REVIEW ARTICLE

Autism: the literature on gender differences

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BACKGROUND

Literature on autism spectrum disorders over the years has documented a male-to-female ratio of approximately 4:1. Yet this gender-ratio is now being questioned with studies showing that this ratio may be lower. Factors underlying this male predominance are mostly unknown. Since the majority of published research on autism includes mostly, and in some cases, exclusively males, much less is known about females with autism.

In this literature review I examined the available published evidence over 7 years on the possible gender differences in autistic girls and boys.

METHODS

A review of the literature was conducted using PubMed with the key words 'autism spectrum disorder' in combination with 'girls and boys' and 'gender differences'. Relevant articles were screened against eligibility criteria leading to 36 final articles which were analyzed in more depth.

RESULTS

Seven key themes on gender differences between autistic girls and boys emerged. These themes include the female camouflage effect, genetic and hormonal mechanisms, autism diagnostic assessment tools which are being increasingly criticized, gender differences in the core diagnostic criteria of autism and differences in comorbidities between girls and boys on the spectrum.

CONCLUSION

Managing to understand gender differences better may lead to more accurate and earlier diagnosis of females on the spectrum. Future research should focus on including larger number of females and developing instruments which are better suited to diagnose the female phenotype of autism and to understand the specific needs of females on the spectrum.

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INTRODUCTION

Autism spectrum disorder (ASD) consists of a heterogeneous group of neurodevelopmental disorders,[1] which according to the latest edition of the *Diagnostic and Statistical Manual of Mental Disorders (DSM-5, 2013)* is characterized by 'persistent deficits in social communication and interaction as well as restricted and repetitive patterns of behaviors, interests and activities'. These symptoms need to be present from early childhood, particularly before the age of three years or, when demand outweighs capacity.[2]

The first attempts at identifying and describing autism were made as early as 1943 and 1944 by Leo Kanner and Hans Asperger respectively. Since then, definitions and criteria for diagnosis have been updated several times. Autism is being seen as a spectrum of conditions with different levels of severity.[1] Autism is a life-long condition and is known to affect 1% of the population[3-4] with a well-documented predominance in males, which is now being questioned.

Literature over the years has documented a male-to-female ratio of approximately 4:1.[3, 5-8] Even the DSM-5 states that 'ASD is diagnosed four times more often in males than in females'.[2] However this gender-ratio commonly reported in studies is being questioned.[9-10] In fact, according to Rynkiewicz and colleagues, studies conducted during recent years have shown that this ratio may be lower at the rate of 2.0-2.6 males: 1 female.[3] This was also reported by Beggiato and colleagues, where male to female ratio was found to be approximately 3:1. Despite these lower proportions, the diagnosis of autism still seems to be more common in males than in females. Factors underlying this male predominance are mostly unknown.[8]

Since the majority of published research on ASDs includes mostly, and in some cases, exclusively males, much less is known about females with autism.[11] For a long time it was assumed that females with autism had the same neurobiology and behaved in a similar way to males with autism. This probably may have led to a diagnostic bias 'towards a male stereotype of ASD',[12] leading to different professionals to unknowingly hold gender stereotypes and as a result are less sensitive to symptoms of autism when they occur in girls.[4]

Several studies have reported that early identification of autism is crucial since it is linked to early educational interventions, better communication skills, lower rates of problematic behaviors and less parental stress.[13] Misdiagnosis in females can also lead to similar problems since the young girl on the autism spectrum may be given treatment that she does not need and will not be given access to the necessary services and available support for school and employment.[14] Literature over the recent years has recounted stories of females on the autism spectrum who were not given a timely diagnosis, or no diagnosis at all, and as a result had issues with their identity, low self-esteem and felt as 'outsiders'. When eventually given a diagnosis, it 'was experienced as liberating and resolved a lifelong identity crisis'.[15]

In this literature review I examined the available published evidence over the past 7 years on possible gender differences in autistic girls and boys up to the age of eighteen years. Managing to understand gender differences better may lead to an earlier diagnosis and better support and treatment of ASD in girls and women.[16]

Materials and Methods

An electronic database search was done between April and July 2019 using PubMed. Articles relevant to this literature review published between January 2012 and July 2019 were searched.

The following keywords were used in the search engine: 'autism spectrum disorder' in combination with 'girls and boys' and 'autism spectrum disorder' in combination with 'gender differences'. The initial database search using these keywords identified 824 articles. The titles and abstracts of these articles were screened against inclusion and exclusion criteria. Inclusion criteria included children and adolescents with a diagnosis of autism, up to the age of eighteen years, who were involved in research comparing girls on the spectrum versus boys on the spectrum. Prevalence studies, studies on participants with autism-like traits and studies on adults on the autism spectrum were excluded.

The above process resulted in 48 potentially relevant articles. Then, these 48 articles were read thoroughly to make sure that each article met all inclusion criteria discussed above. This resulted in a further 12 articles being excluded since when reading the whole articles it became evident that 3 studies were on infants with a high-risk of autism and not a diagnosis of autism, another 4 articles did not mention clearly the age of the participants, another 2 articles did not have clear data on the male and female cases who participated and another 3 articles were on neurogenetics. These were not evident when the titles and abstracts were read in the initial screening. This resulted in 36 final studies as seen in Figure 1 according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[17]

These final 36 articles were read in depth, and the topics and patterns which came up repeatedly during this process were highlighted and coded. This process of thematic analysis led to seven key themes on gender differences between girls and boys on the autism spectrum (Table 1).

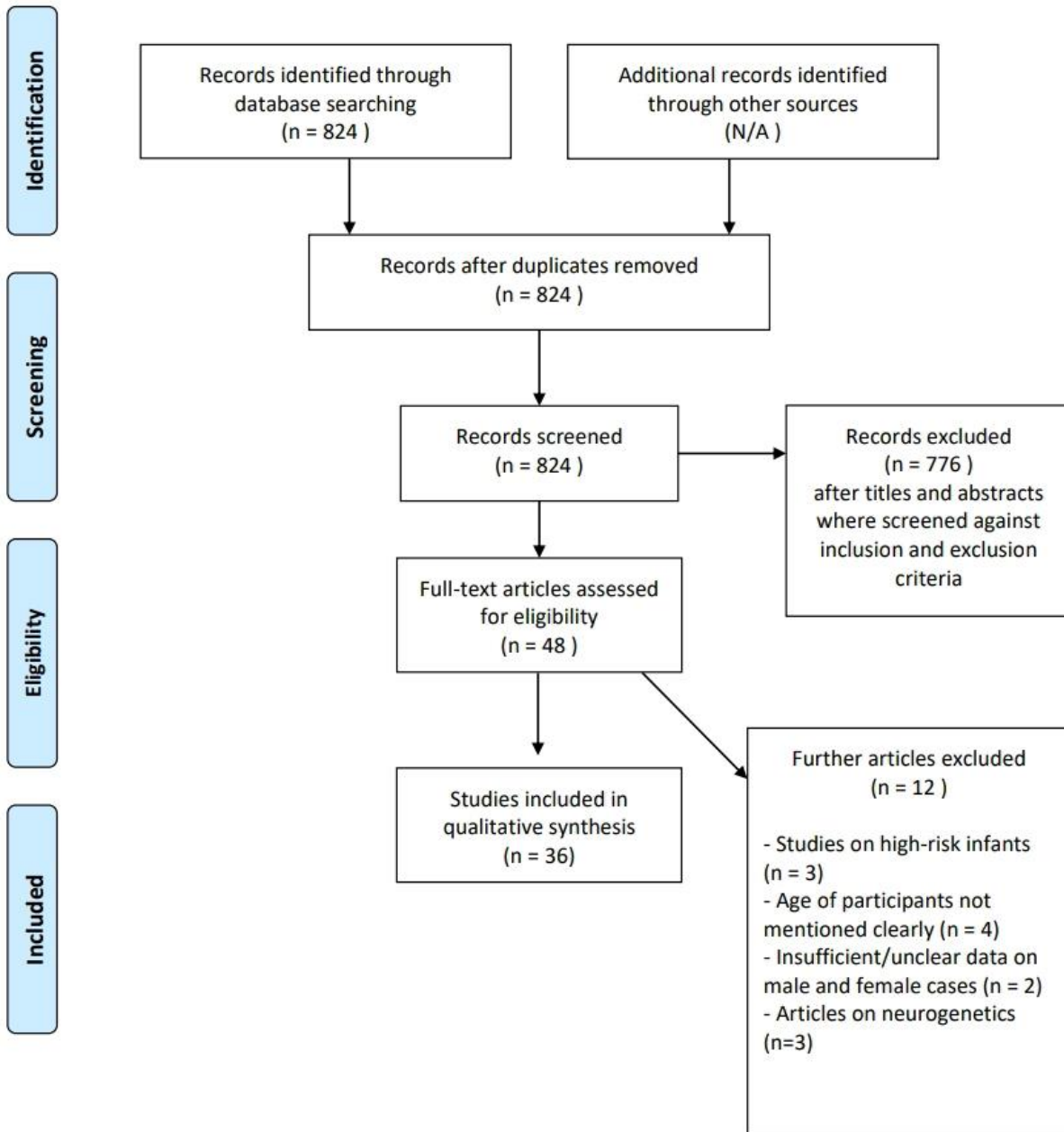**Figure 1**   Flow diagram of study selection according to PRISMA guidelines.

Table 1   The 7 Themes and the Articles addressing each theme

Theme 1	
The Female Camouflage Effect	• Beggiato A et al. (2017) • Dean M et al. (2017) • Fulton AM et al. (2017) • Ratto AB et al. (2017) • Ormond S et al. (2018) • Matheis M et al. (2019)
Theme 2	
Genetic and Hormonal Mechanisms and Theories	• Teatero ML et al. (2013) • Kreiser N et al. (2014) • Schaafsma SM et al. (2014) • Lai MC et al. (2015)
Theme 3	
Diagnostic Assessments	• Kreiser N et al. (2014) • Tierney S et al. (2017) • Young H et al. (2018)
Theme 4	
Core Diagnostic Criteria	• Hiller RM et al. (2014) • May T et al. (2014) • Supekar K et al. (2015) • Duvekot J et al. (2017) • Harrop C et al. (2018) • Antezana L et al. (2019) • Matheis M et al. (2019)
Theme 5	
Social Interaction, Motivation and Interests	• Head A et al. (2014) • Sedgewick F et al. (2016) • Harrop C et al. (2017)
Theme 6	
Social Communication	• Reinhardt VP et al. (2015) • Kauschke C et al. (2016) • Conlon O et al. (2019)
Theme 7	
Behavioural and Emotional Problems	• Dean M et al. (2017) • Duvekot J et al. (2017) • Hull L et al. (2017) • Pisula E et al. (2017) • Margari L et al. (2019)

RESULTS

THE FEMALE CAMOUFLAGE EFFECT

Wing suggested the 'camouflage hypothesis' in 1981 as an explanation for the skewed gender ratio in autism. According to this hypothesis females on the spectrum are able to mask their autistic symptoms, mainly their social deficits, by managing to learn the rules of social situations.[5,18-19] This hypothesis contrasted strongly to the long-standing belief that females are only at a reduced risk of developing autism based on the lower prevalence rates among females over the years.

There is now growing evidence of this camouflaging effect among females on the spectrum, especially among those without intellectual disability.[20] A study by Dean and colleagues, examined and observed closely the social behaviors of 96 children (half autistic and half typically developing (TD) children), all with an IQ of 70 or more, during school recess. Gender differences in social behavior were clearly evident. Boys on the spectrum had more obvious social challenges than the girls on the spectrum. When observed from a distance, the latter were more similar in social behavior to the TD girls. On the other hand, the TD boys were playing structured games and the boys on the spectrum were more easily spotted wandering alone away from these games.[21]

Ormond and colleagues, state that girls are presented to professionals three and a half years after boys and a diagnosis of autism is given approximately five years later than boys.[22] This delay in diagnosis is of concern since it can negatively impact the life of these females.[19, 22] Fortunately, recently researchers are giving increasing attention to female self-

advocates who are describing their difficult experiences to increase awareness both among the professionals and the general public.[20]

Delayed diagnosis occurs especially in girls on the high-functioning end of the autistic spectrum, one possible explanation being the higher intellectual quotient (IQ) scores and thus the increased ability to mask their deficits. In fact, there tends to be underrepresentation of females with a diagnosis of autism at the higher ends of the IQ distribution.[7]

GENETIC AND HORMONAL MECHANISMS AND THEORIES

Given that ASD is known to be genetic, multiple studies have been investigating genes that could be the cause of the male predominance in autism. Sex chromosomal genes which include the male-specific Y-linked genes and many X-linked genes have been found to be associated with autism however the mechanism by which they contribute to the male bias is still unknown.[6, 10]

High levels of prenatal testosterone have been found to activate and masculinize behavior of both boys and girls and seem 'to cause a shift on the ASD scale'. This shift however is not enough for the individual to meet the criteria for ASD. In fact, children who were exposed to the highest levels of testosterone did not meet criteria for diagnosis. Therefore, prenatal testosterone by itself is not able to explain the occurrence of ASD and so is seen as a contributing factor together with other genetic and environmental factors.[6]

Recent literature has shown that maternal stress can activate the maternal immune system and this together with early exposure to high levels of prenatal testosterone can

have a sex specific role in the cause of ASD. These studies are still in their infancy and more research is needed.[6]

Throughout the years, several models were proposed. The most widely studied model is the brain differences model (BDM) which includes the extreme male brain (EMB) hypothesis proposed by Simon Baron-Cohen in 2004.[14] In Baron-Cohen's view, males are better at systemizing by developing rules and guidelines whilst females tend to be better at showing empathy and identifying feelings. Since an extreme male pattern of cognition has been found in persons on the spectrum, males may be more susceptible to develop autism and so this hypothesis may explain the male predominance.[14, 23]

Wing proposed the greater variability model (GVM) which suggested that males are more vulnerable to develop ASD due to a greater genetic variability. A third model known as the liability/threshold model (LTM) proposed that males and females are equally at risk in developing autism, however females have a higher threshold for manifesting the symptoms and so need "more genes" to be affected by the condition. None of these mentioned models have been consistently supported by empirical evidence and they have been heavily criticized. Researchers are now investigating epigenetic mechanisms on the X-chromosome.[14]

DIAGNOSTIC ASSESSMENTS

The Autism Diagnostic Interview – Revised (ADI-R) and the Autism Diagnostic Observation Schedule (ADOS) are two assessment tools used in the diagnosis of autism. For a formal diagnosis to be reached the ADI-R and ADOS are most commonly used together in combination with direct observation of the child's behavior.[1]

Recent literature has shown researchers and professionals criticizing these diagnostic assessments. Main reason being that sex has not been taken into account during the development and validation of these tools.[9] In fact only 'one female for every four to seven males' were included during the validity of the ADI-R whilst an unequal sample size of eight females and seventy one males were included during the development of the ADOS.[14] Different studies have stressed the lack of sensitivity of the ADOS towards identifying girls on the spectrum.[9, 24] Apart from using predominantly male samples, further criticism was related to the fact that parental reports are used for the ADI-R and parents themselves can be unknowingly causing a bias due to gender stereotyping and expectations that more boys are on the autistic spectrum than girls. In addition, since the ADOS is based on observing the child for an average of forty minutes whilst administering the test, it is possible that girls go undiagnosed since their expression of autistic symptoms may be more subtle or different from those of boys.[1]

CORE DIAGNOSTIC CRITERIA

To date, research on gender differences in the core diagnostic criteria of autism still presents with inconsistent results. The most consistent finding shown in the literature is related to the restricted interests and repetitive behaviors domain.[25] Restricted Repetitive Behaviors (RRBs) consist of repetitive body movements and mannerisms [26] which are persistent, at an increased frequency and interfere with learning of children on the spectrum.[11]

Current literature suggests that girls on the spectrum show less repetitive use of objects and adherence to rituals when compared to boys on the spectrum.[5, 11, 25-28] Robust evidence for reduced levels of RRBs in girls with ASD

was found in a large study by Supekar and colleagues using the National Database for Autism Research (NDAR) dataset.[27] Nevertheless there are also several studies which have reported no significant gender differences in RRBs.[29-30] Certain studies showed that girls have interests which are less typical of ASD whilst on the other hand boys have more atypical movements, restricted interests and repetitive use of objects such as repetitive playing with wheels.[11, 25, 28]

SOCIAL INTERACTION, MOTIVATION AND INTERESTS

A persistent deficit in social communication and social interaction is one of the core diagnostic criteria. Individuals on the spectrum often experience difficulties in creating and maintaining friendships and understanding social relationships.[31]

A study by Head and colleagues found that girls on the spectrum scored higher on the Friendship Questionnaire (FQ) than boys on the spectrum, and similar to TD boys. Reports by parents showed that girls on the spectrum had better social skills and were more socially motivated than the boys.[32] A similar study was conducted by Sedgewick and colleagues focusing on the adolescents' motivation for social relationships and their experiences with friends. Again, this study showed that girls with ASD were more socially motivated than the boys as demonstrated by the higher scores on the Social Responsiveness Scale (SRS). Boys with ASD were less concerned with making and maintaining friendships.[31]

Many children with ASD may express themselves and connect with other people through play. Research was done to explore any gender differences during play by Harrop and colleagues. However, no significant differences were found in either play complexity or toy engagement between girls and boys on the spectrum between the ages of 2 years and 4 years 11 months participating in this study. Nonetheless it is possible that differences become apparent later on in development and so more research is needed.[33]

SOCIAL COMMUNICATION

Problems in communication have always been considered as one of the core features of individuals on the spectrum.

One way to assess pragmatic language is through storytelling or narratives measured by The Expression, Reception and Recall Narrative Instrument (ERRNI). Conlon and colleagues conducted a study to investigate possible gender differences in pragmatic communication in a closely-matched sample of 8-year-old boys and girls on the spectrum. Girls told stories which were richer in content and described more salient features of the story and the characters than the boys. Overall, this study suggested that some differences in social communication may exist between girls and boys with ASD and effective tools may be developed to measure these differences.[34]

A study by Kauschke and colleagues was conducted to investigate gender differences in narrative competence and internal state language (ISL) using stories elicited from a wordless picture book. Results showed no significant differences in narrative skills namely story length, coherence and cohesion between girls and boys with ASD and between the ASD group and the control group. However, a difference was found in ISL where girls on the spectrum verbalized characters' internal states and emotions more than the boys on the spectrum.[12]

Literature on gender differences in early social communication shows conflicting results. A study by Reinhardt and colleagues revealed no significant differences in developmental functioning and social communication skills between girls and boys with ASD. However it is possible that gender differences in communication and language become more apparent as children become older and acquire more language skills.[35]

BEHAVIOURAL AND EMOTIONAL PROBLEMS

Different comorbidities are often present in individuals on the autism spectrum and may obscure the clinical presentation.[36] There is literature which indicates that since boys on the spectrum are more likely than girls to show externalizing behaviours which include hyperactivity, aggressive and disruptive behaviours, boys are significantly more likely to be referred by teachers and parents.[21] Girls on the spectrum on the other hand are more likely to show internalizing and emotional problems including anxiety and depression. Nonetheless literature over the years shows inconsistent results about the presence of these behavioural and emotional problems in girls and boys.[28]

These inconsistencies in the literature may be linked with differences in the age and developmental levels of children participating in the study.[36] A meta-analysis by Hull and colleagues found age-related patterns for internalizing and externalizing problems. Therefore the levels of internalizing and externalizing problems in girls and boys became more similar as the children with ASD became older.[37]

Margari and colleagues found high rates of comorbidities in 159 high-functioning children and adolescents including Attention Deficit Hyperactivity Disorder, anxiety, depression, bipolar affective disorder, obsessive-compulsive disorder and anorexia nervosa. Anxiety was found at a high percentage in both sexes but there was no statistical significant difference. Also for the other comorbidities mentioned, except for anorexia nervosa, no statistical significant differences were found between girls and boys on the spectrum.[38]

DISCUSSION

Seven key themes on gender differences in autism emerged from this review of literature since 2012. These findings should be interpreted with caution and a number of limitations should be borne in mind. In this study only one database, PubMed, was used to identify potential eligible studies. Also most studies included have relied on the ADOS and ADI-R for diagnosis of autism, even though these instruments are thought to be male-biased themselves. Another limitation was that several of the studies included were underpowered in terms of number of female participants. Future studies should aim to include more females in order to draw stronger and more consistent conclusions.

The most common theme mentioned was the possibility that current diagnostic assessments are not sensitive enough to diagnose females on the spectrum. Since most of the research conducted on autism has included mostly or only male participants, this may have created a male-biased understanding of autism and assessment tools which are themselves gender biased.[5, 10, 14] It is also possible that the DSM diagnostic criteria we use describe symptoms mostly manifested in males but not in females. Even though females were included in the DSM-IV field trials, all participants had already been diagnosed with autism and were recruited from clinical settings. Therefore the

females in the samples may not be representative of females on the spectrum in general.[14]

Increasingly, literature is showing that girls may be missed diagnostically unless they present with additional problems, mainly behavioral or intellectual problems.[39] In fact females may need to exceed a higher threshold of severity than the males to receive a correct diagnosis of autism.[14, 20]

Early identification and accurate screening of autism is an essential clinical priority since early treatment and intervention are becoming increasingly linked to better outcomes for these children. Attwood et al. developed a Questionnaire for Autism Spectrum Conditions (Q-ASC) which includes characteristics which are potentially unique to females on the spectrum in the areas of play, friendships, social situations, interests and sensory profiles.[40] Ormond and colleagues piloted this questionnaire and results showed significant gender differences. Parents reported more sensory sensitivity, social masking, imitation skills, use of imagination and certain interests in girls when compared to boys.[22]

Another interesting theme which emerged from this review of literature is the female camouflage effect where females on the spectrum possibly try to mask certain autistic symptoms to try and fit better in social situations.[18] However this concept of 'masking' or 'camouflaging' was recently debated by Lawson and colleagues (in press) where they argue that these terms can be misleading since they can imply an intent to deceive and cheat deliberately. Their argument is that 'masking' may be a misleading term as it implies deliberate deception, when in reality trying to

stay safe may mean the need for camouflage. This need is a strategy to survive which is nurtured over many years. In fact, individuals on the spectrum may cover up aspects of themselves which they want to keep hidden. Sometimes this may be done subconsciously and at other times intentionally, however the intent would not be to deceive. These strategies used by individuals on the spectrum to feel safe and adapt themselves to certain social situations can be compared to the behavior of chameleons which can change their color to match their surroundings. Like in chameleons, individuals with ASD make use of this state of 'adaptive morphing' in order to fit into social settings.[41]

CONCLUSION

Despite several inconsistencies in the literature, seven main themes on gender differences in autism were found in this descriptive review of literature since 2012.

Since the majority of research on autism includes mostly or exclusively males, not much is known about females with autism and as a result females may be missed or misdiagnosed. Many autistic female self-advocates talk about the importance of accurate and early diagnosis. As a result, future research should focus on including larger numbers of females in studies and developing instruments which are better adapted and fit to identify and diagnose the female phenotype of autism.[16] More research is needed to provide a comparison between girls and boys on the spectrum and typically developing children to improve services and resources available and better understand the specific needs of females on the spectrum.

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