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Review

Review of gender differences in core symptomatology in autism spectrum disorders

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ABSTRACT

A preponderance of males with autism spectrum disorders (ASD) has been evident since the initial writings on the topic. This male predominance has consistently emerged in all ASD research to date in epidemiological as well as clinical populations. Despite this long recognized gender disparity in ASD, surprisingly there is a paucity of research addressing gender as it relates to core ASD symptom presentation. Gender differences may manifest with regard to symptom domains, severity, breadth, and so forth. The present review will discuss background (e.g., history, prevalence), assessment issues, gender differences in typically developing individuals in domains relevant to ASD, an in depth review of the literature base on the nature and etiology of gender differences in ASD, as well as future research directions and implications.

Contents

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1. Introduction

A preponderance of males in autism spectrum disorders (ASD) has been evident since the two seminal publications associated with the origin of the disorders (Asperger, 1944; Kanner, 1943). In 1943, Leo Kanner published *Autistic Disturbances of Affective Contact,* describing 11 cases, 8 of whom were boys. In 1944, Hans Asperger published '*Autistic Psychopathy*' *in Childhood* (translated title) describing 4 "prototypical" cases (all male). Asperger (1944) wrote about the gender disparity. He wrote, "It is fascinating to note that the autistic children we have seen are almost exclusively boys" (Asperger, 1944; Frith, 1991, p. 84). He noted that some girls had "contact disturbances which were reminiscent of autism," though none had the "fully formed" or "fully fledged" picture as did the four boys (Asperger, 1944; Frith, 1991, pp. 84–85).

Upon exploring the current literature and hypotheses for the gender disparity in ASD, Asperger's original writings on gender differences have significant relevance. Asperger admitted that the etiology was unknown (Asperger, 1944; Frith, 1991). He noted some girls had developed the traits after encephalitis. He purported, "There is certainly a strong hint at a sex-linked or at least sex-limited mode of inheritance" (Asperger, 1944; Frith, 1991, p. 84). Further, he noted that it could just be chance that he had not encountered autism in girls, or that autistic traits in girls are not apparent until post-puberty. Asperger also observed that several of the mothers had autistic features (Asperger, 1944; Frith, 1991). Finally, Asperger related symptoms of autism to a number of purported important gender variables (e.g., cognition, emotions, instincts), writing:

> The autistic personality is an extreme variant of male intelligence, of the male character. Even within the normal variation, we find typical sex differences in intelligence. In general, girls are better learners. They are more gifted for the concrete and the practical, and for tidy, methodical work. Boys, on the other hand, tend to have a gift for logical ability, abstraction, precise thinking and formulating, and for independent scientific investigation. This is the reason, too, why in general boys at older age levels do better than girls in the Binet test. The narrowly logical and abstract items which start at the ten-year level are simply more congenial to boys! In the autistic individual the male pattern is exaggerated to the extreme. In general, abstraction is congenial to male thought processes, while female thought processes draw more strongly on feelings and instincts. In the autistic person abstraction is so highly developed that the relationship to the concrete, to objects and to people has largely been lost, and as a result the instinctual aspects of adaptation are heavily reduced. (Asperger, 1944; Frith, 1991, pp. 84–85)

This gender disparity has been consistently reported to date, with estimates of a male to female ratio of approximately 4.3:1 (Fombonne, 2003, 2005, 2007). Although there is a long history of an identified gender disparity, a paucity of research has addressed gender as it relates to core symptom presentation. The present review will present background on ASD, such as diagnostic classifications and prevalence, a brief discussion of assessment considerations and findings of gender differences in typically developing children in relevant domains, and finally, an in depth review of the literature base on the nature and etiology of gender differences in ASD.

1.1. Diagnostic classifications and prevalence

The *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision* (DSM-IV-TR; American Psychiatric Association [APA], 2000) includes five disorders under the category of Pervasive Developmental Disorders (PDD): autistic

disorder; Asperger's disorder; PDD not otherwise specified (PDD-NOS); Rett's disorder; and childhood disintegrative disorder (CDD). Rett's disorder and CDD are both rare disorders characterized by the presence of regression in skills (Volkmar, State, & Klin, 2009). Moreover, Rett's and CDD are typically not viewed as included under ASD (Matson & Mahan, 2009; Volkmar et al., 2009). Core symptoms of ASD include qualitative impairments in social interaction and communication, and restricted, repetitive, and stereotyped patterns of behavior, interest, or activities (Brim, Townsend, DeQuinzio & Paulson, 2009; Loukusa & Moilanen, 2009; Matson, Matson & Rivet, 2007; Niklasson, Rasmussen, Oskarsdottir, & Gillberg, 2009.

Rett's disorder is unique in that it is the only PDD that occurs almost exclusively in females and has an identified genetic cause (Amir et al., 1999; Hagberg, Aicardi, Dias, & Ramos, 1983; Rett, 1966). Most individuals (most estimates are approximately 95% ranging from 85 to 100%) with classic Rett's disorder have MECP2 (methyl-CpG binding protein) mutations at Xq28 (Deidrick, Percy, Schanen, Mamounas, & Maria, 2005; Erlandson & Hagberg, 2005). Diagnosis of Rett's disorder must be made clinically, as MECP2 mutations result in a wide variety of phenotypes within and outside of Rett's disorder (Erlandson & Hagberg, 2005; Hagberg, Hanefeld, Percy, & Skjeldal, 2002; Hammer, Dorrani, Dragich, Kudo, & Schanen, 2002; Matson, Dempsey, & Wilkins, 2008; Matson, Fodstad, & Boisjoli, 2008).

Regarding prevalence, no epidemiological study (excluding Rett's disorder) has yielded more females than males (Fombonne, 2003, 2007). The male to female ratio has ranged from 1.33:1 (16:12; McCarthy, Fitzgerald, & Smith, 1984) to 16:1 (Wing, Yeates, Brierley, & Gould, 1976) (average 4.3:1; Fombonne, 2003, 2005, 2007). This varies according to cognitive ability, with a median sex ratio of 5.5:1 for IQ in the normal range, compared to 1.95:1 for moderate to severe intellectual disability (ID) (Fombonne, 2005, 2007). The co-occurrence of ID and ASD in general has been an important topic. It has frequently been reported that the majority with autism have ID; however, current rates may be lower than previous estimates (Bryson, Bradley, Thompson, & Wainwright, 2008; Edelson, 2006; Ritvo & Ritvo, 2006).

2. Gender issues in ASD assessment

A number of considerations are important relative to gender differences in ASD assessment. Koenig and Tsatsanis (2005) pointed out that gender differences in presentation have not been sufficiently addressed in studies of key instruments used in the field such as the ADI [*Autism Diagnostic Interview* (Le Couteur, Rutter, Lord, & Rios, 1989), *ADI-Revised* (ADI-R; Lord, Rutter, & Le Couteur, 1994)] and ADOS [*Autism Diagnostic Observation Schedule* (Lord, Rutter, Goode, & Heemsbergen, 1989), *Pre-Linguistic ADOS* (PL-ADOS; DiLavore, Lord, & Rutter, 1995), *ADOS-Generic* (ADOS-G; Lord et al., 2000)]. Standardization samples for ASD instruments consist of predominately males, with a sex ratio of approximately 3:1 (Koenig & Tsatsanis, 2005). For disorders such as ASD with such a pronounced gender difference, Rutter, Caspi, and Moffitt (2003) noted that there is a paucity of research addressing the validity of diagnostic criteria by gender. In addition, symptom criteria or assessment items may be biased in that they are more typical of one gender, raising the issue of whether separate criteria content or requirements or different norms or cutoff scores based on gender are appropriate (Bell, Foster, & Mash, 2005; Rutter et al., 2003). Therefore, during assessment, careful consideration should be given to gender, age, and cognitive/adaptive level, as opposed to only comparing females to typically developing males or males with ASD (Koenig & Tsatsanis, 2005; Matson & Minshawi, 2007).

3. Gender differences in the general population

Quite a large literature base exists concerning gender differences in the general population in a multitude of variables (Hyde, 2007). However, this is beyond the scope of this topic. This section will encompass a brief review of the research in gender differences in the general population which have potential implications related to ASD symptoms as discussed by Koenig and Tsatsanis (2005). Nonetheless, it is notable that even in typically developing populations, some research has yielded mixed findings, and some differences are slight rather than meaningful (e.g., Charman, Ruffman, & Clements, 2002; Jarrold, Butler, Cottington, & Jimenez, 2000; Koenig & Tsatsanis, 2005; Wallentin, 2009). The large majority of these variables have not been sufficiently examined in ASD (Koenig & Tsatsanis, 2005).

Regarding socialization, Koenig and Tsatsanis (2005) reviewed some evidence to suggest a potential female advantage in decoding facial expressions and nonverbal cues, empathizing, and theory of mind (e.g., Bacon, Fein, Morris, Waterhouse, & Allen, 1998; Brown & Dunn, 1996; McClure, 2000; Nydén, Hjelmquist, & Gillberg, 2000). If so, Koenig and Tsatsanis (2005) hypothesized that females with ASD could either appear less or more impaired, compared to males with ASD or typically developing females, respectively. Koenig and Tsatsanis (2005) pointed out that gender differences in the number of peers, types of activities, and social roles in peer groups could pose differing social demands (e.g., McLennan, Lord, & Schopler, 1993).

With regard to communication, females show a slight advantage in early language development, though this does not persist, and other purported gender differences have been frequently cited but are not supported in the research base (Wallentin, 2009). However, Koenig and Tsatsanis (2005) emphasized some aspects of language with social implications. For example, Koenig and Tsatsanis (2005) reviewed evidence suggesting females build relationships by sharing thoughts and emotions requiring more social communication skills, while males build relationships on object/activity related themes (e.g., sports and hobbies).

Less research has addressed gender differences in restricted interests and repetitive behavior. In typically developing children (8–72 months), Evans, Leckman, Carter, and Reznick (1997) did not find significant differences in compulsions, routines, and rituals. In typically developing 2-year olds, Leekam et al. (2007) found boys had greater overall repetitive behavior, and preoccupations with restricted patterns of interest. Koenig and Tsatsanis (2005) cited evidence indicating greater difficulties with self-regulation and inhibition control in boys, hypothesizing that if repetitive behavior in ASD serves to reduce arousal or provide sensory stimulation, girls may have less difficulty decreasing reliance on these behaviors (Koenig & Tsatsanis, 2005).

4. Gender differences in ASD

4.1. Intelligence (IQ)

4.1.1. Gender differences in IQ in ASD

Early on in epidemiological studies and the literature, differences regarding intelligence consistently emerged. In the first epidemiological study, Lotter (1966) found that 100% of girls ($n = 9$) had an IQ score below 55 compared to 57% of boys ($n = 13$), a sex ratio of 1.4:1. In a review of epidemiological studies, Fombonne (2005) found a median sex ratio of 5.5:1 with IQ in the normal range, compared to 1.95:1 in moderate to severe ID. Numerous researchers have found lower IQ scores in females with ASD (Banach et al., 2009; Lord, Schopler, & Revicki, 1982; Pilowsky, Yirmiya, Shulman, & Dover, 1998; Tsai & Beisler, 1983; Tsai, Stewart, & August, 1981; Volkmar, Szatmari, & Sparrow, 1993; Wing, 1981). Regarding male to female ratios, Wing (1981) found 1 girl compared to 16 boys with an autism diagnosis. In a separate group with the triad of language and social impairments, ratios were 9.5:1 in those with IQ above 50, compared to 2.2:1 for IQ between 20 and 49, and 0.9:1 for IQ between 0 and 19 (Wing, 1981). Tsai et al. (1981) found a ratio of 4.7:1 when IQ was greater than 70 compared to 2.9:1 when IQ was below 50. Lord et al. (1982) found a ratio of 5.2:1 ($IQ > 80$) versus 3.3:1 ($IQ < 40$). Tsai and Beisler (1983) found a ratio of 4.43:1 ($IQ > 50$) compared to 1.31:1 ($IQ < 50$). Significantly more females had IQ scores below 50 (Tsai & Beisler, 1983). Lord and Schopler (1985) found that females with ASD were more prevalent when IQ was less than 34. Volkmar et al. (1993) found higher sex ratios when IQ was greater than 70. Males with autism were 8.8 times (1.5 times for PDD-NOS) more likely to have an IQ over 70 (Volkmar et al., 1993).

Findings of lower cognitive ability in females with ASD and greater male to female ratios in the absence of ID have continued to be replicated. In a study of 8-year olds with ASD in South Carolina, Nicholas et al. (2008) found that 72.7% of girls had an IQ below 70 compared to 56.4% of boys. The ratio was 4.9:1 ($IQ > 70$) compared to 2.4:1 ($IQ < 70$). Finally, the proportion of males to females with ASD was similar when IQ was below 34 (Nicholas et al., 2008). Bhasin and Schendel (2007) found a higher sex ratio in children with ASD and an IQ above 70 (4.6:1) compared to those with ASD and an IQ below 70 (3.5:1). In simplex (single incidence) families, Banach et al. (2009) found that 54.8% of females compared to 20.3% of males had an IQ below 50. The sex ratios were similar when IQ was below 50, compared to 8.3:1 when IQ was above 70 (Banach et al., 2009). In contrast in multiplex families, where more than one child has ASD, gender differences in IQ have not been found (Banach et al., 2009; Spiker et al., 2001).

In contrast to the previously mentioned studies which used an ASD population, Bryson et al. (2008) used an epidemiological study of ID in Ontario to examine the prevalence of autism in adolescents with mild ($IQ = 50–75$) or severe ($IQ < 50$) ID. Consistent with previous research, the overall sex ratio for autism was 2.3:1, with higher ratios in mild ID (2.8:1) compared to severe ID (2:1; Bryson et al., 2008). In further analyzing the frequency data, regardless of ID, overall, males were more likely to have autism. Regardless of autism, females were more likely to have severe ID versus mild ID. However, males with severe ID were significantly more likely to have autism than males with mild ID or females. The authors highlighted the increased risk of autism in males with severe ID (Bryson et al., 2008).

In conclusion, findings related to ID are one of the earliest and most consistent findings in this literature (Matson, Mahan, Hess & Fodstad, 2010; Njardvik, Matson & Cherry, 1999). Females with ASD have lower average intellectual ability than males, and the male to female sex ratio in ASD is highest when ID is not present. Given the evidence for significant gender differences in ASD associated with ID, it follows that factors related to ID must be considered in evaluating the research that has been conducted in this area.

4.1.2. Relationships between gender differences, IQ, and ASD

Researchers have pointed out methodological issues associated with IQ (Matson & Shoemaker, 2009). The relationships between gender differences, IQ, and autism symptoms have not yet been determined (Lord & Schopler, 1985; Volkmar et al., 1993). Previous research has not distinguished between severity of autism and severity of ID (Lord & Schopler, 1985; Volkmar et al., 1993). Furthermore, Volkmar et al. (1993) noted that the appropriateness of controlling for IQ depends on whether low IQ is a cause or consequence of gender differences in ASD. If low IQ is a separate associated feature, controlling for it may result in overmatching (i.e., controlling for factors that are not confounding variables) and inhibit understanding of true differences (Volkmar et al., 1993). Research and hypotheses have since been put forth concerning these issues.

Nishiyama et al. (2009) evaluated gender differences in genetic and environmental factors underlying the relationship between IQ and autistic traits via twins with ASD. Genetic factors impacting autistic traits were highly similar to those impacting IQ for boys (−0.94) and girls (−0.95). Regarding individual specific environmental factors influencing autistic traits, there was a moderate association to those influencing IQ for boys (−0.29) and girls (−0.59). Thus, no significant gender

differences were found in the genetic and environmental factors influencing autistic traits and IQ, and genetic factors underlying both ASD and IQ were highly similar (Nishiyama et al., 2009). This is consistent with evidence suggesting overlap in genes contributing to ID and ASD (Gupta & State, 2007; Laumonnier et al., 2004; Marshall et al., 2008). Reviewing genetics and ASD, Gupta and State (2007) noted that the majority of findings implicate mutations that could result in cognitive or social impairment, or both. It is important to note that Nishiyama et al. (2009) measured autistic traits as a whole via the *Childhood Autism Rating Scale* (CARS; Reichler & Schopler, 1971; Schopler, Reichler, DeVellis, & Daly, 1980; Schopler, Reichler, & Renner, 1988). However, based on previous research with different assessment instruments and populations, these authors purported that autistic traits in socialization appear orthogonal to IQ, while communication and repetitive behaviors appear to be moderately related to IQ. Hence, further research into gender differences in IQ and ASD is needed, particularly in light of recent research on the dimensional and fractionable nature of autistic traits (see Happé & Ronald, 2008; Happé, Ronald, & Plomin, 2006; Mandy & Skuse, 2008; Skuse, 2007; Volkmar et al., 2009; Waterhouse, 2008; Yirmiya, 2008).

Skuse (2007) put forth a hypothesis about the relationship between gender, IQ, and autistic traits. Skuse (2007) discussed that ASD and autistic traits frequently present in individuals with both idiopathic ID or ID associated with genetic conditions (e.g., Fragile X, tuberous sclerosis; Zafeiriou, Ververi, & Vargiami, 2007). In addition, particularly in genetic studies, strict diagnostic criteria have been employed in an attempt to reduce heterogeneity, yielding samples with mostly moderate to severe ID (Skuse, 2007). Furthermore, Skuse (2007) cited evidence from the general population that autistic traits are continuously distributed (i.e., dimensional not categorical) and, in contrast to studies of samples with ASD, uncorrelated with verbal or nonverbal IQ. Skuse (2007) concluded that despite their association, ASD and ID do not typically have common causes. Rather, the genes that have been implicated in ASD are instead important for developing aspects of cognitive ability needed to compensate for vulnerability to underlying autistic traits (i.e., social-cognitive processing; Skuse, 2007). These autistic traits lead to a clinically identifiable disorder in individuals with low IQ, males, or those with "independent neurodevelopmental vulnerability owing to a wide range of gene mutations, chromosomal anomalies or environmental insults" (Skuse, 2007, p. 387). It may be that "females are equally at risk, in terms of genetic predisposition, but a factor relating to genetic or hormonal sex differences enables them to compensate for that risk. They are, therefore, less likely to manifest the full range of autistic symptoms, as conventionally measured" (Skuse, 2007, p. 393).

In summary, there is a multitude of evidence to suggest overlap in genetic factors related to ASD and IQ; however, Nishiyama et al. (2009) did not identify gender differences in this relationship. Further research is needed as symptom areas in ASD (e.g., social, communication, behavior) may be differentially associated with IQ. Autistic traits frequently present in ID and have been found to be associated with IQ. Conversely, in the general population, autistic traits have been found to be continually distributed and not related to IQ. Skuse (2007) purported that ASD and ID do not have common causes. Rather, females may be similar in genetic predisposition to ASD, but more able to compensate for that risk than males. Thus, the causal relationships between ID, ASD, and gender differences remain unclear and complicate investigation of the nature and etiology of gender differences in ASD.

4.2. ASD symptoms

Despite the long recognized predominance of males with ASD, few researchers have examined gender differences in ASD symptoms (Matson & LoVullo, 2009). There is a dearth of research (fewer than 10 studies) on gender differences in ASD symptoms in an ASD population. Regarding IQ, methodology has differed, with researchers either not controlling for IQ (Hus, Pickles, Cook, Risi, & Lord, 2007; Nicholas et al., 2008; Tsai & Beisler, 1983; Tsai et al., 1981), limiting inclusion to participants within the average IQ range (Holtmann, Bölte, & Poustka, 2007; McLennan et al., 1993), using IQ as a covariate or matching participants based on IQ (Carter et al., 2007; Pilowsky et al., 1998), or conducting the analyses both with and without IQ as a covariate (Banach et al., 2009; Lord et al., 1982; Volkmar et al., 1993). Regarding age, the large majority of the research involved children, with one researcher focusing on toddlers (Carter et al., 2007) and three researchers including adult participants, up to mid-thirties (McLennan et al., 1993; Pilowsky et al., 1998) or early-fifties (Hus et al., 2007) in age. Researchers have also examined gender differences in ASD symptoms in the general population, sometimes including a subgroup of participants with ASD (Allison et al., 2008; Ronald et al., 2006; Williams et al., 2008), with one study focusing on an adults (Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001) and one on toddlers (Allison et al., 2008). Following is a review of the literature on gender differences in ASD based on the core symptom areas, as well as the literature in the general population on gender differences in ASD symptoms.

4.2.1. Socialization

Lord et al. (1982) found lower *Vineland Adaptive Behavior Scales* (VABS; Sparrow, Balla, & Cicchetti, 1984) Social Quotients in females ages 3–8 years with ASD, though this difference disappeared when IQ was included as a covariate. No significant differences were found on *Psychoeducational Profile* (PEP) scales involving inappropriate affect and relating/human interest (Lord et al., 1982). Tsai and Beisler (1983) found that boys had greater social (as measured by the *Developmental Profile* Social Subscale) and play (*Symbolic Play Test*) abilities than girls with ASD. In a population-based study, Nicholas et al. (2008) found no significant gender differences in 8-year olds with ASD on the *DSM-IV-TR* social impairment criteria. In children with ASD (age: $M = 9$, $SD = 6$), Banach et al. (2009) found no significant gender differences on the ADI-R or VABS social domains in simplex or multiplex families, and this finding held both with and without IQ used as a covariate. In toddlers ages 18–33 months, Carter et al. (2007) examined gender differences with age and nonverbal ability (*Mullen Scales of Early Learning*

Visual Reception Scale) as covariates. Girls showed more Social Interaction impairment (ADI-R), poorer socialization skills (VABS), and poorer Competence in the areas of Mastery Motivation (e.g., claps for self, curious, persists on difficult tasks, wants to do things independently, likes figuring things out like stacking blocks) and Empathy (*Infant-Toddler Social and Emotional Assessment*; ITSEA). No significant gender differences were found in Reciprocal Social Interaction (ADOS-G) or Social Relatedness (ITSEA; Carter et al., 2007).

Researchers have examined gender differences in samples with higher cognitive abilities and ASD. McLennan et al. (1993) examined gender differences on the ADI for participants with ASD matched on nonverbal IQ (all $>$ 60) and age (range: 6–36 years). Females had greater impairments in current friendships and reciprocal social interaction, while males had greater separation anxiety and impairments in reciprocal social interaction and communication prior to age of 5. No significant gender differences were found for nonverbal social behaviors or sharing enjoyment/modifying behavior to context (McLennan et al., 1993). Holtmann et al. (2007) examined gender differences on the ADI-R, ADOS, and *Child Behavior Checklist* (CBCL) for participants with ASD matched on IQ (all $>$ 70) and age (range: 2–20 years). Females had greater impairments in ADI-R current group play with peers and CBCL Social Withdrawal and Social Problems, while males had greater impairments on inappropriate facial expression (4–5 years) and showing/directing attention (current). No significant differences were found on ADI-R or ADOS overall social domains (Holtmann et al., 2007).

4.2.2. Communication

Tsai and Beisler (1983) found that boys had greater receptive and expressive language abilities (*Sequenced Inventory of Communication Development*) than girls with ASD. Nicholas et al. (2008) found no gender differences in *DSM-IV-TR* communication criteria. Banach et al. (2009) found no significant gender differences in children with ASD on the ADI-R or VABS communication domains in multiplex families, and this finding held both with and without IQ used as a covariate. In contrast, in simplex families, girls exhibited less communication impairment (ADI-R) and lower adaptive communication skills (VABS); however, not with IQ covaried. (2008)Knickmeyer, Wheelwright, and Baron-Cohen (2008) found that females with ASD ages 4–14 years engaged in more pretend play (*Children's Play Questionnaire*). In toddlers, Carter et al. (2007) found girls with ASD to have greater communication impairments (ADOS), and lower expressive and receptive communication (VABS). No significant gender differences were found on nonverbal communication (ADI-R) or in receptive and expressive language (Mullen; Carter et al., 2007).

In samples with higher cognitive abilities and ASD, McLennan et al. (1993) found that females with ASD demonstrated less impairment in social play at 4–5 years of age (ADI), with no significant differences in the areas of gesture, conversation, language abnormalities, prosody/intonation, or communication (current and ever). Holtmann et al. (2007) found no significant gender differences in communication (ADI-R or ADOS).

4.2.3. Restricted interests and repetitive behavior

In perhaps the earliest study focusing on gender differences in ASD, Tsai et al. (1981, p. 168) described greater abnormal motor movements in females with ASD, which they described as "dystonia, abnormal posture and gait, dystonic posturing of hands and fingers, hand flapping, tremor, tic-like movement, ankle clonus, and emotional facial paralysis (i.e., asymmetry of the lower portion of the face when children smiled or spoke spontaneously)." This has not been supported in further studies. Lord et al. (1982) found that boys with ASD had more peculiar visual interests (CARS) and inappropriate, routinized, and stereotypic play (PEP), with IQ covaried out. Banach et al. (2009) found no significant gender differences in children with ASD on ADI-R restricted, repetitive, and stereotyped behavior domain in simplex or multiplex families, and both with and without IQ covaried. Nicholas et al. (2008) found that boys with ASD had more preoccupation with parts of objects, routines and rituals, and stereotyped mannerisms based on *DSM-IV-TR* criteria; but no differences regarding restricted interests. In toddlers with ASD, Carter et al. (2007) found no significant differences on ADI-R or ADOS restricted, repetitive, and stereotyped behaviors. Finally, in studies of samples with higher cognitive abilities and ASD, no significant gender differences were found on restricted, repetitive, stereotyped behaviors on the ADI (McLennan et al., 1993) or ADI-R (Holtmann et al., 2007).

4.2.4. All ASD symptoms

Several studies have included a range of intellectual ability levels and failed to find any gender differences in ASD symptoms. Volkmar et al. (1993) used IQ as a covariate and found no significant gender differences on the *Autism Behavior Checklist* (ABC; Krug, Akick, & Almond, 1980), *ICD-10* criteria, or VABS. In participants ages 20 months to 34 years, Pilowsky et al. (1998) matched groups on mental age and found no significant gender differences on the ADI-R or CARS. Finally, in participants ages 4–52 years ($M = 8$, $SD = 5$), Hus et al. (2007) found no significant gender differences in groups based on ADI-R items involving: word or phrase acquisition, repetitive sensory motor actions (i.e., hand and finger or other complex mannerisms, repetitive use of objects, unusual sensory interests, and rocking), insistence on sameness (i.e., resistance to trivial change in environment, compulsions/rituals, difficulties with change in routine or environment), or savant skills (i.e., visuospatial, memory, musical, and computational ability).

4.2.5. Conclusion

In summary, overall relatively few differences in ASD symptoms have been found between males and females. Three studies found no significant gender differences in any ASD symptom areas. Some findings of greater socialization and

communication impairments and abnormal motor movements in girls appear to have been related to lower IQ. Some studies found greater impairments in females via interview but not observation, or in current but not early functioning. Regarding specific findings, in socialization, one toddler study found girls had greater impairments (e.g., social interaction, adaptive social skills, empathy). In the average IQ range, females have been found to have greater impairments in some areas (e.g., friendships, reciprocal interaction, group play), but fewer impairments in others (e.g., social anxiety, showing/directing, and early reciprocal interaction, communication, and inappropriate facial expressions). Regarding communication, in toddlers, one study found girls to have greater communication abnormalities (via interview but not observation) and adaptive communication impairments (on the VABS but not the *Mullen*). In the average IQ range, no significant gender differences have been found in communication with the exception of females having less impairment in social play at 4–5 years. Regarding restricted, repetitive, and stereotyped behaviors, some research has found that boys had greater peculiar visual interests, inappropriate/stereotypic play, preoccupation with parts of objects, routines/rituals, and stereotyped mannerisms. In studies of toddlers or individuals in the average IQ range, no significant gender differences in this behavioral domain have been found.

4.2.6. In the general population

A number of studies have examined gender differences in ASD symptoms in the general population, some with a subgroup of participants with ASD. In the general population, boys ages 7–9 have been found to score significantly higher (Posserud, Lundervold, & Gillberg, 2006) on the *Autism Spectrum Screening Questionnaire* (ASSQ; Ehlers & Gillberg, 1993; Ehlers, Gillberg, & Wing, 1999; Posserud et al., 2006), and males ages 7–15 have been found to score significantly higher (Constantino & Todd, 2003) on the *Social Responsiveness Scale* (SRS; Constantino, 2005; Constantino & Todd, 2003), with higher scores indicating the presence of more autistic traits. In a population study of the *Childhood Autism Spectrum Test* (CAST; Scott, Baron-Cohen, Bolton, & Brayne, 2002) on children ages 4–10 years, boys scored higher than girls, and these results held when ASD and a mixed special needs group were removed (Williams et al., 2008). In a study of twins at 8 years of age (90 with ASD), Ronald et al. (2006) also found that boys scored higher on the CAST. In a study of 8-year-old twins, Loat, Haworth, Plomin, and Craig (2008) found greater social impairments in boys; however, boys and girls did not differ significantly on other CAST domains or relationship problems as measured by the *Relationships Problems Questionnaire*. On the *Autism Spectrum Quotient* (AQ), males in the control group scored significantly higher than females, while there were no significant gender differences in those with high functioning autism or Asperger's on the child (Auyeung, Baron-Cohen, Wheelwright, & Allison, 2008), adolescent (Baron-Cohen, Hoekstra, Knickmeyer, & Wheelwright, 2006), and adult (Baron-Cohen et al., 2001) versions. This same pattern held in a sample aged 19–63 months on the *Quantitative CHecklist for Autism in Toddlers* (Q-CHAT; Allison et al., 2008). Males in the control group scored higher than females; however, not in the ASD sample (Allison et al., 2008). To summarize, in general population studies, males have been found to have more autistic traits; however, in subgroups of participants with ASD, no gender differences have been found.

4.3. Age

Much of the literature in ASD has involved children and adolescents rather than adults (Matson & Neal, 2009). Regarding epidemiology, in Fombonne's (2003, 2005, 2007) reviews, only one study included participants up to age 27 years (Ritvo et al., 1989). In studies of gender differences in ASD symptoms, most research has been on children, with some emphasis on toddlers (Allison et al., 2008; Carter et al., 2007) and adults (Baron-Cohen et al., 2001; Hus et al., 2007; McLennan et al., 1993; Pilowsky et al., 1998). Several studies of gender differences in ASD either matched groups on age or entered age as a covariate. Studies concerning onset, course, and adult outcome are examined below.

4.3.1. Onset

Few studies have addressed gender differences in onset of ASD, and this issue has not been examined systematically as the focus in any studies. In participants with ASD and an IQ above 60, McLennan et al. (1993) reported that males were more likely to have an overall onset and play deficits before age 3 as measured by the ADI, while no gender differences were found in the frequency of onset of language and social deficits before age 3. Volkmar et al. (1993) noted no significant gender differences on age of onset.

4.3.2. Course

Only one study directly addressed gender differences in the course of ASD. McLennan et al. (1993) found different patterns of gender differences based on time period of ADI items (i.e., early items prior to age 5, current items, and "ever" items). Females showed less impairment in early social and communicative behavior (e.g., social imitative play, seeking and offering comfort). However, this pattern was reversed in older children, adolescents, and adults, where females showed greater social impairments in friendships. The researchers posed several possible explanations for these differences. For older females, peer activities are heavily dependent on social interests and communication, whereas males may have social options (e.g., spectator sports) which are less verbal and interactive. In addition, females in the study had often been in special education settings predominately with males, thus limiting opportunities to meet females with common interests. Finally, items on the ADI are different across time period. For example, early items focus on brief, responsive interactions with caregivers (e.g., imitation and social play), while later items focus on friendships and initiation of social behavior such as greeting and sharing activities (McLennan et al., 1993).

Lord et al. (1982) examined their findings according to age groups and found significant differences; however, no significant interaction emerged between age and gender. Regarding age, both with and without IQ covaried, children ages 5–8 years showed greater eye–hand coordination and perceptual skills than 3–4-year olds, while children ages 3–6 years showed greater adaptive social skills than 7–8-year olds. With IQ as a covariate, 5–6-year olds showed fewer peculiar visual interests than the other age groups (Lord et al., 1982).

Studies of ASD traits in the general population with a subgroup with ASD have yielded comparable results across the lifespan for children, adolescents, and adults without ID (Auyeung et al., 2008; Baron-Cohen et al., 2006; Baron-Cohen et al., 2001), as well as for toddlers (Allison et al., 2008). These studies have all revealed greater ASD traits in males in the general population. However, no gender differences were found in the subgroups with ASD.

4.3.3. Outcome

Howlin, Goode, Hutton, and Rutter (2004) conducted a follow-up study of outcome in 68 adults with ASD and a performance IQ above 50. The average age when first seen was 7 years (range 3–15) and the average follow-up age was 29 years (range 21–48). Only 7 women were included in the sample, and they were similar in age, IQ, language, reading, and spelling ability (Howlin et al., 2004). No significant gender differences were found on measures of language level, abnormal use of language, repetitive, stereotyped behaviors, or overall social outcome. However, no females were rated as having a "Good" outcome, and five were rated as having "Poor" or "Very Poor" outcomes in areas of educational, vocational, residential, and social status (Howlin et al., 2004). Billstedt, Gillberg, and Gillberg (2007) conducted a follow-up study of 75 males and 30 females using the *Diagnostic Interview for Social and Communication DisOrders* (DISCO; Wing, Leekam, Libby, Gould, & Larcombe, 2002). The follow-up period ranged from 13 to 22 years and the average follow-up age was 26 years (range 17–40). Female gender was predictive of greater abnormalities in social interaction, but not impairments in reciprocal communication and limitation in self-chosen activities (Billstedt et al., 2007). It is notable that more females in this study had epilepsy, which has been associated with ID/greater brain dysfunction and, hence, risk for poorer outcomes (Danielsson, Gillberg, Billstedt, Gillberg, & Olsson, 2005).

4.4. Diagnosis

Compared to males with ASD, females have been found to experience a lack of diagnosis, delay in diagnosis, and misdiagnosis with regard to ASD. In an early epidemiological study, Wing and Gould (1979) found that even when sex ratios were the same for severity of social impairment, males were 15 times more likely to be diagnosed with ASD compared to females. In a follow-up report of the 11 children seen in 1943, Kanner reported that the girls were referred to the clinic at later ages (6–8 years) compared to boys (2–6 years; Kanner, 1971). Kopp and Gillberg (1992) reported case histories of 6 females between 6 and 10 years with ASD and an IQ above 60. None were diagnosed with ASD prior to age 6 (4 were over 8 years), even though abnormal development and social, communicative, and imaginative deficits had been identified before 2 years. Previous impressions had included ADHD, minimal brain dysfunction, developmental delay, and speech and motor concerns (Kopp & Gillberg, 1992; Miniscalco & Sandburg, 2010). Finally, researchers have found undiagnosed ASD in females with anxiety (Kopp & Gillberg, 1997) and anorexia nervosa (Nilsson, Gillberg, Gillberg, & Råstam, 1999).

Two more recent studies have examined gender differences in diagnostic experiences in ASD. Goin-Kochel, Abbacchi, and Constantino (2007) found that girls were diagnosed later for Asperger's disorder (average of 8.9 versus 7.0 years) and PDD-NOS (5.1 versus 3.9 years), but not autistic disorder (3.7 versus 3.3 years). No significant gender differences were found for number of professionals seen, though this was positively correlated with age at diagnosis. Earlier age at diagnosis was associated with greater parental education, income, and satisfaction with the diagnostic process (Goin-Kochel, Mackintosh, & Myers, 2006). Siklos and Kerns (2007) found that parents of a female with ASD experienced significantly more difficulty during the diagnostic process. The time frame from the first visit to a health care professional to a final diagnosis was significantly longer for females (average of 4 years 2 months) compared to that for males (2 years 2 months). Age at diagnosis was later for females (6 years 1 months) compared to males (4 years 8 months). Despite these differences, there were no significant gender differences in the number of professionals seen during the diagnostic process or reports of satisfaction and stress levels (Siklos & Kerns, 2007).

4.5. Psychopathology

Rutter et al. (2003) reviewed the literature on gender differences in psychopathology in general, grouping these differences into two main categories. First are neuropsychiatric disorders (e.g., autism, ADHD, reading disorder), characterized by onset during childhood and greater prevalence in males (Rutter et al., 2003). The second category encompasses emotional disorders (e.g., depression, eating disorders), characterized by onset during adolescence and greater prevalence in females (Rutter et al., 2003). Although antisocial behavior has adolescent onset and male preponderance, the male to female ratio is much higher when onset is during childhood (Moffitt & Caspi, 2001; Moffitt, Caspi, Rutter, & Silva, 2001).

Few studies have examined gender differences in psychopathology in ASD. In participants with ASD and an IQ above 70, Holtmann et al. (2007) found females had higher thought problems and attention problems (CBCL), but no significant gender differences on the CBCL Somatic, Anxious/Depressed, Delinquent, or Aggressive Behavior subscales. Bölte, Dickhut, and

Poustka (1999) found no significant gender differences in individuals with ASD ages 4–18 on the CBCL with age and IQ covaried. Matson and Love (1990) examined parent-reported fears in 2.5–17-year olds with and without ASD. Overall, average fear scores on the *Revised Fear Survey Schedule for Children* were higher for females compared to males (Matson & Love, 1990). In toddlers with ASD, Carter et al. (2007) found a trend towards more Atypical Depression/Withdrawal (ITSEA) in females with ASD, but no significant differences on the Externalizing, Internalizing, Dysregulation, or Maladaptive subscales.

4.6. Developmental, self-help, and motor skills

Some researchers have examined gender differences in developmental, self-help, and motor skills in ASD. Tsai and Beisler (1983) found that boys had greater perceptual-motor abilities (Developmental Profile Physical and Self-Help subscales) than girls with ASD, but not when matched on age and receptive language. Wing (1981) found boys more likely to be ambulatory, though ID was not accounted for. In ambulatory participants, the sex ratio was similar (Wing, 1981). Volkmar et al. (1993) found no significant gender differences on the VABS with IQ covaried. In toddlers with ASD, Carter et al. (2007) found no significant gender differences in daily living skills (VABS). Boys had better gross motor skills (VABS) and gross and fine motor skills (*Mullen)* (Carter et al., 2007). In individuals with ASD and IQ above 70, Holtmann et al. (2007) found no significant gender differences in developmental milestones, though females did achieve them earlier.

4.7. Neuropsychological/cognitive

Two studies examined gender differences in ASD from a neuropsychological perspective with the *Wechsler Intelligence Scales for Children-III* (WISC-III). They included children with ASD and average IQ. The authors discussed cognitive theories related to ASD (e.g., executive functioning, theory of mind, weak central coherence) (for a review see Tsatsanis, 2005).

Nydén et al. (2000) examined neuropsychological performance in 8- to 12-year olds with average IQ ($N = 34$). Participants included clinic referred boys and girls with either ASD or ADHD, and a typically developing comparison girl group. Clinic girls performed worse on tests of global executive functions (*Tower of London*) and theory of mind (*Cartoon Explanation Tasks – Mental*). No significant differences were found on other tests of executive functions (i.e., inhibiting prepotent response, stopping an ongoing response, and interference control) and cognitive ability (i.e., WISC-III Freedom from Distractibility, Processing Speed, and a Block Design task), though clinic boys performed better than clinic girls except on Processing Speed (Nydén et al., 2000).

Koyama, Kamio, Inada, and Kurita (2009) examined sex differences on the WISC-III Japanese version in 26 girls (mean age 8 years) and 116 boys (mean age 9 years) with ASD and average IQ. Girls performed significantly better on the Processing Speed Index (Coding and Symbol Search), possibly reflective of the distractibility, extreme slowness, circumstantiality, and drive for perfection in high functioning autism (Ehlers, Nydén, Gillberg, & Dahlgren Sandberg, 1997). Boys' performance on Block Design was significantly better than girls, supportive of a detail focused cognitive style and the weak central coherence hypothesis in ASD (Happé, 1999; Happé & Frith, 2006; Shah & Frith, 1993). Boys scored higher on Block Design compared to other performance subtests, while girls demonstrated a more even profile across performance subtests. No significant sex differences were found on Full Scale, Verbal, or Performance IQ, or on the verbal subtests. Both boys and girls performed worse on Comprehension relative to other verbal subtests, reflective of difficulty understanding social contexts and solving social problems (Koyama et al., 2009).

4.8. Family size and birth order

Researchers have examined gender differences in family characteristics such as birth order, family size, and so forth. However, Volkmar et al. (1993) cautioned that in familial studies, stoppage (i.e., not having more children after the birth of a child with a disability) may be higher in females due to greater ID, resulting in fewer siblings and underestimation of risk in siblings of females. Tsai et al. (1981) found females with ASD were more often first-born, only child, and were from smaller families. Pilowsky et al. (1998) found no significant gender differences in parental age at birth, birth order, or number of siblings. In individuals with ASD and nonverbal IQ above 60, Lord, Mulloy, Wendelboe, and Schopler (1991) found that females with ASD were from smaller families, and were more likely to be first-born whereas males with ASD were more likely to be first- or fourth-born or later. In a more recent larger sample familial aggregation study, Goin-Kochel et al. (2007) found no gender differences in family size of individuals with ASD.

4.9. Neurological, genetic, and medical comorbidity

Researchers have examined gender differences as related to pre-, peri-, and post-natal complications, birth defects, dysmorphic features, identified syndromes, and epilepsy. Tsai et al. (1981) found greater evidence of neurological impairment in females with ASD, such as abnormal EEGs, history of epilepsy, evidence of brain damage on Rutter and Lockyer's (1967) criteria, and enuresis. However, they did not account for the gender disparity in ID. Research in the area of comorbid neurological, genetic, and medical factors in ASD has since continued. Some researchers have since proposed subgroups of ASD based on these factors. Following is a review of the literature base related to gender differences in ASD in pregnancy and birth complications, birth defects, dysmorphic features, identified syndromes, and epilepsy.

Gender differences in pre-, peri-, and post-natal complications in individuals with ASD have been examined. Several researchers have found no significant gender differences in pre-, peri-, and post-natal complications in individuals with ASD (Gillberg & Gillberg, 1983; Mason-Brothers, Ritvo, Guze, & Mo, 1987; Zwaigenbaum et al., 2002). However, results are complicated by the small number of females and the presence of ID (Lord et al., 1991). In individuals with ASD and nonverbal IQ above 60, Lord et al. (1991) obtained similar results (no significant gender differences). In contrast, in a sample of 23 males and 23 females with IQ above 70, Holtmann et al. (2007) found that females had more pre-, peri-, and post-natal complications, but no differences in neurological soft signs. Finally, Schendel and Bhasin (2008) found that girls with low birth weight had a significant fourfold increased risk for ASD and ID, but not for ASD alone.

Miles et al. (2005) have classified cases of "complex autism" versus "essential autism" and examined gender differences. Complex cases were classified by having more dysmorphic features and/or microcephaly, and comprised all 11 cases in this study with an identified syndrome (i.e., chromosomal; single gene disorders such as tuberous sclerosis and Sotos; fetal valproate exposure) (Miles et al., 2005). Miles et al. (2005) found a higher sex ratio in essential compared to complex autism (6.5:1 versus 3.2:1). In addition, more individuals with essential autism had a family history of ASD, siblings with ASD, higher IQ, and regression at onset (Miles et al., 2005). Conversely, more individuals with complex autism had seizures and an abnormal EEG and brain MRI (Miles et al., 2005). In an earlier study, Miles and Hillman (2000) found comparable results in that the male to female ratio decreased with physical anomalies and abnormal brain MRIs. Specifically, compared to an overall sex ratio of 4.2:1, the sex ratio was significantly lower for those with both abnormal morphology and brain MRI (2.1:1 versus 23:1), as well as for those with abnormal morphology alone (1.7:1 versus 7.5:1) (Miles & Hillman, 2000). Six cases (1 female) in this study had genetic syndromes (i.e., ring chromosome 8, del 8q22, der 15, Sotos, tuberous sclerosis) (Miles & Hillman, 2000).

In a population-based study in Atlanta, Georgia, Schendel, Autry, Wines, and Moore (2009) examined major birth defects (e.g., central nervous system/eye, cardiovascular, genitourinary, musculoskeletal, chromosomal syndromes, etc.) in ASD in relation to gender differences. Inconsistent with Miles and Hillman's (2000), Miles et al.'s (2005) findings, sex ratios were higher in children with ASD and major birth defects (6.8:1) compared to the overall ASD sex ratio of 3.8:1. However, of those with major birth defects, the sex ratio was lower in those with a DD (i.e., ID, cerebral palsy, vision loss) in addition to ASD compared to ASD only (6.3:1 versus 8:1), though it is notable that few participants had birth defects and ASD without another DD (Schendel et al., 2009).

Amiet et al. (2008) conducted a meta-analysis of epilepsy in ASD as related to ID and gender. Females had an increased relative risk of epilepsy, and the sex ratio of ASD was higher in individuals without epilepsy (3.5:1) than with epilepsy (close to 2:1). The prevalence of epilepsy was higher for individuals with ID (Amiet et al., 2008). Follow-up studies of adults diagnosed with ASD in childhood have shown higher rates of epilepsy in females (Billstedt et al., 2007; Danielsson et al., 2005), and epilepsy has been shown to be associated with the presence of greater intellectual and adaptive impairments (Danielsson et al., 2005).

4.10. Genetic models and linkage

Twin studies have been employed to evaluate gender differences in models examining the contribution of genetic and both shared and unique environmental factors to ASD. In a general population study using the SRS, Constantino and Todd (2003) found no significant gender differences in the model. Similarly, Mazefsky, Goin-Kochel, Riley, and Maes (2008) did not find model differences by gender in an ASD only sample using the ADI-R. In contrast, in a primarily general population sample, Ronald et al. (2006) found gender differences in the model using the CAST. Using multiple measures of social, behavioral, and cognitive measures as well as the CAST in the general population, Loat and colleagues (Loat, Asbury, Galsworthy, Plomin, & Craig, 2004; Loat et al., 2008) found higher heritability estimates in males, but hypothesized this was more indicative of X-linked quantitative trait loci. In summary, results have been inconsistent in the few studies which have been conducted, and these studies have varied widely in methodology, namely the population and instruments employed. Finally, as mentioned previously, Nishiyama et al. (2009) did not find significant gender differences in genetic and environmental factors in the relationship between autistic traits and IQ.

Several researchers have found differential results of linkage studies based on gender. Sex-specific linkages have been found on chromosomes 17 (Cantor et al., 2005; Duvall et al., 2007; Stone et al., 2004; Strom et al., 2009), 7 (Lamb et al., 2005; Schellenberg et al., 2006), 11 (Autism Risk Genome Project Consortium et al., 2007; Duvall et al., 2007; Schellenberg et al., 2006), and 15 (Autism Risk Genome Project Consortium et al., 2007; Lamb et al., 2005), as well as on chromosome 16 (Lamb et al., 2005), 4, 8, and 10 (Duvall et al., 2007), and 5 and 9 (Autism Risk Genome Project Consortium et al., 2007). In addition, Lamb et al. (2005) found parent of origin effects on chromosomes 7 and 9. Therefore, stratifying genetic linkage analyses based on gender and whether genes were inherited from the mother or father has yielded differential results on a number of chromosomes.

5. Etiology of gender differences in ASD

A wide range of hypotheses on the etiology of gender differences in ASD have been proposed, implicating a number of different mechanisms. Given the evidence for high heritability of ASD, the large majority of researchers turned to genetic hypotheses to account for the significant gender differences, and this is evident even in the initial early hypotheses put forth. This focus on genetics is consistent with the ASD literature base in general (Matson & LoVullo, 2009). Miles and Hillman

(2000, p. 251) declared "It is commonly acknowledged that in order to understand the genetic basis of autism, we will have to understand the male predominance." Other hypotheses have implicated gender differences in typically developing populations, brain lateralization, and hormonal influences. Finally, while most have focused on biological etiologies, some have noted environmental factors such as diagnostic issues and gender biases.

5.1. Multifactorial liability/threshold model

Tsai and colleagues (Tsai & Beisler, 1983; Tsai et al., 1981) applied the multifactorial genetic transmission hypothesis to account for gender differences in ASD. According to Tsai and colleagues, in this model, "liability" is a normally distributed underlying variable comprising all genetic and environmental factors relevant to the etiology. All people have some liability, but they do not become affected unless it exceeds a certain critical value (the threshold). Males have a lower threshold for brain dysfunction and less significant genetic "liabilities" are required for a male to end up with ASD. Females require a higher "dose" of genes to be impacted. Therefore, as the less frequently affected sex, females would have more severe deficits, more affected relatives, and more relatives with more severe deficits (Tsai & Beisler, 1983; Tsai et al., 1981). Tsai and colleagues (Tsai & Beisler, 1983; Tsai et al., 1981) found support for this model in that females with ASD had more first-degree relatives with cognitive/language impairments or ASD.

Further research has not yielded any support for this liability/threshold model. Risk for the broader autism phenotype has not been found to be higher in relatives of females with ASD (Bolton et al., 1994; Pickles et al., 2000; Szatmari et al., 2000). Boutin, Maziade, Merette, and Mondor (1997) did find more first degree relatives with cognitive disabilities (i.e., language delay, ID, learning disabilities) in females with ASD and an IQ less than 50; however, in their sample, there were no gender differences in IQ. Pickles et al. (2000) did not find significant differences in severity or type of phenotypic expression in relatives by sex of the proband, nor were there elevated rates on the mother's side for male probands. In a recent large sample study, Goin-Kochel et al. (2007) did not find an increased risk of ASD in relatives of females with ASD, even when controlling for IQ. Goin-Kochel et al. (2007) concluded that there is a lack of support for increased genetic liability for ASD in families of females with ASD, and that earlier findings (Tsai & Beisler, 1983; Tsai et al., 1981) may be accounted for by lower IQ in females. Consistent with Goin-Kochel et al. (2007) conclusion, in multiplex families, Banach et al. (2009) did not find a significant difference in IQ, severity of autistic symptoms, or adaptive social and communication functioning in male siblings with ASD based on whether they had a brother versus a sister with ASD (with the exception of slightly greater socialization impairment in males with ASD with a brother with ASD, which is in the opposite direction predicted by the model).

5.2. Genetic variability

Wing (1981) applied Taylor and Ounsted's (1972) hypotheses about gender differences in developmental disabilities to ASD. Taylor and Ounsted (1972) reported that a wide variety of disabilities (e.g., Down's syndrome, cerebral palsy) have a higher prevalence in males, and those with the lower prevalence tend to be more severely impaired. Taylor and Ounsted (1972) also hypothesized that higher prevalence and less severity in males may be due to their greater genetic variation in the majority of measurable characteristics. Wing (1981) noted that, therefore, more males may show mild ASD features as a direct result of this genetic variability, while females may show these features only as a result of some type of pathology.

This model would predict higher rates of identifiable organic conditions in females compared to males with ASD. In support of this, Wing (1981) found that identifiable organic conditions were more frequently associated with profound ID in girls versus severe/moderate ID in boys. However, Tsai and Beisler (1983) examined the percentages and rates of organic conditions based on Wing's (1981) data, and found them similar overall in boys and girls (56% and 65%, respectively). When IQ was below 50, rates for boys and girls (67% and 68%) were similar (Tsai & Beisler, 1983; Wing, 1981). In participants with IQ above 50, boys had more identifiable organic conditions (27% versus 0%); however, only one girl was included (Tsai & Beisler, 1983; Wing, 1981). Finally, inconsistent with Wing's (1981) prediction, Schendel et al. (2009) found higher sex ratios in children with ASD and major birth defects; however, the ratio was lower in those with a ASD and ID compared to ASD only.

Wing's (1981) genetic variability hypothesis has not been further researched directly. However, researchers have expanded upon the notion of greater genetic variability in males in relation to epigenetic hypotheses (see X-inactivation/X-linkage and X-linked male extremes hypotheses below). Rutter et al. (2003) pointed out that genetic variability has been posed as an explanation for a number of disorders, though without substantial systematic research evidence. Regarding Wing's (1981) hypotheses about gender differences in pathology and ID in ASD, some related data, albeit limited, has emerged. This area of research is impacted by the type of pathology and related ID, rare conditions resulting in small sample sizes, and sex linked genetics. In children without physical anomalies and/or an identified syndrome or etiology (essential versus complex autism), Miles et al. (2005) found more males compared to females, higher IQ, and more ASD relatives. Based on this data, Beaudet (2007) noted that the gender ratio in cases with identified genetic mutations is likely equal. In contrast, Schendel et al. (2009) found a higher sex ratio in children with ASD and major birth defects.

5.3. Language and visuospatial skills

Wing (1981) described another hypothesis of gender differences in ASD based on available research at that time on gender differences in typically developing populations. She quoted Asperger (1944) describing the syndrome as "an extreme

variant of male intelligence and male character" (Wing, 1981, p. 135). Wing (1981) reported that in the general population, females have better language skills, and poorer visuospatial and math skills. Males may be more susceptible to communication deficits such as those in ASD, but more likely to have useful visuospatial abilities (Wing, 1981). Females may be less vulnerable to communication deficits, but those with ASD may have fewer compensating visuospatial skills and be more likely to have profound ID (Wing, 1981). Wing (1981) further noted that visuospatial skills may be implicated in developing repetitive routines involving manipulating objects.

Wing (1981) did point out data available at the time which were inconsistent with this hypothesis. First, differences in visuospatial and language skills are seen in adolescence in comparison to ASD symptoms emerging in infancy/early childhood. Second, although speech and language disorders are more frequent in boys, developmental receptive language disorder, which has overlap with ASD, is low in frequency for both boys and girls. Finally, higher functioning individuals with ASD score higher on verbal versus performance subtests on the Wechsler intelligence scales (though this may reflect rote memory and not understanding), and have poor coordination. Wing (1981) also noted that it has not been fully established that typically developing girls have superior social interaction skills.

Gillberg, Winnergård, and Wahlström (1984) expanded upon Wing's (1981) hypothesis, suggesting a link between autism and the sex chromosomes based on a case with XYY syndrome. These authors (1984, p. 353) cited Wing (1981) as hypothesizing that autism "might result from the pathological exaggeration of typically male behavioral traits." Visuospatial skills and some ASD symptoms (e.g., insistence on sameness, restricted interests, preoccupation with objects) could be characterized as exaggerations of male characteristics (Kopp & Gillberg, 1992). Conversely, communication impairments in ASD could be characterized as an exaggeration of male language development (i.e., slower and more vulnerable), and social communication impairments as an area typically less well-developed in males (Kopp & Gillberg, 1992). In line with Wing's (1981) association of autism with too much male or insufficient female influence, Gillberg et al. (1984) cited possible links between autism and excess male chromosome material (as in XYY syndrome or long Y chromosomes) or a deficiency in female chromosome material (as in fragile X and Lesch-Nyhan).

Two researchers evaluated Wing's (1981) hypothesis. Lord et al.'s (1982) results varied depending on whether IQ was accounted for. Boys did perform better than girls on eye–hand integration and perceptual tasks, though not when IQ was covaried. These skills may reflect developmental differences for both genders, as older children did better on these tasks (Lord et al., 1982). Regardless of IQ, boys exhibited more unusual visual responses than girls. When IQ was covaried, boys also demonstrated more routinized and stereotypic play. Finally, no gender differences emerged in affect and relating to people, nor receptive language with IQ covaried (Lord et al., 1982). With IQ above 60, McLennan et al. (1993) found males did show greater deficits in early social and communicative behavior, though this was reversed in older age groups. No gender differences were found in restricted, repetitive, stereotyped behaviors (McLennan et al., 1993), contrasting Lord et al.'s (1982) findings.

5.4. Lateralization of brain function

Lord et al. (1982) derived hypotheses based on available research at the time relating to brain function in the general population. As reported by Lord et al. (1982), language deficits have been attributed to left hemisphere damage, while perceptual skills suggest intact right hemispheric functioning. Females have been shown to have less lateralization (i.e., smaller differences in left–right hemisphere function). Applied to ASD, in females, more extensive bilateral brain damage would be needed to produce specific deficits as in ASD. In contrast, for males, more limited dysfunction or smaller lesions in a specific area may be sufficient to result in ASD. Lord et al.'s (1982) reported that their findings of lower performance across cognitive measures in females could be interpreted as evidence for more extensive brain dysfunction in females with ASD.

5.5. Extreme male brain (EMB) theory

Baron-Cohen and Hammer (1997) argued that autism is an extreme form of the male pattern of neurodevelopment. They linked this idea back to Asperger's (1944) writings describing how "the autistic personality is an extreme variant of male intelligence" (Frith, 1991, p. 84). The EMB theory proposes that ASD is an extreme form of the male brain, where empathizing is hypo-developed and systemizing is hyper-developed (Baron-Cohen, 2002). Empathizing (folk psychology) refers to a drive or capacity to identify others' emotions (e.g., theory of mind) and thoughts and respond with an appropriate emotion, while systemizing (folk physics) refers to a drive or capacity to analyze variables in a system, derive underlying rules governing a system, and construct systems in order to predict lawful events (Baron-Cohen, 2002; Baron-Cohen & Hammer, 1997). Baron-Cohen (2002) asserted that systemizing predicts weak central coherence (i.e., focus on details as opposed to global information processing) in ASD. Baron-Cohen (2008) asserted that hypersystemizing can explain preference for and success in predictable/lawful systems (e.g., math, spinning objects, calendar dates, engines) in ASD, as well as difficulties (e.g., resistance to change) in the unlawful social world of human behavior. Baron-Cohen and colleagues (Baron-Cohen, 2002, 2008; Baron-Cohen & Hammer, 1997; Baron-Cohen, Knickmeyer, & Belmonte, 2005) reported evidence in the general population of strengths in females in empathizing (e.g., turn taking, body language, cooperative and emotional conversation, early eye gaze), and in males in systemizing (e.g., occupations, tasks involving matching, assembly, mental rotations, map reading), while individuals with ASD show impairments in empathizing (e.g., false belief tasks, emotion recognition) and strengths in systemizing (e.g., calculation, memorization, attention to detail, picture-sequencing). Though these differences

have been found, there was still considerable overlap, effect sizes were variable, and they reflect population and not individual differences (Baron-Cohen, 2008).

Baron-Cohen has further proposed that exposure to fetal androgens are involved in the masculinization of the brain (Baron-Cohen, 2002; Baron-Cohen & Hammer, 1997; Baron-Cohen et al., 2005). This is related to earlier writings (e.g., Geschwind & Behan, 1982; Geschwind & Galaburda, 1985; Hines & Shipley, 1984; Leboyer, Osherson, Nosten, & Roubertoux, 1988) concerning lateralization of brain function and fetal androgen exposure. In support, Baron-Cohen and colleagues (Baron-Cohen & Hammer, 1997; Baron-Cohen et al., 2005) cited additional research linking male gender and ASD with left-handedness, brain differences, and lower 2D:4D (i.e., ratio between length of 2nd and 4th digit as proxy for first trimester testosterone), and masculine traits and ASD traits in individuals with congenital adrenal hyperplasia (CAH; causes excess adrenal androgen production) (e.g., Knickmeyer et al., 2006). Much debate has ensued surrounding this theory and how to evaluate it (Auyeung et al., 2009; Barbeau, Mendrek, & Mottron, 2009; Baron-Cohen, Auyeung, Ashwin, & Knickmeyer, 2009; Falter, Plaisted, & Davis, 2008a, Falter, Plaisted, & Davis, 2008b; Klin, 2009; Knickmeyer, Baron-Cohen, Auyeung, & Ashwin, 2008). Carter (2007) implicated arginine vasopressin (which is androgen-dependent) in the development of ASD traits in males; and further, oxytocin (estrogen-dependent) as protective to females. Yamasue, Kuwabara, Kawakubo, and Kasai (2009) implicated oxytocin, hypothesizing a role in social reciprocity and brain regions implicated in social behaviors. Researchers have recently emphasized additional mechanisms as well (i.e., epigenetics), which may be impacted by a multitude of environmental and biological factors, but also occur independent of hormonal influences (Craig, Harper, & Loat, 2004; Davies & Wilkinson, 2006; Gabory, Attig, & Junien, 2009; Skuse, 2000). These epigenetic mechanisms will be reviewed following.

5.6. X-chromosome epigenetics

Given the pronounced sex ratio found in ASD, traditional explanations have been proposed and explored somewhat (e.g., X-linked recessive inheritance, sex limited or sex influenced expression, multifactorial inheritance, death in females, genetic heterogeneity; Miles & Hillman, 2000), though none have fully panned out (Schanen, 2006). While some findings suggest X-chromosome involvement (Jacquemont et al., 2006; Jamain et al., 2003; Klauck et al., 2006; Laumonnier et al., 2004; Liu et al., 2001; Marshall et al., 2008; Shao et al., 2002; Thomas et al., 1999; Vincent et al., 2005), no consistent X-chromosome cause has been identified excluding Rett's disorder (O'Roak & State, 2008). Given this complexity, researchers have implicated epigenetic theories with evolutionary components (Marco & Skuse, 2006). Epigenetic processes can impact gene expression without changing DNA sequence (Delcuve, Rastegar, & Davie, 2009). Skuse (2006) described a number of epigenetic ways X-linked genes could be implicated in gender differences (e.g., X-inactivation, differential expression of X-linked genes based on chromosomal and gonadal sex, and genomic imprinting).

5.6.1. Imprinting

In imprinting, alleles are differentially marked for expression or silencing, which depends on which parent genes are inherited from. As an example, Prader-Willi syndrome and Angelman syndrome were the first identified disorders in humans involving imprinted genes (Horsthemke & Buiting, 2008). In addition, Rett's disorder is caused by a mutation in MeCP2 (Amir et al., 1999), a gene involved in imprinting regulation (LaSalle, 2007).

Skuse (1999, 2000) and Skuse et al. (1997) proposed the imprinted-X liability threshold model based on findings in females with Turner's syndrome (monosomy X). Skuse et al. (1997) found that females who had inherited the X from the father (verses the mother) had superior social-communicative skills. The imprinted-X liability threshold model holds that the threshold for expression of ASD symptoms is influenced by an imprinted genetic locus on the X, which influences development of skills needed for social communication. This locus is silent in the one X males get from the mother. In males, having a single X reduces the threshold of ASD phenotypic expression. Females have a higher threshold because they have a second paternal X in which the locus is expressed. The model proposes that genetic vulnerability is primarily due to effects from autosomal loci, and ASD symptoms largely result from genetic or environmental influences independent of the sex chromosomes (Skuse, 1999, 2000; Skuse et al., 1997). Donnelly et al. (2000) presented an additional case of a female with autistic disorder, Turner's syndrome, and a maternally inherited X-chromosome. Thomas et al. (1999) presented eight females (three with autistic disorder) with deletions on the short arm of the X. In contrast, in female probands, Pickles et al. (2000) did not find higher rates of the broader autism phenotype in paternal grandmothers or daughters of paternal uncles. In Turner's syndrome, researchers have investigated Skuse's hypothesis related to memory (Bishop et al., 2000), ADHD (Russell et al., 2006), physical/medical variables and academic achievement (Sagi et al., 2007), and mouse models (see Lynn & Davies, 2007).

Evolutionary models have been proposed as to why imprinting may have evolved. Shaner, Miller, and Mintz (2008) proposed that imprinting serves to alter the fitness sensitivity of a parent-selected fitness indicator (i.e., early social/communicative behaviors), due to resource allocation needed for sons by mothers. Badcock and Crespi (Badcock & Crespi, 2006; Badcock & Crespi, 2008; Crespi & Badcock, 2008) hypothesized an evolutionary struggle between parents based on cost/benefit during early and later development; and that ASD (i.e., mechanistic, male brain) is the diametric opposite of psychotic spectrum conditions (schizophrenia, bipolar, major depression; mentalistic, female brain), which are of more paternal versus maternal benefit, respectively. Debate has ensued surrounding this theory (see commentaries and replies in Crespi & Badcock, 2008).

5.6.2. X-inactivation/X-linkage hypothesis

Loat et al. (2004) and Loat et al. (2008) proposed the presence of quantitative trait loci (QTL) on the X-chromosome for social, behavioral, and cognitive traits found in ASD. In addition, Loat et al. (2008) proposed that gender differences in ASD arose due to X-inactivation (see Craig et al., 2004; Skuse, 2006). In males, genes subject to random X-inactivation will be fully expressed because they have a single X (Skuse, 2006). However, some genes escape inactivation and some do not have a Y homologue, resulting in two active copies in females versus one in males (Craig et al., 2004). Males may lack a functional copy on the Y for X-linked genes that escaped inactivation (Skuse, 2006). Also, inactivation may be skewed either by chance or as a result of X mutations (Craig et al., 2004). Loat et al. (2004) and Loat et al. (2008) hypothesized that in monozygotic (MZ) twins, female twins would be less similar on these X-linked traits due to random X-inactivation. Conversely in dizygotic (DZ) twins, female twins would be more similar on these traits, due to the presence of an active paternal X in half of the cells, compared to males having either the mother's maternal or paternal X (Loat et al., 2004; Loat et al., 2008).

Some evidence has been found in support of the X-inactivation/X-linkage hypothesis. Loat et al. (2004) found stronger correlations in MZ male compared to female twins for prosocial behavior at 2 years, verbal ability at 3 years, and peer problems at 4 years of age. Regarding DZ twins, female twins were more similar in the areas of prosocial behavior and verbal ability at 3 years (Loat et al., 2004). Further, Loat et al. (2008) found evidence for the same pattern for teacher reported prosocial and problem behavior at 7 years, and parent reported social impairments (CAST) at 8 years. Female MZ twins were less similar in hyperactivity and problem behavior, while female DZ twins were more similar on the CAST composite and communication and non-social domains (Loat et al., 2008). Trends of less similarity in MZ female twins were found in the areas of peer problems, academic achievement, language achievement, and nonverbal IQ (Loat et al., 2008). In a primarily general population sample, Ronald et al. (2006) found significantly higher MZ twin correlations for social impairments and overall ASD symptoms in males, while female MZ twin correlations were significantly higher in the area of restricted, repetitive behaviors and interests (CAST). In an ASD population, Mazefsky et al. (2008) found a trend towards higher correlations for both MZ and DZ twins in males on nonverbal communication and social dysfunction (ADI-R).

5.6.3. X-linked male extremes

In the general population, males exhibit greater variance than females for many traits (e.g., IQ) and thus are overrepresented at the extremes of distributions (e.g., Hedges & Nowell, 1995; Johnson, Carothers, & Deary, 2008; Lehre, Lehre, Laake, & Danbolt, 2009). The X-chromosome contains a high density of genes important for brain development and reproduction, and ID is approximately three times more often related to genes on the X versus autosomes (Zechner et al., 2001). These genes for IQ on the X may have evolved due to selection in males by females (Zechner et al., 2001). Regarding extremes, in females, X-linked gene expression is averaged out across cells via X-inactivation (Craig et al., 2004; Lehre et al., 2009). In contrast, males exhibit extreme X-linked phenotypes, due to impact of X-linked genes without a Y homologue (Craig et al., 2004; Skuse, 2005, 2006; Zechner et al., 2001). Skuse (2005, 2006) described how males are more impacted by these X-linked traits (e.g., intelligence, social cognition, emotion regulation), resulting in more exceptional abilities in some areas, but more mental impairments due to mutations.

Some researchers have examined gender differences in variability in ASD traits. As discussed earlier, across the lifespan in the general population, males exhibit greater autistic traits. In addition, studies have found gender distinct distributions, as well as larger standard deviations in males (Auyeung et al., 2008; Baron-Cohen et al., 2001; Constantino & Todd, 2003; Posserud et al., 2006; Williams et al., 2008). In contrast, in twins 2–4 years, Loat et al. (2004) found similar gender variances for traits (i.e., anxiety, prosocial behavior, hyperactivity, conduct problems, peer problems, and cognitive ability).

5.6.4. Skewed X-chromosome inactivation

Researchers have investigated non-random, or skewed, X-chromosome inactivation. In an initial investigation using peripheral blood cells, Talebizadeh, Bittel, Veatch, Kibiryeva, and Butler (2005) found that skewed X-inactivation was more common in females with autism than without autism, and was more heritable in females with autism compared to general population rates. In contrast, Gong et al. (2008) did not replicate this. Using frontal cortex and blood samples, Nagarajan et al. (2008) did not find more frequent X-inactivation skew in females with autism or mothers of males with autism. However, further research is needed using a variety of samples and methodologies (Nagarajan et al., 2008). Finally, the role of X-linked genes which escape inactivation in the etiology of gender differences in ASD has not been explored (Gong et al., 2008).

5.6.5. Mosaic X-chromosome aneuploidy

Iourov, Vorsanova, and Yurov (2006) and Iourov, Yurov, and Vorsanova (2008) hypothesized that the sex ratio in ASD was the result of an abnormal number (aneuploidy) of X-chromosomes in some cells (mosaicism) in the brain. One study found that unexplained autism in males was associated with low-level mosaic aneuploidy in peripheral blood cells (Yurov et al., 2007).

5.7. Sporatic and inherited genetic models

Researchers have discussed gender differences in ASD as related to sporadic (simplex) versus inherited or familial (multiplex) models. These models have been examined in relation to essential (idiopathic) versus complex (syndromic) autism (Miles et al., 2005), and inherited versus *de novo* copy number variations (CNV; non-inherited sequence changes in

sections of DNA; Jacquemont et al., 2006; Marshall et al., 2008; Sebat et al., 2007; Zhao et al., 2007). Beaudet (2007) discussed Miles and Hillman's (2000), Miles et al.'s (2005) findings along with recent findings of *de novo* CNV (Jacquemont et al., 2006; Sebat et al., 2007). Beaudet (2007) estimated that only half of these *de novo* mutations have been identified. Furthermore, the gender ratio in cases with identified mutations is likely equal, excluding X-linked disorders (Beaudet, 2007). This leaves a large number of people with ASD without identified DNA sequence changes, a group which is predominately male, with higher IQs and normal features in appearance (Beaudet, 2007). Thus, overall, Beaudet (2007) proposed a mixed etiology model for autism, where each case could have genetic or epigenetic mutations which could be *de novo* or inherited. Similarly, Zhao et al. (2007) proposed "a unified genetic theory for sporadic and inherited autism," comprised of two groups. The vast majority of ASD occurs in simplex (low-risk or sporadic) families resulting from *de novo* mutations which have poor penetrance in females (i.e., they have the mutation but do not express the clinical phenotype) and high penetrance in males (Zhao et al., 2007). A small minority of ASD occurs in multiplex (high-risk or inherited) families, where female carriers transmit the mutation dominantly, and the risk to male offspring is 50/50 (Zhao et al., 2007). Lastly, Banach et al. (2009) found lower IQ in females with ASD from simplex but not multiplex families. These authors pointed out that *de novo* CNV have been found to be more common in simplex versus multiplex families and may be more common in females with ASD (Marshall et al., 2008; Sebat et al., 2007). Banach et al. (2009) purported that there may be a greater frequency of genomic risk factors in simplex families, particularly in females, associated with both ASD and lower nonverbal IQ, versus males having a more familial form of ASD and higher IQ. This line of research points to impact of stratification of ASD samples in genetic research based variables such as gender, simplex or multiplex families, presence of other conditions (e.g., genetic syndromes, birth defects, dysmorphic features, ID, medical conditions, language impairment), and ASD symptom areas (Folstein, 2006; Happé & Ronald, 2008; Happé et al., 2006; Skuse, 2007; Waterhouse, 2008).

5.8. Diagnostic issues with gender

Kopp and Gillberg (1992) hypothesized that ASD is underdiagnosed in females because the diagnostic criteria and behavioral phenotype have been derived from typical male cases. Thus, the phenotype may differ in girls. Kopp and Gillberg (1992) contrasted the behavioral presentation of six girls with autism to that typical of males with autism. Socially, in contrast to "extreme autistic aloneness," these girls "tended more towards 'clinging' to other people, imitating their speech and movements without a deeper understanding of the silent laws of ordinary social interaction, inability to understand the emotional content of facial expressions as they show in real-life interaction, treating people as objects and only brief periods of aloofness" (Kopp & Gillberg, 1992, p. 96). Some presented similar to Wing's (1989) "active but odd" classification. They exhibited extreme echolalia and repetitive questioning. In contrast to preoccupation with objects and circumscribed interests in boys, the girls demonstrated an "overall lack of initiative" (Kopp & Gillberg, 1992, p. 97). Gillberg (2007) noted that typically developing girls are less hyperactive and aggressive, behaviors associated with ASD and reason for referral. Kopp and Gillberg (1992, p. 97) purported that difficulties in boys may be difficult to ignore or dismiss, as boys "may be both aggressive and domineering and show strong initiative in their insistence on sameness." Gillberg (2007) also noted that typically developing girls speak sooner and more frequently, and greater language and social imitation skills may mask a core deficit (e.g., empathy) in girls (Kopp & Gillberg, 1992). Finally, girls may not exhibit visual self-stimulation behaviors typical of autism because they lack exceptional visuospatial skills (Kopp & Gillberg, 1992).

A number of diagnostic barriers may ensue for girls with ASD. Only the most severe cases may be referred for evaluation (Gillberg, 2007). They may receive vague diagnoses (e.g., learning disorder) or other diagnoses such as obsessive-compulsive, conduct, paranoid, depressive, personality, or eating disorders (Gillberg, 2007; Kopp & Gillberg, 1992). As described previously, females with significant ASD impairments have experienced misdiagnosis, delayed diagnosis, greater difficulty in the diagnostic process, and lack of diagnosis.

5.9. Gender biases

Some researchers (Carter et al., 2007; Holtmann et al., 2007; McLennan et al., 1993) have discussed possible environmental/social gender biases in ASD (e.g., parent report, parent expectations, upbringing, sex role models, and socialization). In daughters, parents may expect more social and communicative behavior (Carter et al., 2007; McLennan et al., 1993), impacting both their behavior (e.g., more prompts to daughters to behave in an affectionate and social manner) and, as informants, interpretation (e.g., interpreting behavior of daughters to suggest more social interest and motivation; McLennan et al., 1993). Similarly, parents may perceive daughters as having greater impairments resulting in a larger discrepancy between expectations and actual behavior (Holtmann et al., 2007). In toddlers, Carter et al. (2007) found parents rated girls as having lower competence (e.g., empathy) not evident on observation (ADOS). Finally, the social and communicative nature of peer relationships in females may be more demanding (McLennan et al., 1993).

6. Conclusion

For disorders such as ASD that have such a pronounced gender difference, Rutter et al. (2003) pointed out that there is a dearth of research addressing a variety of key issues such as the validity of diagnostic criteria for males and females and gender issues in assessment instruments (Koenig & Tsatsanis, 2005; Rutter et al., 2003). The large body of research literature

concerning the assessment, treatment, and etiology of ASD has been conducted with predominantly male samples (Bell, et al., 2005). Hence, extrapolating this to females with ASD poses concerns (Koenig & Tsatsanis, 2005). Rutter et al. (2003) also pointed out the need for evaluation of gender differences with regard to developmental variables, chronicity and recurrence, and comorbidity and severity.

Despite the long observed male predominance in ASD, there is a paucity of research examining gender differences. A host of methodological issues have plagued this area and contributed to inconsistent findings. Given the large male to female ratio, ascertainment of female participants and thus small female sample sizes has been an obstacle (Koenig & Tsatsanis, 2005). Additionally, a major issue has been how to handle the IQ disparity (Volkmar et al., 1993), which can produce widely varying results (e.g., Lord et al., 1982; Volkmar et al., 1993). Volkmar et al. (1993) emphasized that it is unclear if it is appropriate to control for IQ, as the relationships between IQ, ASD, and gender have not been fleshed out. Additional methodological issues include changes over time in the diagnostic criteria and categories, heterogeneity in presentation, age ranges and developmental changes in symptom presentation, differences in samples (ascertainment bias, stringency of definitions, epidemiological versus clinical), and so forth (Carter et al., 2007; Lord & Schopler, 1985; Volkmar et al., 1993). Hence, the current knowledge base is scant, and additional research is needed. It is unclear how much of the gender disparity is an actual difference in prevalence and/or presentation or reflective of problems in the current system (Koenig & Tsatsanis, 2005). Furthermore, gender differences in severity of impairment related to autistic symptoms, cognitive ability, and adaptive skills in ASD have not been determined (Koenig & Tsatsanis, 2005). Future research should examine gender differences in ASD symptom presentation across a wide span of development, include comparison groups of both males and females without ASD, which is important given increasing evidence for the presence of autistic traits in the general population. Finally, a fine-grained analysis of ASD symptoms is warranted, considering emerging data of the fractionability of the triad of impairments.

Research in this area has significant implications informing assessment and intervention for females with ASD. Differences may manifest with regard to symptom domains, breadth of symptoms, symptom severity, developmental changes in symptom presentation, course, and so forth. This information is important clinically to improve identification and knowledge, and work towards addressing diagnostic pitfalls with females with ASD (e.g., validity of the diagnostic criteria, assessment instruments, comorbidity biases, informant biases in report, expectations, and socialization). In addition, gender differences related to intervention needs, prioritized areas, and potential targets for intervention may become evident. This information is important in both clinical and research realms regarding diagnosis and treatment. As there is a paucity of research, these data would serve to stimulate future research priorities in gender differences in ASD symptoms.

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