ASD.

Early studies examining differences between males and females with ASD found that females with ASD had lower intellectual functioning [4, 12–15] and exhibited less RRBs [13, 16] compared with males with ASD. However, it is important to note that there have been significant changes in diagnostic practices since the publication of these findings. Further, most of the existing research on behavioural differences among males and females diagnosed with ASD has recruited samples across a wide age range. This is a likely consequence of the sex disparity, which makes it difficult to recruit sufficient numbers of females with ASD. Nevertheless,

This article is part of the Topical Collection on *Autism Spectrum*

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exploring differences from toddlerhood to adulthood concurrently may obscure important developmental changes and patterns across the lifespan. Therefore, this review examines contemporary findings on sex-related differences in ASD within different developmental time points from pre-school to adulthood.

Core Autism Characteristics

Pre-school

The literature examining core autism characteristics among pre-school children is quite varied. The most consistent result is that males tend to have more RRBs and stereotyped behaviours than females [17, 18, 19••, 20]. However, one study utilising a high-risk sibling cohort found no interaction between gender and autism diagnosis, indicating that the sex differences in RRBs among pre-school children may not be autism specific [19••]. Further, numerous studies have also identified no sex differences in RRBs [21–26].

Within the social communication domain, the results are split. Some studies identify a female advantage [27, 28], some find females more impaired compared with males [17, 21, 29], and others identify no difference at all [20, 22, 23, 24•, 26]. The varied results here may be related to sample recruitment methods (high-risk cohorts, clinical samples, community samples), which can have a significant impact on the generalisability of findings [30]. More research—particularly longitudinal—is required to track changes in development between the sexes across time.

Childhood

Similar to the pre-school literature, most studies examining school age children with ASD identify more RRBs among males with ASD compared with females [31–33]. Hiller et al. [32] found that if a child did not meet the RRB diagnostic criterion, they were ten times more likely to be female. This was supported by Kumazaki et al. [31] and Supekar and Menon [33] who also identified higher levels of RRBs in males compared with females with ASD. Conversely, Sutherland et al. [34] found no difference in RRB frequency, but found differences in *types* of special interests, such that both sexes had interests along traditional sex lines. This is supported by Nowell et al. [35] who also found no differences in the quantity of interests between males and females, but for both genders the primary reported interest was along traditional sex lines. Hiller et al. [32] further identified that females tended to be less interested than males in the use of objects, vehicular toys, or gaming. However, it is important to consider that a few studies have found no sex differences in RRBs [25, 36–38], though Rynkiewicz et al. [36] identified divergent developmental trajectories, such that RRBs decreased over time in males but not females.

Interestingly, few studies have examined gender differences in sensory issues among children with ASD. Kumazaki et al. [31] identified more sensory difficulties among females than males with ASD. However, a recent study examining a large sample of children with ASD (512 female, 512 male) found no differences in sensory symptoms measured on the Autism Diagnostic Observation Schedule (ADOS, [39, 40]) [25]. Taken together, the evidence appears to support a sex difference in RRBs, such that males with ASD exhibit more and different behaviours compared with females who possibly show more sensory differences and fewer other types of RRBs.

Examining social communication skills, two studies identified a female advantage in the use of non-verbal communication such as gestures [32, 36]. Compared with males, females have also been found to have better social communication skills [38], emotional responsiveness [41], and more skills in reciprocal conversations and sharing of interests [32]. Furthermore, a study examining patterns of social attention identified that females with ASD exhibited more typical patterns of social and non-social attention such that they fixated more to faces, less to objects, and orientated faster to faces compared with males with ASD [42]. Finally, despite finding no sex differences in social communication, based on the findings in this area, it has been suggested that the superior social communication skills identified in females with ASD may contribute to camouflaging other diagnostic features.

On the other hand, two parent-report studies have identified a *male* advantage in communication skills [36, 43]; Banach et al. [43] only found such a difference among simplex individuals, and this was no longer significant after controlling for IQ. Moreover, a number of studies have found no sex differences in social communication skills [31, 33, 34, 37, 44]. These findings highlight the importance of controlling for IQ when examining social communication abilities. Nevertheless, there is preliminary evidence for a female advantage in the use of non-verbal communication skills such as gesture.

Adulthood

Numerous studies examining autism characteristics in adults have utilised self-report questionnaires. Baron-Cohen et al. [45] reported that regardless of diagnosis, females score higher on empathising and males score higher on systemising and autism characteristics. The interaction between sex and diagnosis is also significant, indicating a masculinised profile among individuals with ASD. However, subsequent research has found that adult females with ASD self-report higher autism symptomatology compared with males with ASD [46–48, 49••], while other studies have identified no sex effect

on empathising [47, 50] or systemising skills [47]. The self-report literature provides preliminary evidence for a masculinised profile among females with ASD.

Interestingly, a different profile emerges when examining parent-report (e.g. ADI-R) or observational measures (e.g. ADOS). Lai et al. [48] found no sex differences when examining the ADI-R overall and subdomains—although females were noted to have more lifetime sensory difficulties than males—while on the ADOS, males had more impairment in the social communication and RRB subdomains than females. The more severe profile among males is supported by subsequent studies showing that males present with more severe impairment than females on both the ADOS and ADI-R [49••, 51]. These results support the suggestion of a more severe autistic profile among diagnosed adult males compared with females, which contrasts with findings from the self-report literature. It has been suggested that such a discrepancy may be related to females with ASD being more adept at camouflaging behaviour, thus presenting as less impaired on observational assessments compared with self-reflection of behaviour.

A couple of studies have specifically investigated the possibility of camouflaging behaviour among adults with ASD. Lai et al. [49••] found that, despite substantial variability, females had significantly higher camouflaging scores compared with males, corroborating the suggestion that females with ASD may be more skilled at camouflaging their symptomatic behaviour. In contrast, a thematic analysis of social camouflaging found that similar numbers of males and females with ASD reported camouflaging behaviour, with no consistent differences noted between the sexes [52]. Additional research is required to ascertain the potential sex difference in camouflaging behaviour.

Focusing on objective measurements of emotion recognition and social attention, Ketelaars et al. [53] found no evidence of a sex difference in emotion regulation accuracy between males and females with ASD. However, females had higher levels of alexithymia (an impairment in identifying emotional states) than males, and there was preliminary evidence that females with high levels of alexithymia had difficulties labelling others' emotions. Females with ASD have also been found to have a normal time to first fixation to the face, but overall lower duration of fixation to the face compared with TD females [54], suggesting an initial social interest that is not maintained. Furthermore, females with higher reported autism characteristics had slower time to first face fixation, suggesting reduced social attention. The results from these two studies indicate a potential difference in emotion recognition and social attention for females with ASD. Overall, the evidence reviewed here seems to point toward a different core symptom phenotype for adult females with ASD such that, despite self-reporting more autism characteristics than males, objective and observational measures indicate the existence of camouflaging social behaviour among females with ASD.

Summary

Together there appears to be consistent evidence for increased RRBs among males with ASD compared with females from pre-school to adulthood. However, there is currently no work specifically examining gender differences in RRBs among adolescents on the spectrum, and only one study that showed that males had more RRBs on the ADOS. The evidence surrounding social communication abilities is much more varied. However, there appears to be evidence for a female advantage in the use of non-verbal communication in childhood, which may contribute to the identified increase in camouflaging behaviour among female adults with ASD compared with males. Overall, there is enough evidence for different male and female profiles for core autism characteristics that future researchers examining these behaviours should consider sex as a moderating factor.

Cognition

Pre-school

Most studies investigating cognitive development among pre-schoolers with ASD have found no sex-related differences in clinical- [17, 18, 55] or community-based samples [21, 22]. Carter et al. [29] did find that pre-school females with ASD had higher visual reception and lower language and motor scores compared with males with ASD, but the differences were small. Matheis et al. [26] also found that pre-school females with ASD had lower motor scores, but higher communication skills compared with males with ASD. No differences were found for attention or memory skills [26]. Two other studies also identified that high-risk females had higher scores on the Mullen Scales of Early Learning [56] compared with males [19••, 27]. However, these differences occurred whether or not the children went on to receive an ASD diagnosis, suggesting that sex differences in cognition among pre-school children may not be autism specific. Finally, Postorino et al. [23] found that while females had lower baseline cognition scores than males, this was not maintained over time. Hence, there is no strong support for sex differences in cognitive functioning among pre-schoolers with ASD.

Childhood

Similar to the findings from early childhood, [31] found no differences in cognition among a small sample of children aged between 5 and 9 years (20 female, 26 male). In a larger sample of children aged 8 to 12 years (209 male, 116 female),

Ryland et al. [57] also found no differences in overall cognition, but did find that males had lower visuospatial scores compared with females. Interestingly, Banach et al. [43] investigated sex differences within a sample of children with simplex and multiplex autism, finding no differences in cognition among the multiplex children. In contrast, simplex females had significantly lower non-verbal intelligence quotient (IQ) scores compared with simplex males. However, none of these studies included a comparison non-autistic sample, so it is not possible to determine whether the gender differences are specific to individuals with ASD or exist regardless of diagnosis.

Dworzynski et al. [44] used a population-based cohort to examine sex differences in ASD and compared them to undiagnosed individuals with high levels of autistic behaviours. Among females, those with a diagnosis were 4 to 9 times more likely to have lower cognitive functioning compared with females without a diagnosis. Among males, those with a diagnosis were 2.7 times more likely to have lower verbal cognition compared with males without. This suggests a possible disparate relationship between cognitive functioning and the likelihood of receiving an autism diagnosis among males versus females. Therefore, females may be more likely to receive a diagnosis if they also have lower cognitive functioning.

So, while there is no strong evidence for a sex difference in cognition among children diagnosed with ASD, the results in this area raise an important issue regarding whether sex differences may vary by genotype or as a function of confirmed versus possible diagnosis.

Adulthood

A small number of studies have investigated sex differences in adult cognitive profiles. Lai et al. [51] found poorer performance among males with ASD compared with TD males on executive function tasks involving attention to detail and dexterity, while females with and without ASD performed similarly. No other differences were noted. Lehnhardt et al. [47] found that males with ASD had higher verbal abilities, while females had higher processing speed and executive function. However, a subsequent study found no such sex difference for mental rotation ability [58]. A recent study also identified that females with ASD performed better than males with ASD on a digit symbol test, but there were no sex differences in other tests of executive function [59]. To date, the evidence appears to support the suggestion of differing cognitive profiles among males and females with ASD, particularly concerning executive functioning tasks.

The higher executive functioning and processing speed observed may provide an advantage in developing higher-level social communication skills (i.e. mimicking) leading to social camouflage behaviours among females with ASD. In support of this suggestion, Lai et al. [49••] found that more camouflaging behaviour was associated with better signal detection in females but not males with ASD. Additional work is therefore required to tease apart the relationship between cognition and behaviour for diagnosed males and females.

Summary

Although the existing evidence suggests no sex difference in cognition among children with ASD, there is emerging evidence for a sex difference in executive function, with adult females with ASD exhibiting better executive functioning skills compared with males. Furthermore, the female executive function advantage has also been linked to camouflaging behaviour, providing further evidence for differing profiles among males and females with ASD.

Adaptive Behaviour

Pre-school Children

Relatively few studies have examined sex differences in adaptive behaviour among pre-school children and most have failed to find any significant differences between males and females with ASD [22, 23, 24•, 26, 55]. One study using a high-risk sibling cohort did identify a female advantage on the socialisation and daily living subscales on the Vineland Adaptive Behaviour scales (VABS) [60] among children aged 3 years [27]. However, there was no significant interaction between sex and ASD diagnosis, indicating the female advantage was independent of ASD diagnosis [27]. The existing evidence to date therefore suggests no autism-specific sex differences in adaptive behaviour at this developmental stage.

Childhood

The only study to look specifically at adaptive functioning among a sample of school-aged children with ASD found no sex difference in VABS scores among a multiplex sample [43]. However, parents of simplex females reported significantly more communication impairments than did parents of simplex males, though this effect was no longer significant once cognition was controlled for. Therefore, sex differences in adaptive behaviour among children with ASD may reflect differences in cognitive functioning.

Summary

More work is required to investigate potential sex differences in adaptive behaviour, particularly among adolescents and adults with ASD. However, the limited existing evidence suggests no sex difference exists in childhood.

Psychopathology

Pre-school Children

Only three studies have investigated sex differences in emotional and behavioural difficulties among pre-school children with ASD. Hartley and Sikora [17] found that females had more sleep problems and anxious/depressive affect (as measured by the Child Behaviour Checklist (CBCL) [61]), compared with their male counterparts. However, two other studies found no sex differences on the CBCL [23] or Infant-Toddler Social and Emotional Assessment [62] internalising or externalising domains [29]. The small number of studies makes it difficult to draw strong conclusions here.

Childhood

The literature investigating sex effects in psychopathology within childhood samples has been quite varied. Two studies identified no sex differences in overall psychopathology as measured by the CBCL [41] or in parent-reported subjective well-being [63]. However, Amr et al. [41] found that males exhibited significantly more delinquent behaviour compared with females (albeit in a relatively small sample of 37 males and 23 females).

In a large population-based cohort, Dworzynski et al. [44] measured behavioural profiles among a group of children with an ASD diagnosis and a group with high autistic traits but no diagnosis. While no sex differences presented within the diagnosed group, when looking within the sexes, diagnosed females had significantly higher levels of hyperactivity and were 5.4 times more likely to exhibit behavioural problems compared with non-diagnosed females. Further, females with high behavioural difficulties and lower cognitive functioning were 8.4 times more likely to have received an ASD diagnosis. These results suggest that in absence of additional behavioural issues, females with ASD may be less likely to receive a formal diagnosis.

One study examined the change in psychopathology symptoms over time in a sample of ASD and TD children aged 7 to 12 years [37]. Regardless of the presence of an ASD diagnosis, males were found to be more hyperactive, while females had more social anxiety symptoms. No changes were observed over time or within any of the other behaviour domains (i.e. opposition behaviour, inattention, executive function, or learning problems), suggesting that sex differences in the emotional and behavioural profile may not be specific to children with ASD. These findings add to the picture that emotional and behavioural symptom differences between males and females may contribute to a potential under-diagnosis of ASD among females.

Adolescence

Two studies utilised both parent- and self-report to compare behavioural and emotional difficulties among males and females with and without ASD. Oswald et al. [64] found that, based on both parent and self-report, young adolescent females with ASD exhibited more depression symptoms compared with males with ASD and typically developing (TD) females. No such differences were found for anxiety symptoms. Using the CBCL and Youth Self Report [65], Pisula et al. [66•] further examined these relationships finding no sex differences in behaviour or interactions between sex and diagnosis. Interestingly, when comparing parent- and self-ratings, adolescents with ASD generally rated their problems as less severe than their parents, while TD controls rated their behaviour as more severe than their parents. It is possible that this may be a consequence of adolescents with ASD having poor insight into their own emotions. Alternatively, what might be perceived as problem behaviour by TD individuals, may not by those with ASD. As such it is necessary to consider collecting data from multiple sources when examining psychopathology. However, the limited work here precludes drawing firm conclusions on sex differences in psychopathology among adolescents with ASD.

Adulthood

Relatively few studies have focused on sex differences in psychopathology among adults with ASD. Tsakanikos et al. [67] recruited a sample of 50 males and 50 females with an associated intellectual disability (ID) to examine comorbid psychopathology, finding males to be significantly more likely to have a diagnosis of personality disorder or schizophrenia, while dementia was more common among females. Additionally, males were more likely to be prescribed a combination of pharmaceuticals, while female more often received sedation. While these findings suggest a sex difference in the presentation and management of psychopathology in adults with ASD, restricting examination to those with an associated ID means it is unclear whether the same results would extend to higher functioning individuals.

A few studies examining self-reported psychopathology symptoms have found no sex differences in depression, anxiety, or obsessive-compulsive symptoms [46, 47, 49••, 59]. Nevertheless, Lai et al. [49••] found that more camouflaging behaviour was associated with higher self-reported depressive symptoms among males but not females with ASD. This sex difference could suggest that males with ASD are more susceptible than females to the burden of engaging in camouflaging behaviour. However, additional research is required to fully understand the potential sex differences in psychopathology throughout adulthood.

Summary

From the limited evidence, there is no strong evidence to suggest an ASD-specific sex difference in psychopathology symptoms during childhood, adolescence, or adulthood. However, there is some evidence that psychopathological sex differences often identified in the typical population (e.g. females exhibiting higher anxiety and depression, and less disruptive behaviour compared with males; [68]) may be reflected in the ASD population and may contribute to the under-diagnosis of females, as females without associated behavioural difficulties are much less likely to receive an ASD diagnosis.

Peer Relationships

Childhood

A small number of studies have examined whether or not peer relationships vary by sex among children with ASD. Hiller et al. [32] found that females were able to initiate friendships but had trouble maintaining them. Dean et al. [69] further compared peer relationship behaviour between children with ASD and typically developing peers, finding that males tended to be overtly excluded, while females were overlooked rather than deliberately excluded. Another study found that females with ASD used more compensatory behaviours (e.g. staying in close proximity to peers, and weaving in and out of activities), while males with ASD preferred to play alone [70]. These results highlight different social behaviours among males and females with ASD—particularly when compared with their TD peers—and that even within childhood, females with ASD may engage in more camouflage behaviours than males.

Adolescence

A number of studies have focused on differences within peer relationships among male and female adolescents with ASD. To date, two studies have used phenomenological analyses to examine accounts of social experiences for females with ASD. The first identified that although females with ASD were motivated to develop meaningful friendships, this was reported as increasingly difficult during adolescence [71]. Many respondents revealed that they learned specific coping strategies to manage friendships, including masking and imitation, and these accounts provide evidence for the 'social camouflaging' theory of females with ASD. These findings were corroborated by Vine Foggo and Webster [72], who also identified that females with ASD had the desire to create friendships, but reported conflict with peers and difficulty determining the expectations of others or socialising in groups. Nevertheless, the absence of male comparison groups in these studies makes it difficult to determine whether this situation is unique to females with ASD.

Sedgewick et al. [73] utilised a mixed methods approach to investigate social motivation and friendship among both males and females with ASD and TD controls. Females with ASD had a similar level of motivation to form friendships and they also had similar friendship quality to the TD females. In contrast, males with ASD reported less motivation for friendships and different quality friendships compared with all other groups, suggesting greater social difficulties may be specific to adolescent males with ASD. A follow-up mixed methods study also identified that females with ASD had similar friendships and social experiences compared with TD females, but that those with ASD faced more social challenges and had difficulty managing their conflicts [74].

Using the Friendship Questionnaire (FQ) [75] to assess peer relationships, Head et al. [76] found that independent of ASD diagnosis, females had higher levels of sociability, emotionality, and friendship compared with males. An additional comparison of parent- and self-report data revealed that adolescents' self-reported higher scores on the FQ compared with parent ratings. A discrepancy between informants was also identified by Kuo et al. [77] who found that adolescents with ASD identified more friends than were reported by their parents. Therefore, these findings indicate that adolescents with ASD may define friendship different to their parents and highlights the importance of gathering information from multiple sources.

Summary

Together, the literature on peer relationships appears to indicate that among children and adolescents, females with ASD demonstrate better skills than males with ASD. Furthermore, these skills appear to be related to improved camouflaging skills, similar to differences identified in the social communication literature. Therefore, females with ASD appear to be more likely to use skills, such as masking and imitation, and gesture to camouflage with their peers.

Conclusion

This review has highlighted the highly variable results concerning sex effects in ASD. Methodological issues likely contribute to the inconsistent findings in this area, including small female sample sizes, IQ disparity, and changes in diagnostic criteria (for a review, see [78]), making it difficult to determine which sex effects reflect an actual difference rather than some confounding factor

or spurious result. Nevertheless, some findings emerge more consistently than others. For example, while there does not appear to be evidence of a sex difference in early childhood cognitive functioning, there is emerging evidence for executive functioning differences in adulthood. Importantly, a recent meta-analysis identified that these may not be specific to individuals with ASD, highlighting the importance of including non-autistic comparison samples in future investigations [79••].

In regard to autism characteristics, the most consistent finding is that males exhibit more RRBs than females, a difference that presents from childhood onwards, though a recent meta-analysis identified the difference as present only from 6 years of age [80]. In addition to the disparate frequency of RRBs, there is also a sex difference in the *type* of RRBs, with females presenting more gender 'typical' interests, which may not be identified by traditional assessments. Similarly, there appears to be relatively consistent evidence for a difference in peer relationships between males and females with ASD, such that females have more motivation toward developing friendships and use more compensatory behaviours than males such as may contribute to an under-identification of ASD among females.

While the current review focused on behaviour differences between males and females with ASD, it is important to note the existence of substantial research on brain development, hormone exposure, and physical differences that fell beyond the scope of this review [81–86]. Nevertheless, there is emerging evidence for a female behavioural phenotype of ASD. What remains to be shown is how stable this phenotype is from early childhood and throughout adulthood, including among older adults.

Compliance with Ethical Standards

Conflict of Interest The author declares that there are no conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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