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Sex/Gender Phenotypes and the Diagnosis and Treatment of Autism Spectrum Disorder: Implications for Applied Behavior Analysts

Bryan J. Blair[1] · Sam Blanco[2,3] · Fernande Ikombo-Deguenon[3] · Alyssa Belcastro[1]

Abstract

Research has consistently reported a higher rate of autism spectrum disorder (ASD) diagnoses in males than in females, but until recently, the impact of sex/gender differences has received little attention from applied behavior analysts. The underlying reasons for the difference in rates of diagnosis could be related to genetic or hormonal differences, sociocultural expectations of behavior based on sex/gender norms, or biases built into the assessment and observation of ASD symptoms. It is necessary to engage in further discussion and research in order to improve the treatment and quality of life of persons with ASD because misdiagnosis or late diagnosis can delay the start of early intervention and limit its proven benefits. Furthermore, differences in symptom presentation can impact interventions selected. We suggest that applied behavior analysts should be knowledgeable of these issues and the implications they may have on the field of applied behavior analysis in general.

Keywords Applied behavior analysis · Autism spectrum disorder · Diagnosis · Sex/gender

Behavior-change procedures and skill-acquisition protocols based on the principles of applied behavior analysis (ABA) are currently the most empirically supported methods for improving outcomes for people diagnosed with autism spectrum disorder (ASD; Foxx, 2008; Lovaas, 1987; Makrygianni, Gena, Katoudi, & Galanis, 2018; Rosenwasser & Axelrod, 2001). Research has indicated that the earlier a child with ASD receives treatment, the better his or her quality of life becomes (Behavior Analyst Certification Board [BACB], 2014a; Harris & Handleman, 2000; Koegel, Koegel, Ashbaugh, & Bradshaw, 2014; Lovaas, 1987). Early intensive behavioral intervention, based on the principles of ABA, has been shown to produce substantial improvements in language, social skills, and adaptive behaviors in persons diagnosed with ASD (Peters-Scheffer, Didden, Korzilius, & Sturmey, 2011). A diagnosis of ASD opens educational, financial, and, in

some cases, social doors to the person who is diagnosed, as well as his or her family and caretakers. For example, a diagnosis of ASD might result in services that are funded by insurance companies or provide access to a community of parents who are in similar situations. So, any factors that impact diagnosis or access to services are important to consider; one of these factors is the sex/gender of the individual being diagnosed or assessed.

According to a recent report by the Centers for Disease Control and Prevention (CDC) Autism and Developmental Disabilities Monitoring Network, approximately 1 in 59 children are diagnosed with ASD (CDC, 2018), and many studies have reported approximately a 4–5:1 male to female ratio of diagnosis (Lai, Lombardo, Auyeung, Chakrabarti, & Baron-Cohen, 2015). However, some studies have suggested that it is possible that the often-reported 4–5:1 male to female ratio for diagnosis of ASD is not accurate and thus requires further investigation (Lai et al., 2015). As mainstream media coverage continues to improve the general awareness of the public about ASD, and research improves diagnostic tools, assessment methods, and treatment interventions, it is essential that the role of sex/gender differences also be addressed to ensure that applied behavior analysts are using functional and targeted interventions for symptomatic behavioral topographies rather than general diagnostic labels. (Note: Like Lai et al., 2015, we chose to use the dual

✉ Bryan J. Blair
bryan.blair@liu.edu

1 Long Island University - Brooklyn, Room 228, 1 University Plaza, Brooklyn, NY 11201, USA

2 The Sage Colleges–Albany and Comprehensive Behavior Supports, Albany, NY, USA

3 Comprehensive Behavior Supports, Brooklyn, NY, USA

term *sex/gender* given how difficult it is to separate the biological and socially constructed aspects of the definitions of *male* and *female*.)

Given that two thirds of practicing applied behavior analysts currently work with persons diagnosed with ASD (BACB, n.d., 2015), we must accept some responsibility for better educating consumers of our services, including parents and guardians, school psychologists, and teachers, about potential differences in behavioral symptomatology and clinical presentation across sexes/genders by conducting research with those differences in mind and, for those working in school settings, by better identifying students who may benefit from assessment and intervention based on factors related to different phenotypes. Practicing behavior analysts may mistakenly assume that males are more likely to exhibit symptoms of ASD given participant selection biases in published research and the academic and clinical training of practitioners, which might have included more content and experience with males with ASD than with females with ASD. These experiences might result in unintentional biases with regard to the objective identification, assessment, and treatment of challenging behaviors associated with ASD across sex/gender.

The following discussion will address the impact of sex/gender differences in ASD diagnoses on the referral and assessment process and on educational and behavioral outcomes—in particular, the consequences of the underdiagnosis of females with ASD will be examined. In addition, the existence of possible sex/gender-specific phenotypes of ASD will be considered. Finally, given how imperative it is to recognize the sex/gender diagnostic imbalance, specific recommendations will be made for how applied behavior analysts can help improve the referral process for ABA services, continue to learn more about sex/gender differences, and ensure compliance with the BACB's *Professional and Ethical Compliance Code for Behavior Analysts* (BACB, 2014b).

A Brief History of the Diagnosis of ASD

The term *autism* has been included in one form or another in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) since the first edition (APA, 1952), but the diagnostic criteria have changed considerably over the years. In the DSM-5 (APA, 2013), the diagnostic criteria for ASD include "persistent deficits in social communication and social interactions" and "restricted, repetitive patterns of behaviors, interests, or activities" (p. 50). Furthermore, symptoms must be present in early childhood and must "cause clinically significant impairment in social, occupational, or other important areas of current functioning" (APA, 2013, p. 50). Although previous editions of the DSM categorized ASD into separate diagnoses, the DSM-5 was the first edition to differentiate between three different levels of ASD based on severity and

required support. These changes in the definition of autism are critical to the acquisition of appropriate services, especially because the diagnosis of ASD is usually determined by conducting subjective behavioral observations rather than through genetic or neurological testing.

Initially, pediatricians and developmental specialists used the criteria in the DSM to provide an ASD diagnosis (Silverman, 2011). Over time, however, formal assessments were developed to provide a more systematic, effective, and valid protocol for providing a diagnosis. The Autism Diagnostic Interview–Revised (Lord, Rutter, & Le Couteur, 1994) and the Autism Diagnostic Observation Schedule (Lord et al., 1989) are now considered to be the gold standards of assessment instruments for diagnosing ASD (Lai et al., 2015; Silverman, 2011). However, in many cases, physicians still rely on the diagnostic criteria from the DSM-5 when a patient presents with symptoms that might be indicative of ASD in order to characterize the behaviors and skill deficits.

Sex/Gender Bias in the Referral and Diagnostic Process

As stated, it is commonly accepted that the male to female ratio for ASD diagnoses is approximately 4:1 (Lai et al., 2015). One reason that might account for this ratio is that many researchers intentionally selected participants to reflect the accepted ratio given their own training and experience, causing an ascertainment bias as the participant selection in the original published research was substantially biased toward males (Mandy et al., 2012; Werling & Geschwind, 2013), and leading to a further lack of clarity. However, in studies that used a general population sample, the ratio decreases to approximately a 2:1 male to female ratio of diagnosis (Lai et al., 2015).

A second consideration regarding differential diagnoses of ASD across males and females is that the commonly accepted 4–5:1 male to female ratio encompasses *all* levels of ASD. If the severity of symptoms is accounted for, the ratio for Level 3 diagnoses (or more severe cases) of males to females is as low as 1.3:1, whereas for Level 1 diagnoses, the ratio is closer to 8–14:1 (Young, Oreve, & Speranza, 2018). This indicates that current systems for referral, assessment, and diagnosis are possibly failing to capture instances of Level 1 and Level 2 ASD in females, although it is also possible that Level 1 and Level 2 are more prevalent in males. In either case, more research needs to be conducted in this area to ensure that accurate diagnostic tools are available.

Just as diagnostic criteria may have been biased by the male predominance in case studies, assessment tools were also developed and standardized based on a largely male subject population (Lai et al., 2015). Lai et al. (2015), argued that assessment should focus on narrower constructs and a wider

Table 1 DSM-5 Diagnostic Criteria and Behavioral Symptoms of ASD (APA, 2013) by Phenotype (Kopp & Gillberg, 2011; Lai et al., 2015; Young et al., 2018)

DSM Diagnostic Criteria	Male Phenotype Examples	Female Phenotype Examples
A.1. Social-emotional reciprocity	• Less likely to engage in social approach or has an abnormal social approach • Failure to initiate social interactions	• Passive; more likely to be labeled as "shy" • More advanced linguistic skills, especially in early childhood • Social difficulties masked by same-age caretaker in elementary school years
A.2. Deficits in nonverbal communication (e.g., eye contact)	• Total lack of facial expressions and nonverbal communication	• Frequently engages in verbal and nonverbal imitation of peers (might be exhausting for peers)
A.3. Forming relationships	• Difficulty or lack of interest in forming relationships	• Forms new relationships, but unable to maintain relationships • Able to engage in imaginative play, but frequently nonreciprocal, scripted, or controlled
B.1. Stereotypy (includes echolalia)	• Motor stereotypy, lining up objects, echolalia, idiosyncratic phrases	• Similar to males but less likely to engage in lining up objects
B.2. Insistence on sameness	• Extreme distress at small changes, difficulties with transitions, requirements to take same routes or eat same foods	• Similar to males, but more frequently reported • Difficulties with completing daily activities; perfectionist
B.3. Highly restricted, fixated interests	• Activities are less social; restricted interests tend to focus on objects	• Restricted interests tend to focus on animals or people (e.g., pop culture, fashion, horses)
B.4. Hyper- or hypo-reactivity to sensory input	No reported differences in the literature	

range of behavior exemplars in order to accurately assess females. Some researchers have begun the process of revising assessments in order to do just that. For example, Kopp and Gillberg (2011) created a revised and extended version of the validated and widely used Autism Spectrum Screening Questionnaire (ASSQ; Ehlers, Gillberg, & Wing, 1999) that included 18 additional questions intended to capture more symptoms that are specific to the female phenotype of ASD. They compared scores between multiple assessments, including the ASSQ and their revised and extended version, the ASSQ-REV. Although the results were similar across boys and girls with ASD, there were statistical differences, with more girls with ASD reported to have the following items: "has a different voice/speech," has "difficulties in completing daily activities because of compulsory repetitions," "avoids demands," and "interacts mostly with younger children" (Kopp & Gillberg, 2011, p. 2880). The results of this study suggest that standard diagnostic tools have undergone significant revisions and that further refinement of the assessment and diagnostic process is likely to occur as more is learned about the etiology, prevalence, and distribution of ASD.

A final consideration relates to the cultural perceptions of ASD, which is considered to be primarily a male disorder. Some have suggested that ASD might simply be a manifestation of extreme forms of male behavior, possibly related to biological or physiological characteristics of men themselves (Baron-Cohen, 2002). Recent studies have demonstrated that not only are girls diagnosed later than boys but the time between a guardian expressing concern about symptoms and the diagnosis of ASD is longer for girls than for boys (Begeer et al., 2013; Shattuck et al., 2009). It is difficult to pinpoint why this discrepancy in identification and diagnosis exists, but recognizing differences in the topographies or perception of ASD-related behaviors between males and females is a necessary step toward better identifying and assessing individuals who present with clinically relevant challenging behavior or skill deficits.

Sex/Gender Phenotypes of ASD

The possible existence of male and female phenotypes (Table 1) consisting of variations of behaviors associated with ASD (Bargiela, Steward, & Mandy, 2016) is an important development in the contemporary history of the diagnosis, assessment, and treatment of ASD. Anecdotal descriptions of characteristics that may be more common in girls with ASD than in boys with ASD have also been widely documented (Kopp & Gillberg, 2011; Lai et al., 2015; Young et al., 2018), and these differences span the domains within the ASD diagnosis: deficits in social interactions and

communication and restrictive or repetitive patterns of behaviors, interests, or activities (APA, 2013). However, like the diagnostic process itself that categorizes subjective observations of behavioral symptoms into discrete pathologies and levels of severity, the differences between male and female phenotypes of ASD should be considered with caution and with a commitment to analyze this process and minimize subjective biases that may be present.

The documented differences between the male and female phenotypes of ASD appear to be of several types. The first type includes differences in the topographies and modalities of stereotypic behaviors (e.g., motor stereotypy, echolalia, and idiosyncratic phrases), restricted interests, and sensory-related issues (Kopp & Gillberg, 2011; Lai et al., 2015; Young et al., 2018). For example, whereas males might line up or order objects, females tend not to be as likely to line up objects in rows, or whereas males and females diagnosed with ASD both have restricted interests, female interests tend to be focused on animals or people.

Another general category of differences is that females with ASD tend to score considerably higher in assessments of linguistic skills, social deficits for females tend to be camouflaged in elementary school, and females tend to form new relationships more easily than males do (Kopp & Gillberg, 2011; Lai et al., 2015; Young et al., 2018). However, these differences in social skills might also mask other more problematic behaviors, particularly challenging behaviors related to following routines, difficulties with transitions, and challenges related to completing common daily tasks, that might be significant enough to warrant a referral for further assessment and evaluation. Additionally, several researchers have suggested that social deficits related to ASD might be mitigated in young girls because of the social behaviors of typically developing girls in general (Bargiela et al., 2016; Young et al., 2018). Furthermore, Bargiela et al. (2016) hypothesized "that the female tendency to have internalising (e.g., anxiety, depression) but not externalising (e.g., hyperactivity/impulsivity, conduct problems) difficulties is also a risk for non-detection" (p. 3291). This apparent lack of obvious challenging or disruptive behaviors might make the female phenotype appear to be less severe, even if covert behaviors (e.g., thoughts) are possibly as serious. A third difference that is commonly observed is that females diagnosed with ASD tend to not be diagnosed with a developmental disability, thus possibly masking other symptoms or mitigating their effects in certain settings (e.g., school) even if challenges are present in other settings such as at home or in the community (Young et al., 2018). ASD in males might be diagnosed at higher rates because of comorbid developmental disabilities that can exacerbate symptoms associated with ASD. For example, males who are diagnosed with ASD who are also diagnosed with other developmental disabilities, particularly intellectual disabilities related to communication or daily living skills, might

engage in higher rates or intensities of dangerous behaviors relative to females who are diagnosed with ASD because of the additional challenges related to accessing preferred and necessary stimuli and social interactions.

Finally, differences related to differential referral and diagnostic rates might be due in part to the severity of the behaviors themselves. It has been documented that behavior exhibited by females might need to surpass a higher threshold of relative severity than behavior exhibited by males to receive a diagnosis (Kreiser & White, 2014). As a result, females are at a higher risk of going undiagnosed when presenting with more moderate symptoms even if the behaviors present similar challenges. Research has suggested that women who received diagnoses late in life frequently reported that an attempt was made to obtain a diagnosis earlier in life; however, because their symptoms presented differently than the typical topographies and severities associated with males with ASD, they did not receive the diagnosis (Baldwin & Costley, 2016; Bargiela et al., 2016). And, in some cases, women have reported being misdiagnosed with clinical disorders, such as multiple personality disorder or depression, or being overlooked due to their symptoms presenting as shyness or other social characteristics that are considered to be more socially acceptable for typically developing females (Bargiela et al., 2016). When all of these differences are considered, the reasons that females are not diagnosed with ASD as often as males become more obvious.

Discussion

Applied behavior analysts are trained to identify the functional relations among behaviors and environmental stimuli. For challenging behavior, behavior analysts attempt to identify the environmental origins and controlling variables for the behavior itself. When teaching new skills, ABA practitioners are primarily concerned with how they can arrange the environment in ways that maximize the functional outcomes for individual learners. In most cases, diagnoses are not the most relevant factors when we decide how to develop and implement interventions or systems of supports. However, applied behavior analysts work within settings in which formal evaluations and diagnoses can dictate the provision of services (BACB, n.d., 2015), and we must be aware of the variables that lead to the referral, assessment, and evaluation of persons who might require services and the variables that lead to the diagnosis of ASD. It is possible that behaviors associated with the female phenotype of ASD are so different from those associated with the male phenotype that even with the extensive training and clinical practice on the part of practitioners, socially relevant behavioral deficits and problem behaviors might not be immediately recognized as ones in need of intensive intervention.

Practitioners should be aware of the fact that diagnoses can sometimes be misleading and not overly informative for treatment decisions and, in some cases, might inadvertently exclude individuals from receiving direct treatment for their behavior. The preceding discussion provides ABA practitioners with a brief history of the prevalent sex/gender biases in the referral, assessment, and diagnostic processes for persons with ASD. As a result of this summary review of the inconsistent and unreliable diagnoses of ASD and the possible existence of sex/gender phenotypes, applied behavior analysts, along with the greater society, must question the validity of the diagnostic process and how it might impact the relationship between ASD and the provision of ABA services. Whereas some have conceptualized ASD as a form of extreme male behavior or biology (Baron-Cohen, 2002), contemporary analyses suggest that ASD is not consistent with that characterization. Rather, ASD appears to be a complex disorder with a wide array of behaviors across both sexes/genders even if those behaviors are currently more difficult to identify in females due to societal expectations, the learning history of females, and possible practitioner biases (Young et al., 2018). When considering the potential underdiagnosis of females, we must ensure that we are providing services to those that truly need them instead of being guided by cultural norms related to a specific diagnosis and outdated and unreliable diagnostic tools (Kopp & Gillberg, 2011).

We are well aware that there are more than a few ways to categorize phenotypes of ASD, but for the purposes of this paper, we felt it was important to consider sex/gender phenotypes specifically given the serious risks inherent in the late diagnosis, underdiagnosis, or misdiagnosis of females, which often results in lack of treatment or, in some cases, contraindicated treatment. ABA practitioners are strongly encouraged to continue to work closely with researchers to develop the characteristics of sex/gender phenotypes in order to help refine diagnostic criteria and to further the development of effective interventions for all individuals. At its core, ABA is focused on promoting socially significant change to improve lives, and an understanding of the sex/gender phenotypes and implications for treatment is necessary to fulfill our ethical obligation as a field and to continue to remain true to that optimistic core.

An insistence on the use of individualized and empirically supported direct assessment protocols based on specific behavioral symptoms will ensure that referrals made by, and interventions created by, applied behavior analysts are not developed according to diagnostic categories or labels (BACB, 2014b), but rather according to a more refined descriptive and functional system. Behavior analysts are trained to assess and treat behaviors and, in most cases, not the presumed pathology. But it is clear that in the case of individuals with ASD, behaviors related to core symptoms must be described, characterized, and measured for effective treatment to occur.

Given the identified issues with the diagnosis, referral, and treatment of females with ASD, we would like to provide several suggestions for actions that applied behavior analysts can take in order to ensure that all individuals with symptoms of ASD can access empirically supported and socially valid interventions. The following suggestions are directly linked to specific items (in parentheses) from the BACB's *Professional and Ethical Compliance Code for Behavior Analysts* (BACB, 2014b).

1. **Advocacy.** Applied behavior analysts should ensure that referrals for ABA services consider behaviors across sex/gender phenotypes (Table 1) and that any learned biases related to the identification of skill deficits or problem behaviors in the referral process be mitigated (1.01, 2.03a). Advocacy for appropriate referrals and assessment is particularly important because professionals who are responsible for identifying students that may need a referral for additional services (e.g., classroom teachers or school psychologists) might not be well versed in the sex/gender phenotypes of ASD. Moreover, teachers and other school personnel might be more likely to refer students who engage in disruptive behaviors than those who are struggling with daily routines or are withdrawn during social activities.

2. **Professional development.** Applied behavior analysts should pursue continuing education and training related to diagnostic, referral, and treatment issues associated with sex/gender phenotypes of ASD (1.02a, 1.03). Given learned societal, cultural, and diagnostic biases that appear to make it more challenging for females with symptoms of ASD to be formally diagnosed with ASD, it is crucial for all professionals to be aware of these biases, as their individual training and clinical experiences in ABA or with ASD might have been more focused on the male phenotype.

3. **Train and disseminate.** Applied behavior analysts must ensure that the content of all behavior-analytic training that they create includes case exemplars and clinical vignettes that are balanced across sex/gender phenotypes. Given that research suggests that the actual male to female ratio for the prevalence of ASD might be closer to 2:1 when other factors are considered, we must ensure that all trainings and informational sessions for ABA include an appropriate number of examples of skill deficits and problem behaviors associated with both male and female phenotypes of ASD (2.03b).

4. **Clinical programming.** Applied behavior analysts should individualize behavior-change programs based on clinical presentations and functions of behaviors and use evidence-based practices as indicated. Although applied behavior analysts are well trained to identify functions of behaviors and to use empirically supported

interventions, it is possible that in some circumstances, without an awareness of biases with regard to sex/ gender phenotypes, they might inadvertently use interventions to treat a pathological topography of behavior associated with ASD given their histories and clinical experience with certain males with ASD (1.02a, 4.03a).

5. **Research.** Applied behavior analysts should ensure that the representation of participants in research is appropriately distributed across sex/gender. In addition, it is important for the field of behavior analysis to continue to conduct research on the differences between the male and female phenotypes of ASD from a behavioral perspective as scientist-practitioners. For example, if a female client presents with a specific challenge that has not responded well to interventions based on empirical research with males with ASD, then it is important to further investigate if the presentation is possibly related to a particular phenotype of ASD (9.02d, 9.02f, 9.02h).

These recommendations represent first steps toward ensuring that function-based behavior-change procedures designed by applied behavior analysts are sensitive to idiosyncratic behavioral symptoms and not based on general diagnostic criteria or overly influenced by biased clinical training and experiences.

One of the core tenets of procedures based on ABA is that they are supported by principles derived from rigorous experimental analyses of behavior and that those principles can, and will, change over time as new data are collected and synthesized. It is clear that the data for differentiating ASD phenotypes, in particular by sex/gender, suggest that the commonly held belief that males are more likely to present with symptoms associated with ASD might not be justified. As applied behavior analysts, like all other clinical professions, we must grapple with how cultural norms and our own histories of reinforcement, or lack of exposure, affect our behavioral observations, clinical experiences, and decision-making. Given this new data, applied behavior analysts must adapt and refine their own practices in order to meet the needs of all current and future clients, regardless of sex/gender. We hope that this paper helps applied behavior analysts better identify their own biases based on how they were trained and their exposure to research on ABA, ASD, and diagnostic tools, and results in more consistent, reliable, valid, and relevant referrals for ABA services based on empirical need and not on unsupported assumptions.

Author Note Bryan J. Blair - Department: Counseling and School Psychology; Sam Blanco - Department: Esteves School of Education. Fernande Ikombo-Deguenon - Department; Comprehensive Behavior Supports. Alyssa Belcastro - Department: Counseling and School Psychology.

Compliance with Ethical Standards

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