Autism in Women

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KEYWORDS

• Female autism • Autism spectrum disorder • Sex differences • Male bias

KEY POINTS

- Autism has long been considered a predominantly male disorder, which may affect identification and diagnosis of women on the spectrum.
- Women with autism may have differences in autism spectrum disorder (ASD) symptom expression compared to men due to social and biological differences and therefore not follow the prototypical male profile of ASD symptoms.
- Women on the spectrum have a unique profile with often more subtle presentations, greater number of co-occurring conditions and later diagnosis, resulting in less access to interventions and support.
- We recommend that clinicians have a higher index of suspicion for ASD in women and provide referrals for psychological diagnostic evaluations, to help support their clinical needs.

According to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition classification, autism spectrum disorder (ASD) is a set of behaviorally defined brain-based conditions characterized by social communication impairments and restricted repetitive patterns of interest and behavior (RRBs).[1] ASD is a heterogeneous condition with a wide range of cognitive abilities from intellectual disability (ID) to giftedness, core language abilities from typical or advanced to nonverbal, and motor coordination abilities from typical to motor apraxia. ASD is frequently accompanied by medical and mental health comorbidities such as epilepsy, feeding disorders, constipation, attention-deficit hyperactivity disorder (ADHD), anxiety, and depression, which have the potential to influence ASD presentations. ASD has been reported as more prevalent in men than women since originally described.[2,3] Importantly, the wide variation in symptom expression of ASD and nature of a behavior-defined condition without biomarkers creates diagnostic and treatment challenges, resulting in lower identification and access to services groups with less prototypical autism presentations, particularly for women.

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In recent decades, there has been a steady increase in the prevalence of ASD in the United States and the rest of the world.[4,5] Over a hundred genes have been identified in the expression of autism,[6] but no evidence suggests that autism should be more prevalent in specific racial or ethnic groups. The most recent composite Autism and Developmental Disabilities Monitoring Network prevalence estimate (1.85%), using 2016 data, was higher than the previous estimate (1.68%) found using 2014 data.[7] This increased prevalence has led to an explosion of research on autism, ranging from basic science to applied clinical studies. This research has led to more clearly defined diagnostic criteria, better and more systematic diagnostic tools, and broadening of the autism spectrum to include individuals with presentations of high functioning mild ASD and moderate-to-severe ID. The explanation for the global increase in the ASD prevalence is multi-factorial and includes these recent diagnostic changes as well as a significant increase in public and professional awareness and the number of clinicians with expertise in autism diagnosis.

The male-to-female ASD ratio has been reported to be 4 to 5:1 in population prevalence review studies.[8,9] However, the first ASD patient databases and research studies overrepresented men,[10–12] influencing the development of the diagnostic tools and criteria that are used today. The overrepresentation of men in research has reinforced a male bias in the public and even health and school professionals' perception of this condition.[13,14] As discussed in this paper, women with autism can have a different, more subtle, clinical presentation as they may compensate better for their social communication impairments and present with less unusual and intense RRBs.[15,16] As a result, women often have a delayed or missed ASD diagnosis, further increasing the burden of this condition by delaying a diagnostic label that promotes better understanding of ASD-related challenges, reducing access to treatment services, and perpetuating the prevalence gap between men and women. More recent population review studies, which only include studies using high methodological quality with active case ascertainment methods, found lower male-to-female ratios of 3:1[14] or 2.5:1.5 The studies that actively looked for ASD cases, regardless of whether they had already been identified by clinical or educational services, found a lower male-to-female odds ratio of 3.25. The passive studies, which only identify cases that have already been diagnosed, have a larger male-to-female odds ratio of 4.56.[14] One possible explanation for these findings is that there are women in the general population who would meet diagnostic criteria for this condition if evaluated, yet have not been identified due to their unique clinical presentation and the male bias in ASD. These changing ratios may also reflect the broadening of ASD diagnostic criteria over time, allowing more high-functioning women to be identified[17] as well as increasing community awareness and the public health response.[5]

When discussing ASD in females, both biological and sociocultural factors should be considered.[18] Although biological sex is understood as a trait assigned at birth, gender socialization also begins at birth,[19] making it difficult to separate the effects of sex and gender on ASD presentation. Moreover, children typically form their own gender identity between the ages of 3 and 5, meaning that they begin noticing gender socialization and stereotypes in their immediate social contexts at a young age.[19] Importantly, for some children, their gender identity may not match how they are treated and perceived by others. There is very limited research on the effects of biological sex and gender identity on ASD symptoms as separate constructs, or on how ASD symptoms may present in children who fall outside of the "male" and "female" binary. As such, given the scope of this paper, our discussion focuses primarily on individuals who were assigned female sex at birth and who have been socialized to

present as female in their sociocultural environments while acknowledging that this is a relatively limited discussion of these concepts. In research cited in this review paper, we describe sex and gender based on how it is reported, including for girls/boys (age 0 to 17) and women/men (age 18 or older). However, studies may have varied in how sex and/or gender was assessed.

The objective of this article is to increase awareness of the male bias in autism and unique sex/gender clinical presentations that contribute to women having a delayed or missed ASD diagnosis. Biological and sociocultural factors contributing to the male/female gap in autism will be explored. Finally, the importance of a timely diagnosis in women is discussed as well as strategies that clinicians can use to promote earlier identification and access to treatment of women with ASD.

NEUROBIOLOGICAL FACTORS

Sex differences in autism provide an opportunity to study causal mechanisms and etiologic models for this heterogeneous condition. At the biological level, sex differentiation originates from the interplay of genetic variations, prenatal environments, and epigenetic effects,[20] all of which are candidate mechanisms for the sex-differential liability of autism.[17,21] The main theoretic models that attempt to explain sexual dimorphism in ASD and the evidence supporting them are presented in this section. These models are unable to explain all sex characteristics and differences and can be seen as complementary to each other.

Extreme Male Brain Theory

The extreme male brain (EMB) theory is an extension of the empathizing-systemizing (E-S) theory of typical sex differences.[22] The E-S theory proposes that, on average, women have a stronger drive to empathize (ie, identify and respond to another person's mental state), whereas men have a stronger drive to systemize (ie, analyze or build a rule-based system). According to the EMB theory, men and women with ASD manifest an extreme profile of the typical male E-S dimensions and a more "masculine" brain type.[23] Further, men may need smaller psychological and physiologic changes to present with ASD than women, potentially explaining sex differences in prevalence rates.

Neuroimaging studies identifying anatomic and functional "male brain" patterns in men and women with ASD provide support for this theory. Infant males on average have a larger brain than females[24] and children with autism tend to have even larger brains early in life.[25] The amygdala in typical control (TC) men tends to be larger than in TC females.[26] Males and female toddlers with ASD have a larger amygdala than TC males.[27] Ypma and colleagues,[28] identified the "male brain" pattern using resting-state functional connectivity, in which TC females had an increased DMN connectivity compared with control males and all study participants with ASD. A functional brain connectivity study demonstrated that women and men with ASD tended to follow the typical male pattern of developmental changes in interhemispheric connectivity.[29]

Steroid hormones and their receptors can act as epigenetic fetal programming influences on early brain development. Through their nuclear hormone receptors, steroids can alter gene expression via direct or indirect influence on multiple epigenetic processes.[30] Animal studies have confirmed that early exposure to androgens (eg, testosterone) has a long-lasting impact in the developing brain, causing sex differences in its anatomy and function and leading to differences in cognition and behavior.[31] Human men present three surges of testosterone levels during life:

between 8 to 24 weeks of gestation reaching puberty levels,[32] soon after birth until 4 to 6 months of age when testosterone levels become undetectable,[33] and puberty. The sex differences in fetal androgen levels have been well documented through amniotic fluid studies.[34] In the Danish Historic Birth cohort study of amniotic fluid samples, increased testosterone and other steroidogenic activity was demonstrated during fetal development for men that were later diagnosed with ASD.[35] Another study found that boys and girls who had been exposed to high levels of testosterone in utero had social, communication, and play patterns commonly associated with ASD.[36]

Female Protective Effect

The multiple threshold liability or female protective model states that multiple genetic factors contribute to the presence of ASD, resulting in a higher genetic threshold for women to manifest ASD relative to men.[37–39] The fact that men show higher rates of ASD than women,[37] and the greater risk of ASD for siblings and co-twins of women with ASD than siblings and co-twins of men with ASD[37,40] supports this theory.

Neuroimaging studies show greater changes in brain anatomy and function among women with ASD compared with female TCs relative to men with similar levels of ASD compared with male TCs. A study using diffusion tensor imaging found that girls and young women with ASD showed white matter (WM) integrity reductions in a distributed network compared with female TCs, whereas no WM integrity differences were found between boys and young men with ASD and without ASD.[41] Deng & Wang[42] analyzed a selective high-quality data subset from an open data resource showing that TC men have a more leftward brain asymmetry than TC women.[42] This study found that girls and young women with ASD presented with more leftward gray matter brain asymmetry compared with girls and young women TCs, whereas there was no difference between boys and young men with ASD and TCs. This interaction pattern is supportive of the female protective effect (FPE) theory by showing greater gray matter changes in women with ASD compared with men with ASD.

Gender Incoherence Theory

The gender incoherence (GI) theory suggests that ASD is associated with androgynous features in both men and women.[43] This theory was originally supported by a study examining serum hormone levels and anthropometry measures supposedly related to androgen influence among 50 adult men and women with ASD and age- and sex-matched TCs.[43] Women with ASD had higher testosterone levels, less feminine facial features, and a larger head circumference than female TCs. Men in the ASD group were found to have similar testosterone levels as TCs yet had less masculine body characteristics (ie, higher 2D:4D ratio on the right hand and a nonsignificant trend for larger head circumference compared with male controls) and voice quality. In the total sample, androgynous facial features were also found to correlate well with ASD traits (measured with the Autism-Spectrum Quotient).

Neuroimaging research studying the relation among ASD, sex, and brain measurements has supported the GI theory by finding a shift toward masculinization patterns in the brains of women with ASD and shift toward feminization patterns in the brains of men with ASD. In a pattern consistent with the GI hypothesis, one study of amygdala connectivity found that ASD is associated with attenuated sex differences in amygdala connectivity.[44] Other studies have found single side GI (ie, shift toward masculinization or shift toward feminization).[45,46]

Sexual dimorphism has been strongly connected to sex steroids exerting permanent organizational effects prenatally and transient activating effects later in life.[47] Sexual differentiation and sexual steroid levels have an important evolutionary

role. They affect mating behaviors by influencing male/female physical characteristics.[48] Sexual steroids appear to regulate social recognition, social imitation, nonverbal communication, and social reciprocity and mating behavior through its influence on the development of neuronal circuits. All these social communication functions are affected in ASD.[43] Vasopressin and oxytocin, which are influenced by sex steroids and display sexual dimorphism, have received attention due to their impact in social behaviors.[49] Both have been implicated in the biology of ASD.[50,51]

The theories presented here only partially explain sex differences in ASD. Neuroimaging studies demonstrate that some aspects of typical sex differences in brain structure are preserved in individuals with ASD, whereas others are not. Further, although some neuroimaging findings are supportive of these theories, others are inconsistent, do not support the theories, or are supportive of more than one model.[44,45]

CULTURAL AND SOCIAL FACTORS

In addition to the biological factors that may impact the expression of autism symptoms in women, there are also many social and cultural influences. Although children with large developmental delays may be raised with unique developmental expectations, children with autism without large delays are raised under the same social norms as their developmental peers. Children tend to self-segregate by gender, creating distinct social norms.[19] Furthering this distinction, caregivers typically vary their language by their child's sex, resulting in different developmental outcomes.[52] For example, caregivers of girls are more likely to use social language, label emotions, and discuss emotions than caregivers of boys.[53] Mothers of daughters are more likely to increase their vocalizations with their child across development than mothers of sons, resulting in greater vocalizations among daughters.[54] Further, stereotypical "female" toys in early childhood (eg, kitchen sets, dolls), encourage creative and imaginative play and promote modeling of this play by adults and other children interacting with the child.[52,55] Taken together, girls with ASD who do not have notable cognitive delays may have more socialization in activities that tend to attenuate the appearance of "classic" autism symptoms.

The social expectations typically placed on women may also carry stressors in later childhood, adolescence, and adulthood.[56] Social demands and expectations increase throughout development. Interestingly, traditional male friendships are centered largely around activities (eg, attending concerts, sports games, playing video games) and traditional female friendships are centered largely around the exchange of personal information and emotional support.[19] There is a higher requirement of social skills for these female friendships.[57] Therefore, although women with ASD may have more social skill support in early childhood, they also require higher-level social skills to form and maintain friendships into adolescence and adulthood.[56] Additionally, as social awareness increases during adolescence, many young women with ASD begin to recognize and report feelings of "otherness" and difference from their typically developing peers.[58,59]

Emerging research has found that many individuals with ASD engage in "camouflaging" or behaviors that are intended to mask the features of ASD in social situations (ie, social communication differences and repetitive behaviors).[60] Camouflaging is motivated by the desire to connect with others, avoid rejection, and assimilate through strategies such as deliberately copying others' body language and facial expressions, mimicking others' speech patterns, and suppressing repetitive body movements.[60] Although camouflaging is not unique to women with ASD, women report using camouflaging from an earlier age, across more situations, and more frequently than do men.[61] The increased social demands placed on women may lead to increased use

of camouflaging techniques, and greater stress and feelings of overwhelm within social interactions. Regardless of sex, use of camouflaging among adults with ASD is associated with higher self-reported symptoms of generalized anxiety, social anxiety, and depression.[62]

An additional component of social and cultural factors is the clinical interpretation of ASD symptoms by caregivers, teachers, and clinicians participating in developmental screening.[63] Autism symptoms in girls and women may not raise concerns about this condition due to the raters' reliance on gender stereotypes and a male biased understanding of ASD. For example, social withdrawal may be interpreted as shyness in a female but be considered a red flag for ASD in a male. In preschoolers with ASD, parents and teachers reported greater pre-diagnostic concerns about these conditions in boys than in girls.[64]

COMORBIDITIES

ASD is a heterogenous condition. Twin studies have suggested that autism has high heritability (more than 80%).[65] Given that the monozygotic concordance rates are never 100%, this heritability occurs in the context of environmental risks and gene–environment interplay.[66] Genetic testing is recommended to individuals with an ASD diagnosis to investigate potential causes of autism. ASD has a range of medical comorbidities that are observed at higher rates than in the general population and have significant developmental, psychological, and physical health sequela. These include higher rates of genetic (eg, Down syndrome, Fragile X syndrome), neurologic (eg, epilepsy, cerebral palsy, macrocephaly), gastrointestinal (eg, chronic constipation, gastroesophageal reflux), sleep (eg, insomnia), metabolic, and allergic (eg, asthma) disorders.[67,68] Approximately 12% to 20% of individuals with ASD may have a diagnosis of epilepsy.[69,70] Epilepsy onset in autism typically occurs during infancy or adolescence and is associated with developmental regression in approximately 25% of cases (eg, Landau-Kleffner syndrome[69]).[69] Emerging research is investigating shared environmental and genetic causes between these two conditions. For example, the *excitation-inhibition balance theory* purports that dysfunction of excitatory and inhibitory circuits in various brain regions may contribute to shared developmental mechanisms.[71] Although it has long been known that individuals with ASD frequently experience sensory sensitivities that impact eating behaviors, there is growing research on unique gastrointestinal physiology within the gut-brain axis among individuals with ASD. For example, mechanisms such as altered feeding behaviors, reduced gut permeability, and increased biodiversity of the gut microbiome, may lead to the onset of GI symptoms such as chronic diarrhea, constipation, abdominal pain, and gastroesophageal reflux.[72]

Although additional research on sex differences in medical comorbidities is needed, there is growing evidence that women have higher rates of epilepsy, metabolic disorders, endocrine/reproductive health disorders (eg, irregular puberty onset), gastrointestinal disorders, and sleep disorders compared with men with ASD and women without ASD.[73–76] Overall, these findings suggest that women with ASD are more likely to have poorer health outcomes, perhaps due to their higher genetic load leading to co-morbid disorders. Research investigating sex/gender differences in medical comorbidities and the biological basis for ASD and its common comorbidities may lead to novel treatments that reduce symptoms or even prevent comorbidities from developing.

ID was previously reported as being present in approximately 70% of ASD cases and has more recently been reported as being present in 30% of cases.[77] This changing rate no doubt reflects the recent broadening of the autism spectrum to include individuals

with higher cognitive functioning; even so, the more recent prevalence rate may be an underestimate given that intellectually disabled individuals are under-included in ASD research. Relatedly, women have been identified as having higher rates of co-occurring ID than men.[8] Yet again, it is unclear whether this reflects an ascertainment bias in research in which women with typical or above intellectual functioning are under-represented as opposed to a true difference in rates of ID across sex and gender.[17,78]

One meta-analysis estimating the prevalence of comorbid mental health disorders in ASD across the lifespan found higher rates of comorbidities among individuals with ASD than in the general population.[79] The eight most common comorbid mental health diagnoses included ADHD (28%), anxiety disorders (20%), sleep-wake disorders (13%), disruptive/impulse control/conduct disorders (12%), depressive disorders (11%), obsessive-compulsive disorder (9%), bipolar disorders (5%), and schizophrenia spectrum disorders (4%). On average, women with ASD have been found to have higher rates of comorbid mental health symptoms and diagnoses than men, particularly for anxiety, depression, disordered eating, and borderline personality disorder.[79–82] One study found that having a former or initial diagnosis of anxiety or ADHD delays a more appropriate diagnosis of ASD, with a stronger effect for women.[83] Mood or anxiety difficulties, which are more common among women than men in the general population, may be normalized among women, preventing an in-depth investigation of social communication deficits contributing to emotional challenges. Another study found that over one-third of individuals with ASD (47% of women and 27% of men) in the Netherlands Autism Register had one previous mental health diagnosis removed after receiving a diagnosis of ASD,[81] suggesting that earlier diagnoses represented a missed or delayed ASD diagnosis and even more so for women. The overall higher rates of mental health comorbidities among women with ASD can be interpreted as reflecting a truly higher risk for comorbidity, the many barriers that women face to receiving an accurate ASD diagnosis, and/or a greater mental health burden experienced among women with ASD. Overall, these findings suggest that medical providers who have concerns about female patients' social functioning when several comorbidities are present should consider whether an additional ASD diagnosis may provide a more straightforward and comprehensive explanation of presenting concerns and, consequently, facilitate referrals to assessment services that can establish diagnostic clarity.

SEX DIFFERENCES IN CORE SYMPTOM PRESENTATION

A popular quote that has been attributed to autism self-advocate, Dr Stephen Shore, summarizes the heterogeneity within ASD well: "If you've met one person with autism, you've met one person with autism." Although core symptom criteria include social communication deficits and RRBIs, ASD presentations fall across a broad spectrum that ranges from very mild to severe. Further, even though sex differences in symptom presentations are often present, these differences represent averages, and it is unclear whether the range of symptoms on the spectrum varies across sex/gender. Relatedly, given individual differences in ASD expression, there is no simple sex dichotomy in ASD presentation nor a "female autism phenotype" that can be used to form diagnoses.[13] Sex differences in core ASD symptoms are described below.

Social Communication and Social Interaction

Studies of social communication differences are often confounded by study samples that underrepresent women, and by variations in intelligence or language ability.[84] Given the nuances and complexities of social communication, it is imperative to account for cognitive variability. For example, when intellectual functioning was matched

in a sample of adolescents with ASD, sex variations in specific social language components were observed.[85] This study's findings suggested small but consistent differences in which women with ASD demonstrated deficits in social communication skills when compared with TC women, but outperformed men with ASD.[85] Of interest, there were some skills, such as use and knowledge of emotional vocabulary, in which women with and without ASD demonstrated equitable skills (both above men), suggesting that there may be some skills preserved by sex.[85] These small differences may have real impacts on children with autism. In unstructured conversations, women with ASD often make more positive first impressions on others than do men.[86] Further, word choices can have an impact on diagnostics. Cola and colleagues, 2022[87] found specific word choices in verbally fluent children were related to their scores on the diagnostic assessment, the Autism Diagnostic Observation Schedule, Second Edition (ADOS-2).[87] Girls used more "socially-focused" words, specifically regarding friends, than boys despite the samples being matched for intellectual functioning and autism symptom severity. Further, use of these words corresponded to greater ratings of social communication skills. Therefore, equal levels of clinician- and parent-rated autism severity may result in different scores on diagnostic assessments due to sex differences in language use.

Interestingly, when studies use parent-report of social communication and social interaction, they often find no major sex differences.[88,89] However, sex-specific social communication profiles may be more subtle than what can be captured in parent-report measures.

Women with ASD may present as less socially impaired due to their higher social communication abilities. Relative to men with ASD, women with ASD have been shown to have greater expressive social behaviors (eg, reciprocal conversation, sharing of information), more friends, participate in more social groups, and be more aware of exclusion and take steps to reduce exclusion (eg, camouflaging[13,64]).[13,64] Despite having more friendships, women with ASD have been shown to have unique social difficulties relative to men. For example, women may be more skilled in initiating relationships but have difficulty maintaining them or be more likely to experience subtle peer rejection that is poorly understood.[64,90]

Restricted and Repetitive Behaviors

RRBs can include repetitive or unusual motor movements as well as an intense interest in topics or items that range from typical child interests (eg, trains, animals) to atypical interests (eg, patent numbers, flags from around the world). Although there are many facets of RRBs, sex differences are not consistently found in self- or parent-reported number of circumscribed interests (CI). In their review, van Wijngaarden-Cremers and colleagues[78] found that women have lower rates of RRBs and interests.[78] However, the specific topics of CI may vary by sex.[88] CIs may be the most informative RRB to consider as they are more specific to autism and corresponded to eye tracking measures of attention, detail focus and perseveration.[16] Women on the spectrum have been described as having more "random" CIs[64] and thus have less interest associated with the prototypical autism or queried in traditional autism assessments.[64]

Parents often report that, relative to sons on the spectrum, daughters on the spectrum have CIs that are more in line with typically developing peers and that these interests are often associated with positive social interactions.[15,64,91] For example, a girl with ASD may have CIs that are viewed as a common interest for her peer group (eg, pop music band). She may share this interest with her friends, plan social events to watch the band play, or even form a club or online group surrounding the band.

Although this interest is more intense and encompassing than it would be for typically developing girls, she can use it to seek connection socially and thus experience less social impairment as a result of her RRBs than her male counterparts (eg, boy who repetitively talks about airplanes).

Of interest, in some studies, parents report sex differences in repetitive behaviors that are not corroborated by teachers.[89] This may suggest some evidence of female camouflaging of more obvious autism symptom behaviors when outside of the home.[88]

DIAGNOSTIC CHALLENGES

The sex/gender gap between the studies using high methodological quality with active case ascertainment methods and passive methodology studies suggests an underrecognition of ASD in women. A predictive model based on population data estimated that 39% more women should be diagnosed with ASD.[92] Some have suggested that many of the tools designed to assess ASD may not be sensitive enough to capture a female autism presentation and as a result require women to reach a higher diagnostic threshold.[17] However, recent research found that men and women may not vary on their autism severity scores on gold standard measures (eg, ADOS-2[93]) [93] with only small differences when differences are observed.[94] This may suggest that the current diagnostic measures are appropriate for identifying autism in women, when women are referred for evaluation, highlighting the importance of timely evaluation referrals. For additional information on tools that medical providers can use to screen for ASD across the lifespan, see Allison and colleagues[95] and Sappok and colleagues.[96]

IMPORTANCE OF TIMELY DIAGNOSIS

The importance of timely ASD diagnosis is particularly relevant to women. As with any medical condition, timely diagnosis can result in more positive outcomes and reduce the burden caused by a condition. Perhaps most importantly, earlier diagnosis leads to earlier intervention. A meta-analysis investigating improvements in social communication outcomes in children with ASD found that interventions delivered between three and 4 years of age had the largest positive impact on child development, with intervention effectiveness reducing by age eight.[97] Further, social communication skills in infancy predict social skills in middle childhood,[98] highlighting the importance of early intervention for improving outcomes throughout development. Timely diagnosis also allows caregivers to develop effective strategies for managing their child's unique challenges.[99] When an ASD diagnosis is made later in development, it can provide individuals with an increased understanding of their experiences as well as relief that their challenges are not the result of personal failures but instead the unique way in which their brain works. Further, diagnosis empowers individuals to seek appropriate medical treatments (eg, psychotherapy, psychopharmacology) and join community organizations in which they can share their experiences with similar individuals and obtain crucial social support, strategies, and resources.

The harm of late diagnosis for women is significant. Women who receive a later diagnosis describe being labeled as "shy," "rude," and "lazy" throughout their childhood and an emotional and physical toll from years of trying to "appear normal" by masking, compensating, and imitating "neurotypical" social behaviors.[58] Further, given these women's, as well as their families', teachers', and peers', poor understanding of the source of their social challenges, they report persistent social rejection, reduced educational or career obtainment, and elevated rates of victimization including bullying and sexual abuse. The importance of the diagnosis of ASD among

women is highlighted and discussed in detail in Bargiela and colleagues,[58] and Leedham and colleagues.[59]

SPECIFIC SUPPORT FOR WOMEN ON THE SPECTRUM

Although all individuals with ASD generally benefit from support in developing social communication skills, specific treatment recommendations should be informed by the individual's needs. Standard supports often include recommendations for applied behavior analysis (ABA) to target adaptive skill development in young children or cognitive behavior therapy (CBT) for verbally fluent individuals who want to address social challenges, anxiety, and depression, among other needs. Group therapies are often the default for support with social communication skills given that they provide a social context in which to practice social skills. Although there is limited research on health service use, no major sex differences have been found. Nevertheless, a survey of service use in adolescent girls indicated that they use more psychiatry and general emergency room services than do boys.[100] The greater reliance on emergency room services may imply that women with ASD are not having their needs met in routine care and thus do not seek services until difficulties reach the level of a crisis. Additionally, the greater proportion of women in psychiatric care may speak to the higher rates of mental health comorbidities among women with ASD.

In addition to most social skills groups being developed for the prototypical expression of autism, which may better support the needs of men with ASD, these groups will have a predominately male membership, due to the nature of recruitment. For some women, the lack of other women may not be an issue. However, there may still be benefits in having other women in a group, especially for topics related to social skills such as dating, sexual activity, and consent. A more gender-balanced group could offer advantages to all group members to generalize social skills practice and to discuss differences if and as they arise.

General. Clinicians could consider offering a female-specific social skill group which may delve into topics more relevant for women or somewhat gender-specific, such as social expectations, later diagnosis, and a discussion of use, limitations and risks of camouflaging behaviors.

Although not specific to woman, there are additional areas that are common needs for those on the spectrum that should continue to be considered for teens and adults on the spectrum. These include but are not limited to how and when to disclose an ASD diagnosis, sexual and gender identity, general dating and navigating preferences in sexual preferences, and contraception. Some individuals may be more comfortable discussing these topics in a single-sex social group, which could be considered in recruiting and forming appropriate clinical groups.

Comorbid mental health conditions. Women with ASD are likely to have one or more co-occurring condition(s).[101] Therefore, interventions focused on social challenges as well as comorbidities may be more helpful for women with autism. Social skill groups have been found to improve social skills among individuals with ASD and anxiety, yet less so for people with ASD and ADHD.[102,103] Psychopharmacology can be used as an adjunct to psychological interventions to address conditions like anxiety, depression, and ADHD, leading to significant improvements in developmental trajectories and functioning.

Intellectual functioning. Women with intellectual disabilities or other cognitive impairments are more likely to have increased RRBs and a more similar expression of autism to their male peers. For these women, gender-specific supports may be less imperative.

Support for medical testing. One final consideration for clinicians when seeing women on the spectrum should be genetic testing as recommended by the American Academy of Genetics and the American Academy of Pediatric Neurology.

SUMMARY

The active ascertainment population studies have identified a higher proportion of women with ASD (2.5 to 3:1)[14] than was previously documented with passive studies (4 to 5:1).[8,9] The public and often medical professional's male-biased understanding of ASD makes it less likely for parents and caregivers to appropriately identify signs of ASD in women and seek timely evaluations. The male bias in ASD extends to diagnostic criteria and tools, which have developed based on nearly a century of research predominantly focused on men. There is evidence that even clinicians specialized in ASD are more hesitant to diagnose women with ASD than men with similar presentations. However, in the last few years, there is increased awareness of ASD in women and their participation in research has increased.

Women with ASD often have a missed or delayed diagnosis, which increases the burden of this condition by delaying and preventing access to services, leading to less desirable developmental trajectories. Relative to the "prototypical" ASD that is more aligned with a male presentation, the clinical presentation of women is often characterized by more subtle social communication deficits, less intense and unusual RRBs, and the presence of compensatory mechanisms (eg, camouflaging) that may mask otherwise noticeable ASD symptoms. The frequent presence of mental health comorbidities (eg, ADHD, anxiety, depression) also contribute to diagnostic delays and misdiagnosis as well as highlight the heightened emotional challenges experiences by women on the spectrum.

Below are a set of strategies clinicians may use to better support female patients for whom they have concerns about a possible ASD diagnosis.

CLINICS CARE POINTS

- When possible, gather self- and collateral-report (eg, parents and romantic partner) of social functioning. Women with autism spectrum disorder (ASD) may use compensatory strategies (eg, mimicking others' facial expressions, using social language in an appropriate yet scripted manner) at the time of the evaluation that masks their social communication differences.
- Explicitly ask women if they use camouflaging strategies in their daily social interactions. As examples, ask whether women deliberately copy others' body language in conversation, force themselves to make eye contact despite intense discomfort or distress, or actively suppress repetitive finger, hand, or body movements.
- When considering whether signs of ASD are present, including social communication difficulties and restricted and repetitive behaviors (RRBs), mentally compare women with typically developing women, not with expectations of ASD.
- Consider the quality of play and other social skills in girls. If developmental social milestones are "met," inquire about whether these skills appear as frequently and flexibly used as when they are observed in typically developing children (ie, across people, contexts, and objects). Follow up with parents about the details of each skill. For example, girls may have more "character toys" to play with but will still demonstrate repetitive play and language.
- When inquiring about RRBs, provide parents with examples across typically gendered activities, such as "Does your child line up trains or dolls?" or "Is she more interested than others in dinosaurs or boybands?" to prompt parents to think more inclusively when

answering. Even when interests appear developmentally appropriate, consider their quality and intensity.

- Given the high rates of co-occurring diagnoses and the increased risk of miss-diagnosis among women, consider whether ASD provides a more straightforward and comprehensive explanation in complex cases with multiple mental health comorbidities.
- To ensure comprehensive care, provide psychiatry referrals to evaluate and treat mental health comorbidities.
- When in doubt, use standardized tools for ASD screening that are less prone to subjective biases about ASD symptoms. See Allison and colleagues[95] and Sappok and colleagues[96] for ASD screening tools that can be used across the lifespan.
- Provide women with identified social communication deficits and/or RRBs with referrals to evaluators with expertise in working with women on the spectrum.

DISCLOSURE

All authors declare that they have no conflicts of interest.

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