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ORIGINAL PAPER

Autism Spectrum Disorder Risk Factors and Autistic Traits in Gender Dysphoric Children

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Abstract Gender dysphoria (GD) and autism spectrum disorder (ASD) are associated. In 49 GD children (40 natal males), we examined ASD risk factors (i.e., birth weight, parental age, sibling sex ratio) in relation to autistic traits. Data were gathered on autistic traits, birth weight, parents' ages at birth, sibling sex ratio, gender nonconformity, age, maternal depression, general behavioral and emotional problems, and IQ. High birth weight was associated with both high gender nonconformity and autistic traits among GD children. Developmental processes associated with high birth weight are, therefore, likely to underlie the GD–ASD link either directly or indirectly. The present study is the first to provide quantitative data bearing on possible mechanisms that lead GD and ASD to co-occur.

Keywords Gender dysphoria · Autism spectrum disorder · Birth weight · Parental age · Sibling sex ratio

Introduction

Gender dysphoria (GD) and autism spectrum disorder (ASD) are rare conditions. In the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5) (American Psychiatric Association 2013), GD is characterized by distress that accompanies the incongruence between one's experienced or expressed gender and one's assigned gender. ASD is characterized by persistent deficits in social communication and social interaction as well as restricted and repetitive behavior, interests, or activities. Both conditions show low population prevalence rates with between 1 in 10,000 and 1 in 50,000 individuals exhibiting GD (Zucker and Lawrence 2009) and between 1 in 50 and 1 in 500 individuals exhibiting ASD (Blumberg et al. 2013; Fombonne 2005). Also, both conditions show biased male: female sex ratios ranging from approximately 2:1 to 4:1 (American Psychiatric Association 2013; Blumberg et al. 2013; Fombonne 2005; Zucker and Lawrence 2009). Despite being rare conditions characterized by distinct sets of diagnostic criteria, it is not uncommon for GD and ASD to co-occur.

Most literature regarding the link between GD and ASD consists of clinical case reports (e.g., Landén and Rasmussen 1997; Parkinson 2014; Williams et al. 1996); however, some quantitative data have begun to emerge. In one study, 6.4 % (7 of 108) of children and 9.4 % (9 of 96) of adolescents referred for GD were classified as having ASD based on the Diagnostic Interview for Social and Communication Disorders (de Vries et al. 2010). Similarly, a study of adults with GD found that 5.5 % (5 of 91) showed traits consistent with an ASD diagnosis (Pasterski et al. 2014). Both studies concluded that these prevalence rates were significantly higher than estimated population prevalence rates for ASD.

In addition, two studies have examined traits of ASD among individuals with GD relative to comparison groups. Using item responses on the Child Behavior Checklist (CBCL), VanderLaan et al. (2014b) examined intense/obsessional interests and repetitive behaviors, each of which are related to DSM-5 Point B criteria for ASD (American Psychiatric Association 2013).

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In a sample of 534 children clinically referred for GD, their siblings, and the CBCL clinic-referred and non-referred standardization samples, GD children showed elevated intense/obsessional interests relative to all other groups and elevated repetitive behaviors relative to the sibling and non-referred samples. In an adult sample, Jones et al. (2012) demonstrated that female-to-male transsexuals had more traits of ASD on a self-report measure compared to controls. These studies are, therefore, also consistent with the notion that the prevalence of ASD, or traits thereof, is elevated among individuals with GD.

Given this elevation, it is possible that traits of ASD contribute toward cross-gender behavior and identity among a subset of children clinically referred for GD. An alternative hypothesis is that some variable related to ASD might also underlie cross-gender behavior and identity albeit via a different mechanism. Some research has been in line with these hypotheses. In one study, girls with ASD showed less female-typical play behavior, although a similar tendency toward sex-atypical play was not found among boys with ASD (Knickmeyer et al. 2008). In another study, Strang et al. (2014) compared cross-sex wishes—as reported on a single CBCL item—in a sample of 147 children referred for ASD to a non-clinical control sample and the CBCL non-referred standardization sample. By maternal report, ASD children were significantly more likely to exhibit such wishes.

Yet, even though ASD children were more likely to show cross-gender characteristics in these studies, it is unclear whether the play behavior or cross-sex wishes examined were indicative of the extreme and persistent gender nonconformity exhibited by children clinically referred for GD. Data suggesting that cross-gender behavior and identity are associated with early indicators of ASD among some subset of children clinically referred for GD would, therefore, provide a more convincing demonstration that these hypotheses are tenable. One viable approach for doing so is to examine traits of ASD and gender nonconformity in relation to ASD risk factors that are present early in development among children who are clinically referred for GD.

In a sample of children clinically referred for GD, the present study examined maternally reported gender nonconformity and autistic traits in relation to three ASD risk factors: birth weight, parental age at birth, and sibling sex ratio. Regarding birth weight, deviations from an average size at birth (i.e., small size or large size) are associated with an elevated risk of ASD, although the precise mechanisms responsible are unclear (Abel et al. 2013). Advanced parental age at birth is another risk factor for ASD (Lundström et al. 2010; Parner et al. 2012; Sandin et al. 2012), possibly because older parents are more likely to have accumulated genetic mutations or encountered toxic substances that affect gene expression, thus leading to ASD in offspring (Kondrashov 2012; Sandin et al. 2012). A testosterone-rich prenatal environment is a third risk factor for ASD (Knickmeyer et al. 2006) and a high male-to-female sibling sex ratio, which is a putative marker of elevated testosterone exposure in utero, is associated with ASD in children (Mouridsen et al. 2010). If any of these ASD risk factors are associated with autistic traits and gender nonconformity among children clinically referred for GD, then that would provide evidence consistent with hypotheses arguing that ASD has a direct or indirect association with the emergence of GD in children.

Method

Participants

This study utilized patient data from a chart review approved by a hospital research ethics board. Beginning in September 2009, information on autistic traits among children less than or equal to 12 years of age were systematically gathered by our specialty Gender Identity Service using a psychometrically validated parent-report instrument. Data were collected from 47 consecutive patients at the outset of clinical assessment for GD as well as 13 outpatients who had been assessed for GD previously and were continuing to attend the clinic for therapeutic services. Of these 60 cases, 11 were excluded for various reasons: the required maternal reports of all study variables were not completed in two cases; two cases exhibited a co-occurring disorder of sex development; one case was a twin and another was a triplet, which may have impacted birth weight; in four cases, the patients were adopted, in foster care, or under the guardianship of a child protection agency and information was not available on birth weight, biological parents' ages at birth, or biological sibling sex ratio; and birth weight information was missing for one case. Of the 49 remaining cases (40 natal males, 9 natal females) that were retained for analysis, the mean (SD) age at the time that the study measures were completed was 7.19 (2.71) years. Data were collected from 12 cases (11 natal males, 1 natal female) while they were outpatients and 37 cases (29 natal males, 8 natal females) at the time of the initial assessment. Whether cases were outpatients or not at the time the study measures were completed did not vary by sex based on Fisher's exact test, $p = .42$.

Measures

For all parent-report measures, the availability of maternal reports was more consistent across cases compared to

paternal reports. As such, the current study focused on maternal reports with the exception of one measure for one case (noted below). Paternal reports were used to assess inter-rater reliability wherever appropriate.

Autistic traits were assessed using the Social Responsiveness Scale (SRS; Constantino and Gruber 2005). The SRS is a 65-item parent-report questionnaire with a one-factor solution that captures social awareness, social cognition, social communication, social motivation, and repetitive behaviors. It is a well-validated instrument in that it distinguishes between samples of children with ASD, non-ASD clinical controls, and healthy controls. The SRS also distinguishes among subpopulations of ASD children, ranging from those with mild, high-functioning ASD to severe autism. SRS T scores $\geq$60 are defined as being in the clinical range and indicate the presence of autistic traits that are likely to create daily social interference. Whether a case was in the clinical range on the SRS based on maternal report was, therefore, the main outcome measure in the present study. For the present sample, maternal and paternal reports on the SRS were available for 28 cases and their T scores showed significant agreement, $r = .62$, $df = 26$, $p < .001$.

Gender nonconformity was assessed using the Gender Identity Questionnaire for Children (GIQC; Johnson et al. 2004). The GIQC is a 14-item questionnaire in which parents rate their child's preferences in domains such as the gender of preferred playmates, fantasy role-playing or dress-up play, preferred activities and toys, wishes to be the opposite sex, and feelings about sexual anatomy. The rating scale ranges from 1 (stereotypically opposite-sex) to 5 (stereotypically same-sex), but to ease data interpretation the present study reversed the scores such that higher scores reflected elevated gender nonconformity. The GIQC has a one-factor solution and, thus, mean ratings were used to create a gender nonconformity score. This measure provides good discriminant validity between GD versus control children and also distinguishes the magnitude of gender nonconformity within samples of children clinically referred for GD. Maternal and paternal reports on the GIQC were available for 36 cases and their scores showed significant agreement, $r = .56$, $df = 34$, $p < .001$. (Note: a maternal report for the GIQC was not available for one case and the paternal report was substituted.)

With respect to data on ASD risk factors, information on birth weight was available from hospital birth records for 32 cases. For the remaining 17 cases, parent-reported (maternal or paternal) birth weight was used. Parents reported birth weight in pounds and ounces or in grams. All birth weights were converted to kilograms to three decimal places. Hospital-record and parent-reported birth weight information were available for 25 cases and showed significant agreement, $r = .96$, $df = 23$, $p < .001$. This extremely high correlation, which is consistent with previous studies of the agreement between hospital records and parent-reported birth weight (e.g., Blanchard et al. 2002; Gayle et al. 1988; Gofin et al. 2000; O'Sullivan et al. 2000; Tomeo et al. 1999), indicates that the parent-reported birth weight used in the present study is reliable.

Parents' ages were routinely recorded as part of family background information gathering during clinical assessment. Maternal and paternal ages at the time of the child's birth were calculated by subtracting the child's age from each parent's age at the time of the assessment. Paternal ages were missing for three cases in which the father's identity was unknown.

Information on the numbers and ages of siblings were also routinely recorded as part of family background information gathering during clinical assessment. Because sibling sex ratio is a putative proxy of a testosterone-rich prenatal environment (Mouridsen et al. 2010), only siblings who shared the same mother with the patient were considered. Thus, full- and maternal half-siblings were considered in the calculation of the sibling sex ratio whereas paternal half-, step-, and foster-siblings were ignored. The sibling sex ratio was calculated as: (number of male siblings + .5)/(total number of siblings + 1). Thus, lower and higher values reflected female- and male-biased sibling sex ratios, respectively. Also, probands without siblings were retained and represented as having equal proportions of male and female siblings.

A number of control variables were also considered. Given the relevance of age to social skills development, the effect of the patient's age (in years to two decimal places) at the time the SRS was completed was evaluated. IQ scores based on the Wechsler Intelligence Test for Children, Fourth Edition (Wechsler 2003) were included to control for the effect of general intelligence on social skills. (Note: IQ testing was not completed for one case and the sample mean IQ of 111 was imputed to retain the case without biasing effects toward statistical significance.) To control for forms of psychopathology other than ASD (e.g., depression, anxiety) that might also impact social functioning, maternal reports on the CBCL were used. The CBCL is a gold-standard measure for general behavioral and emotional problems in children (Achenbach 1991). Maternal and paternal reports on the CBCL were available for 38 cases and their T scores showed significant agreement, $r = .50$, $df = 36$, $p = .001$. Maternal depression has also been associated with SRS scores (Bennett et al. 2012) and maternal depression was, therefore, taken into account using the mothers' self-reported Symptom Checklist-90-Revised T score on the Depression factor (Derogatis 1994).

Statistical Analyses

All statistical analyses were conducted using SPSS Version 20. Patients were divided into those who did versus did not

have clinically significant autistic traits as indicated by the presence versus absence of a clinical range score on the SRS. These two groups were initially compared on the control and focal variables using independent *t* tests. Also, zero-order correlations among the continuous variables were evaluated across the entire sample. These initial analyses identified relevant variables to consider in subsequent multiple logistic regression analyses comparing the two groups. The regression analyses assessed whether any focal variables that distinguished the groups based on the *t* tests still did so after the control variables were taken into account. The a priori prediction that ASD risk factors, gender nonconformity, and autistic traits would overlap was evaluated directly by examining the interaction between ASD risk factors and gender nonconformity toward the prediction of clinical-range autistic traits. A conventional *alpha* value of .05 was used for making decisions about statistical significance.

It is important to note that none of the patients in our sample exhibited markedly low birth weight (the lowest birth weight in the current sample was 2.27 kg). Thus, even though both small and large size at birth are associated with increased ASD risk (Abel et al. 2013), it was not possible to evaluate whether both low and high birth weight were associated with increased odds of exhibiting clinically significant autistic traits in this sample. Rather, the analyses presented below examined the linear effect of high birth weight on the presence of autistic traits.

Results

Based on maternal-report SRS *T* scores, 44.9 % ($n = 22$; 17 natal males, 5 natal females) of the 49 cases were in the clinical range. The probability of being in the clinical range did not vary by sex based on Fisher's exact test, $p = .71$. The mean (SD) *T* score was 71.05 (9.79) for those cases in the clinical range and 47.78 (5.06) for those in the non-clinical range. Thus, the children in the clinical range exhibited autistic traits ranging from mild to severe with moderate levels on average; the non-clinical range children showed scores that were consistent with unaffected populations (Constantino and Gruber 2005).

Table 1 presents descriptive statistics and summarizes the results of independent *t* tests. Patients in the clinical range were significantly older, had significantly lower IQ scores, had significantly more behavioral and emotional problems based on CBCL total *T* scores, had significantly higher birth weights, and showed significantly greater gender nonconformity. Table 2 presents the zero-order correlations among continuous variables across the entire sample. Of note given the focus of the present study was the significant positive correlation between birth weight and gender nonconformity.

Based on these group and correlation effects, a series of multiple logistic regression analyses were conducted in which the patient's age, sex (dummy coded as natal females = 0 and natal males = 1), IQ, and CBCL total *T* score were entered as control variables. Maternal Depression scores were not controlled given the lack of effects found for this variable (Tables 1, 2). Three separate models examined focal variables and their potential interaction with sex (Table 3). The first and second models showed that high birth weight and elevated gender nonconformity, respectively, were significant predictors of clinical-range autistic traits even after accounting for the control variables. The third model showed that an interaction of high birth weight and elevated gender nonconformity significantly predicted the presence of clinical-range autistic traits. Thus, this latter finding confirms the a priori prediction of an overlap between high birth weight, elevated gender nonconformity, and autistic traits.

Discussion

In a sample of children clinically referred for GD, the present study examined autistic traits in relation to gender nonconformity and three variables that serve as proxies for early-life exposure to ASD risk: high birth weight, advanced parental age, and high sibling sex ratio. These latter two risk factors were not associated with autistic traits or gender nonconformity; however, effects were found for birth weight. Even though both groups showed mean birth weights in the normal range, GD children with clinical-range autistic traits weighed 372 g (11.5 %) more at birth on average, corresponding to a large effect size (Cohen's $d = .76$). Relatively higher birth weight was associated with elevated gender nonconformity and these two factors in combination were associated with clinical-range autistic traits. Thus, relatively speaking, higher birth weight serves as a physical marker of ASD *in statu nascendi* among highly gender-nonconforming children clinically referred for GD. The present findings regarding birth weight were, therefore, consistent with hypotheses suggesting that traits of ASD are associated with the development of the extreme and persistent cross-gender behavior and identity that is characteristic of GD in children.

The present findings also highlight high birth weight as an important clue for helping refine hypotheses regarding the GD–ASD link. Elevated maternal weight prior to and/or during pregnancy might be especially relevant because it is associated with large size at birth (Haugen et al. 2014; Kirchengast and Hartmann 2013) and elevated cognitive and psychiatric problems in offspring (for review, see Van Lieshout 2013), including ASD (Dodds et al. 2011). Although information on maternal pre-pregnancy weight and weight gain during pregnancy were unavailable, the

Table 1 Comparisons of children according to whether they were in the clinical range for autistic traits

	Non-clinical range ($n = 27$)		Clinical range ($n = 22$)		t value	df	p value
	M	SD	M	SD			
Control variables							
Age	6.20	2.47	8.41	2.53	−3.09	47	.003
IQ	115.93	12.82	104.55	14.41	2.92	47	.005
CBCL total T score	53.30	7.30	68.55	7.44	−7.21	47	<.001
Maternal Depression T score	56.15	8.26	59.82	10.84	−1.35	47	.185
Focal variables							
Mother's age at child's birth	34.07	5.51	32.82	6.72	.72	47	.476
Father's age at child's birth[a]	36.00	5.07	35.20	5.61	.51	44	.615
Birth weight (kg)	3.22	.45	3.59	.52	−2.65	47	.011
Gender nonconformity	3.34	.68	3.69	.50	−2.02	47	.049
Sibling sex ratio	.52	.22	.45	.19	1.02	47	.312

[a] Father's age was missing for three cases (one non-clinical range case and two clinical range cases)

Table 2 Correlations among continuous variables across the entire sample

	1	2	3	4	5	6	7	8
1. Age	–							
2. IQ	−.417**	–						
3. CBCL total T score	.449***	−.261	–					
4. Maternal Depression T score	−.027	.020	.324*	–				
5. Mother's age at child's birth	−.204	.417**	−.018	−.112	–			
6. Father's age at child's birth	−.195	.187	−.045	−.038	.689***	–		
7. Birth weight (kg)	.052	.064	.307*	.176	.034	−.041	–	
8. Gender nonconformity	.140	−.039	.214	.185	−.080	−.124	.344*	–
9. Sibling sex ratio	.132	.055	.001	.172	−.007	−.144	.041	.079

* $p < .05$; ** $p < .01$; ***$p < .001$

CBCL and SRS data from the present sample were consistent with this literature. GD children with higher birth weights tended to show more behavioral and emotional problems on the CBCL as well as elevated autistic traits. Importantly, high birth weight was associated with autistic traits even after statistically controlling for general behavioral and emotional problems by covarying CBCL scores. Our results suggest, therefore, that high birth weight has a unique association with autistic traits that cannot simply be explained as part of a more general pattern of psychopathology.

Little is known about the precise mechanisms that link birth weight with ASD risk. Brain overgrowth in particular, as opposed to large size at birth in general, may be responsible. Infants later diagnosed with ASD show greater rates of growth in head circumference during the first year of life (Fukumoto et al. 2011). Furthermore, ASD has been associated with early-life (i.e., prior to age 4) overgrowth in several brain regions, including the amygdala, cerebellum, cingulate cortex, prefrontal cortex, and temporal lobe (for review, see Alley et al. 2014). The amygdala might be particularly relevant because enlarged size and functional abnormalities in the amygdala appear to contribute to deficits in social functioning (for review, see Chasson et al. 2011). Whether these brain regions contribute to GD in children remains to be examined.

It is possible that traits of ASD and/or their neurobiological underpinnings have a direct influence on the emergence of cross-gender behavior and identity. To begin with, the premise that early-onset traits of ASD can lead to a later-emerging GD is tenable given that high birth weight suggests an early predisposition toward ASD. VanderLaan et al. (2014b) suggested that such a developmental sequence could unfold if ASD-based intense/obsessional interests in cross-gender activities or objects gave rise to a cross-gender self-schema and identity. Social communication deficits may also contribute. Robinow (2009) suggested that neurobiological abnormalities associated with reduced

Table 3 Multiple logistic regression comparing clinical versus non-clinical range cases

	B	SE	*β*	*t* value	*p* value
Control variables					
Age	.005	.022	.03	.25	.805
Sex	.012	.131	.01	.10	.925
IQ	−.007	.004	−.21	−1.91	.062
CBCL total *T* score	.031	.005	.66	5.76	<.001
Model 1: birth weight					
Birth weight	.398	.174	.41	2.29	.027
Sex × birth weight	−.301	.206	−.83	−1.47	.150
Model 2: gender nonconformity					
Gender nonconformity	.752	.366	.93	2.06	.046
Sex × gender nonconformity	−.672	.377	−1.49	−1.79	.082
Model 3: birth weight × gender nonconformity					
Birth weight × gender nonconformity	.102	.041	.57	2.48	.017
Sex × birth weight × gender nonconformity	−.079	.046	−.64	−1.73	.091

social functioning in ASD, such as those found for frontal and temporal regions, might make it difficult for some children to acquire concepts regarding gender norms. Social communication deficits might, therefore, underlie the cognitive "lag" that many GD children exhibit in terms of their gender constancy development (Wallien et al. 2009; Zucker et al. 1999). Further, Strang et al. (2014) posited that social communication deficits limit a child's awareness of social cues in response to his or her gender role enactment. If such awareness was limited, a child may not adjust his or her behavior toward more stereotypically masculine or feminine behavior. In concert, these processes may increase the likelihood of cross-gender behavior and identity.

If ASD does influence the emergence of cross-gender behavior and identity in this manner, then the question arises as to why only a particular subset of children showing traits of ASD exhibit marked gender nonconformity. One possibility is that traits of ASD lead to gender nonconformity in a stochastic fashion whereby children with ASD form intense preoccupations with cross-gender activities or objects due to chance. Another possibility is that factors increasing the likelihood of GD are elevated among those ASD children who are gender nonconforming. Cross-gender behavior and identity has a familial (Gómez-Gil et al. 2010; VanderLaan et al. 2013a, b), possibly genetic (Alanko et al. 2010; Heylens et al. 2012), component. It is also associated with excesses of older brothers in natal males and excesses of older sisters in natal females (Blanchard et al. 1995; Schagen et al. 2012; VanderLaan et al. 2014a; Zucker et al. 1997). With respect to psychological correlates, GD is frequently comorbid with internalizing problems such as depression and anxiety (for review, see Zucker et al. 2014). Regarding this last point, in a sample of children with neurodevelopmental disorders (ASD or Attention-Deficit Hyperactivity Disorder), internalizing problems were indeed elevated among those who expressed cross-sex wishes compared to those who did not (Strang et al. 2014). Similarly, in the present study, those GD children with clinical-range autistic traits had elevated behavioral and emotional problems, as indicated by CBCL total *T* scores. Future research should, therefore, continue to consider whether these factors characterize the backgrounds of ASD children who exhibit marked gender nonconformity as well as those of GD children who exhibit traits of ASD.

Rather than ASD contributing to GD in a direct fashion as described above, an alternative hypothesis is that high birth weight is a proxy for some process that indirectly influences both gender nonconformity and traits of ASD. That is, high birth weight might be associated with ASD for reasons such as those noted above while its association with GD is due to some other circumstance(s). For example, high birth weight is inversely associated with prenatal testosterone exposure (Carlsen et al. 2006). In males, lower levels of prenatal testosterone exposure are associated with decreased gender-typical play behavior (Lamminmäki et al. 2012), possibly because low testosterone exposure leads to less masculinization and/or defeminization in neural regions that influence sexually dimorphic behavior. Thus, in natal males of relatively high birth weight, GD may be a consequence of lower prenatal testosterone exposure.

Because high birth weight is associated with lower testosterone (Carlsen et al. 2006), and lower testosterone is associated with greater female-typical play behavior in females (Lamminmäki et al. 2012), it seems unlikely that the GD–ASD link in females would be similarly owing to prenatal testosterone exposure. Instead, some alternate explanation should be sought. For example, research has shown male biases for both ASD (e.g., Blumberg et al. 2013; Dodds et al. 2011; Fombonne 2005) and relatively higher birth weight (e.g., Côté et al. 2003). When present in natal females, these traits may reflect a pattern of male-typical prenatal development. Indeed, higher birth weight in females has been associated with masculinized somatic features such as greater anogenital distance (i.e., the distance between the anus and the fourchette) (Avidime et al. 2011). If such masculinization extends to neural regions that underlie sexually dimorphic behavior, then that might help explain elevated gender nonconformity among high birth weight natal females with GD.

Future Directions

It is important to note that the various hypotheses described above to account for the GD–ASD link are not necessarily mutually exclusive. The processes related to these hypotheses may interact with one another. Another possibility is that each of these hypotheses applies to some subset of children who exhibit traits of ASD and GD. Future research may help discern which is the case.

Interestingly, our data showed a marginally significant interaction between birth weight, gender nonconformity, and sex in the prediction of autistic traits. Specifically, this interaction suggested that the relationship between birth weight, gender nonconformity, and autistic traits might be stronger among natal females. If so, then different processes might influence the GD–ASD link in natal males versus females. Alternatively, the GD–ASD link in natal males and females might be underpinned by the same or similar processes, but the magnitude of the effects of high birth weight on gender nonconformity and autistic traits might be greater among natal females. This speculation is based on a small sample of nine natal females clinically referred for GD and future research on larger samples of such females is needed before firm conclusions can be drawn.

In addition to examining the sexes separately, future research regarding the GD–ASD link should consider using dimensional metrics of autistic traits such as the SRS as well as formal diagnostic criteria. To date, only the study by de Vries et al. (2010) considered formal diagnostic criteria of both conditions. In that study, many of the 16 youth referred for GD who were classified as having ASD were only subthreshold for a diagnosis of Gender Identity Disorder, the formal DSM-IV diagnosis that preceded GD in DSM-5. Even though it is based on a small number of cases, this tendency appears to be somewhat at odds with the current study, which showed that traits of ASD were associated with greater gender nonconformity. As such, it is necessary to question whether the present findings regarding high birth weight would hold in the context of formal diagnoses. If so, then the various hypotheses described above regarding the significance of high birth weight for the GD–ASD link would be tenable across the autism spectrum. If not, then it might be the case that processes related to high birth weight contribute to an association between gender nonconformity and autistic *traits*, but alternate explanations must be sought for cases in which patients satisfy a formal *diagnosis* of ASD. Such an examination was not possible in the current study given sample size limitations; however, future studies employing larger samples may be better able to address these issues.

Lastly, the existing studies examining the GD–ASD link either lacked a clinical comparison group (present study; de Vries et al. 2010; Jones et al. 2012; Pasterski et al. 2014) or did not employ comprehensive measures of GD (Strang et al. 2014) or ASD (VanderLaan et al. 2014b). Further understanding may, therefore, be gained by examining comprehensive measures of ASD in a comparison group of children clinically referred for reasons unrelated to GD or ASD. Such a comparison group would help establish whether increased prevalence of ASD is unique to the GD population. Also, a comparison group would make it possible to evaluate whether an increased presence of ASD risk factors such as high birth weight among GD individuals accounts for any potential group differences in autistic traits.

Clinical Implications

There is currently no consensus regarding best practice when treating children with GD (Zucker 2008); however, one's clinical formulation regarding the bases of GD in a given child may help direct treatment approaches (VanderLaan and Zucker in press). This article outlined hypotheses that may account for GD among children who show traits of ASD and, thus, may also have implications for therapeutic strategies. For example, in the course of psychological therapy, one may wish to explore whether traits of ASD such as intense/obsessional interests or social communication deficits contribute to a child's gender schema and, ultimately, his or her cross-gender behavior and identity. If so, it would be useful to evaluate the likelihood that such ASD traits will continue to do so, especially in light of case studies reporting the desistence of GD among ASD youth (Robinow 2009; Parkinson 2014). Alternatively, if the presence of traits of ASD is reflective of exposure to factors that affected prenatal sexual differentiation of neural areas influencing sexually dimorphic behavior, then traits of ASD may have little or no impact on co-occurring GD. In such a circumstance, ASD may be a treatment consideration, but not necessarily the focus. Instead, one may focus more directly on addressing the lack of congruence between the experienced gender identity and the one assigned at birth.

Conclusions

The present findings identified relatively high birth weight as an important clue that may help explain the link between GD and ASD in children. This study is the first to investigate and identify somatic features (i.e., birth weight) that circumscribe the set of mechanisms that might account for this link. Specifically, a number of factors associated with relatively high birth weight could plausibly influence both GD and ASD either directly or indirectly. Such factors

include neuropsychological abnormalities that influence ASD behaviors; these behaviors may then subsequently contribute to GD. It is also possible that while high birth weight affects brain areas related to ASD, it also reflects exposure to low levels of prenatal testosterone in natal males and somatic masculinization in natal females. It is, therefore, also reasonable to speculate that these latter processes contribute to GD among the subset of children who exhibit both GD and traits of ASD. Detailing which of these hypotheses, or similarly plausible hypotheses, provides an adequate explanation for the GD–ASD link has important clinical implications in terms of informing treatment approaches. Thus, future research is needed to discern whether these hypotheses are indeed accurate.

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