Gender dysphoria and autism spectrum disorder: A narrative review

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Abstract

The current literature shows growing evidence of a link between gender dysphoria (GD) and autism spectrum disorder (ASD). This study reviews the available clinical and empirical data. A systematic search of the literature was conducted using the following databases: PubMed, Web of Science, PsycINFO and Scopus; utilizing different combinations of the following search terms: autism, autism spectrum disorder (ASD), Asperger’s disorder (AD), co-morbidity, gender dysphoria (GD), gender identity disorder (GID), transgenderism and transsexualism. In total, 25 articles and reports were selected and discussed. Information was grouped by found co-occurrence rates, underlying hypotheses and implications for diagnosis and treatment. GD and ASD were found to co-occur frequently – sometimes characterized by atypical presentation of GD, which makes a correct diagnosis and determination of treatment options for GD difficult. Despite these challenges there are several case reports describing gender affirming treatment of co-occurring GD in adolescents and adults with ASD. Various underlying hypotheses for the link between GD and ASD were suggested, but almost all of them lack evidence.

Introduction

The core features of autism spectrum disorder (ASD) are problems in social communication and interaction, together with repetitive behaviour and specific interests (American Psychiatric Association, APA, 2013). ASD reflects different heterogeneous clinical subtypes, formerly described as specific diagnostic entities such as Asperger’s disorder (AD) in the DSM-IV (APA, 2000). In the DSM-5, a more dimensional perspective is used with one ASD classification that can be specified according to the manner of its presentation (Lai et al., 2014). A review of the literature showed that the prevalence of ASD in the general population seems to be increasing and is now estimated at 1% in the most recent studies (Lai et al., 2014). It is uncertain whether there is a true increase or whether higher rates are due to improved methods of detecting ASD (Lai et al., 2014). Additionally, in terms of aetiology, complex interactions between known and unknown genetic predispositions and non-genetic risk factors may lead to development of ASD (Lai et al., 2014).

The first clinical descriptions of ASD stem from the 1940s (Asperger, 1944; Kanner, 1943) with knowledge of ASD expanding tremendously since then. With regard to gender identity for example; it was historically questioned whether children with ASD, who may show difficulties in general identity development, would be able to develop a gender identity. However, Abelson (1981) undertook a study of children with ASD and showed that, although dependent on cognitive abilities and mental age, children with ASD had the potential to develop a gender identity. It could be however, that this merely reflected a cognitive understanding of gender, instead of a core feeling of being a boy or a girl.

Independent from ASD, the term gender dysphoria (GD) is used in the DSM-5 to denote distress resulting from the incongruence between one’s experienced gender and one’s assigned gender, together with a persistent and strong desire to be of another gender (APA, 2013). In the DSM-IV (APA, 2000), gender identity disorder (GID) was used as terminology, and earlier versions used ‘transsexualism’ (APA, 1980). As different forms of terminology exist in the literature, in the current article we use the most recent term described in the DSM-5, i.e. GD when individuals have an official diagnosis. ‘Feelings of GD’ will be used as a broader terminology when an official diagnosis is not applicable but gender nonconformity is meant more broadly.

For people with an official diagnosis, the prevalence of GD in adults is estimated to be in the range of 1:10,000–1:20,000 in birth-assigned men and in the range of 1:30,000–1:50,000 in birth-assigned women.
and transsexualism. We also took into consideration gender identity disorder (GID), transgenderism, Asperger’s disorder (AD), co-morbidity, gender dysphoria terms: autism, autism spectrum disorder (ASD), co-occurrence rates in the current literature. Second, we want to discuss the hypothesized underlying factors that were mentioned in the different studies. Finally, we hope to provide an overview of the implications pertaining to diagnosis and treatment.

Methods

We conducted a systematic search in the following databases: PubMed, Web of Science, PsycINFO and Scopus, using combinations of the following search terms: autism, autism spectrum disorder (ASD), Asperger’s disorder (AD), co-morbidity, gender dysphoria (GD), gender identity disorder (GID), transgenderism, and transsexualism. We also took into consideration studies concerning other variants of ASD, which were mostly labelled with AD or high functioning autism (HFA). The literature search and the manuscript writing were done between December 2014 and August 2015.

All authors assessed the results of the searches on the basis of the title and the abstract. The suitability for inclusion was evaluated on the basis of the full publication. All reference lists of found articles were screened for usefulness. We also included case-series, case reports and expert opinions because of the dearth of systematic studies. Case reports about transvestism, general clinical chart reports and articles in languages other than English were excluded.

Results

Study characteristics

We were able to select 10 original data studies, 10 clinical case reports or case-series, two letters to the editor, one expert opinion article, and two articles in preparation, which covered the period 1996 till August 2015. Table 1 and 2 show the selected case reports and original data studies respectively (including author, focus, method used and participants’ outlines). All original data studies are presented in Table 2 and were of quantitative origin; semi-structured interviews and questionnaires were used. The methods and population were heterogeneous across studies (see Table 2).

In six original data research studies, a total of 1478 children and adolescents with (feelings of) GD were included (age < 21) (de Vries et al., 2010; Di Ceglie et al., 2014; Skagerberg et al., 2015; Vanderlaan et al., 2014, 2015; van der Miesen et al., in preparation, a). In two such empirical quantitative studies the combined sample reached 250 adults with GD (Jones et al., 2012; Pasterski et al., 2014). Four other empirical quantitative studies did not investigate participants with GD, but focused on 19 mothers of children with ASD (Shumer et al., 2015), on 415 adult women with ASD (Pohl et al., 2014), on 147 children and adolescents with ASD (Strang et al., 2014) and on 559 children and adolescents and 803 adults with ASD (van der Miesen et al., in preparation, b).

In the case reports, a total of 14 individuals (five birth-assigned boys, five birth-assigned men, two birth-assigned girls and two birth-assigned women) were described. Some of the case reports included a follow-up of one of the case reports was also described (Tateno et al., 2015). No participants were described in the letter to the editor of Bejerot et al. (2011) and in an expert opinion article (van Schalkwyk et al., 2015).
Eight original data studies reported on co-occurrence rates (de Vries et al., 2010; Jones et al., 2012; Pasterski et al., 2014; Pohl et al., 2014; Skagerberg et al., 2015; Strang et al., 2014; van der Miesen et al., in preparation a, b). Most studies were performed with samples which had (feelings of) GD but three studies reported on samples with ASD. For an overview of the methods used and co-occurrence rates see Table 2.

**Underlying hypotheses**

Authors of the case reports described and original data studies discussed several hypotheses on whether GD and ASD could co-occur. In examining the included studies, we were able to divide the authors’ suggestions into biological, social and psychological assumptions. These are described in the following sections.

**Biological factors**

The extreme male brain theory. In several studies the theory that characterizes ASD as the result of an ‘extreme male brain’ (EMB) (Baron-Cohen, 2002) was promulgated which therefore supports the co-occurrence of ASD and GD (e.g. Jones et al., 2012; de Vries et al., 2010). According to this theory, women have a stronger drive to empathize whereas men have a stronger drive to systemize (Baron-Cohen, 2009). Furthermore, people with ASD are thought to present with an extreme of the male pattern and thus show impaired empathizing and enhanced systemizing abilities (Baron-Cohen, 2009).
| Authors and year of publication | Focus | Method | Diagnosis* | No. of cases and birth-assigned gender | Age | Co-occurrence rates | Control group |
|---------------------------------|-------|--------|------------|----------------------------------------|-----|--------------------|---------------|
| de Vries et al. (2010) | ASD in children and adolescents with GD | Semi-structured Clinician’s Assessed Diagnostic Interview DISCO-10 | GID and GID-NOS confirmed with assessment ASD confirmed by DISCO-10 | n = 204 Children: 70 boys 38 girls Adolescents: 45 boys 51 girls | M 10.8 SD 3.58 | 7.8% of an ASD diagnosis in children and adolescents with GD | No |
| Di Ceglie et al. (2014) | Empathizing and systemizing in adolescents with GD | Parent report questionnaires EQ and SQ | GID attending GIDS | n = 35 parents of adolescents with GD 14 boys 21 girls | M 15.74 SD 1.72 Range 12–18 | Unknown | 156 parents of adolescents recruited from the general population |
| Jones et al. (2012) | Autistic symptoms in adults with GD | Self-report questionnaire AQ online | Transsexuals currently living in their gender role in line with their perceived gender identity | n = 259. 198 male 61 female | M 45.1 Range 16–75 M 34.0 Range 19–52 | 13.6% in birth-assigned men with GD and 21.3% in birth-assigned women with GD using the BAP | 2 control groups: 174 typical individuals and 125 individuals with AS |
| Pasterski et al. (2014) | Autistic symptoms in adults with GD | Self-report questionnaires AQ and modified KHHS | GD and GID formal diagnosis in the course of their treatment at a gender clinic screened by AQ | n = 91 63 male 28 female | M 45.47 SD 27.38 | 5.5% of a threshold score suggestive of an ASD diagnosis in adults with GD | 840 university students |
| Pohl et al. (2014) | Steroidopathy in women with ASD | Self-report questionnaire TMQ online | ASC screened by AQ | n = 415 female | M 36.39 SD 11.98 Year of birth, median 1985 | 3.8% of self-reported GD in adult women with ASD | 415 females without ASC |
| Shumer et al. (2015) | Autistic symptoms in children with Child’s GNC | Parent report questionnaires SRS and Recalled Childhood Gender Identity/Gender Role Questionnaire | ASD identified by their mothers GNC | n = 19 12 male 7 female | M 14.26 SD 2.68 Range 5–18 | Increased amount of autistic symptoms within the mild to moderate range for boys and girls with GD | No |
| Skagerberg et al. (2015) | Autistic symptoms in children and adolescents with GD | Parent report questionnaire SRS | GD attending the GIDS | n = 166 62 male 104 female | M 14.26 SD 2.68 | 5.4% of gender variance was found in children with ASD | No |
| Strang et al. (2014) | Gender variance in children with ASD and ADHD | Parent report questionnaire CBCL Interviews parent and self-report ADI, ADI-R, ADOS | ASD and ADHD reviewed by the neuropsychologist Epilepsy and NF1 reviewed by the neurologist | n = 389 ASD: 123 male 24 female ADHD: 88 male 38 female Epilepsy/ NF1: 60 male 56 female | M 12.21 SD 3.08 M 9.77 SD 2.95 M 10.12 SD 2.88 | 5.4% of gender variance was found in children with ASD | 2 control groups: CBCL standardization sample and controls |
| Vanderlaan et al. (2014) | Obsessional interests in children with GD | Parent report questionnaire CBCL | GD evaluated in a specialized service at an academic health science centre | n = 534 439 boys 95 girls | Unknown | Unknown | 3 control groups: 419 siblings and the referred and non-referred CBCL standardization sample |
| Vanderlaan et al. (2015) | Autistic symptoms and risk factors in children with GD | Parent report questionnaires SRS and GIQC | GD confirmed with clinical assessment | n = 49 40 male 9 female | M 7.19 SD 2.71 | Unknown | No |
Table 2. Continued

| Authors and year of publication | Focus | Method | Diagnosis* | No. of cases and birth-assigned gender | Age | Co-occurrence rates | Control group |
|--------------------------------|-------|--------|------------|--------------------------------------|-----|---------------------|---------------|
| van der Miesen et al., in preparation, a | Autistic symptoms in children and adolescents with (feelings of) GD | Parent report questionnaire CSBQ | Children and adolescents referred to a centre for GD | n = 542 | M 11.1 | 14.5% in children and adolescents with GD using a cutoff indicating a probable clinical diagnosis for ASD | 2 control groups: 2507 typical developing children and 196 children and adolescents with ASD |
| van der Miesen et al., in preparation, b | Gender variance in children and adults with ASD | Self-report questionnaires YSR and ASR | ASD confirmed with clinical assessment | n = 1262 | Children: M 5.98 | 7.2% of gender variance was found in the sample of children with ASD and adults |

*Original diagnosis described in the articles.

AD, Asperger’s disorder; ADHD, attention deficit hyperactivity disorder; ADI, Autism Diagnostic Interview; ADI-R, ADI – Revised;ADOS, Autism Diagnostic Observation Schedule; ASC, autism spectrum conditions; AQ, autism spectrum quotient; ASD, autism spectrum disorder; ASR, Adult Self Report; BAP, broader autistic phenotype; CBCL, Child Behavior Checklist; CSBQ, Children’s Social Behavior Questionnaire; DISCO-10, Diagnostic Interview for Social and Communication Disorders 10th revision; EQ, empathy quotient; GD, gender dysphoria; GID, gender identity disorder; GID-NOS, gender identity disorder – not otherwise specified; GIDS, Gender Identity Development Service; GQC, Gender Identity Questionnaire for Children; GNC, gender nonconformity; HFA, high-functioning autism; KHS, Kinsey Heterosexual Homosexual Scale; M, mean; NF1, neurofibromatosis; OCD, obsessive-compulsive disorder; SD, standard deviation; SQ, systemizing quotient; SRS, Social Responsiveness Scale; TMQ, Testosterone-related Medical Questionnaire; YSR, Youth Self Report.

Other factors associated with the EMB. In a letter to the editor, Bejerot et al. (2011) speculated about a role of an extreme form of the male brain not consistent with it. Indeed, the neurobiological basis of an extreme form of the male brain is not yet clear. Like individuals with ASD, typical men have more lateralization of the brain and ASD in men therefore remains unexplained in these studies. In conclusion, there is some evidence for the EMB theory but the latest research on GD and ASD was inconsistent with it. Indeed, the neurobiological basis of an extreme form of the male brain is not yet clear. The question of whether prenatal testosterone levels and autistic traits are linked (Auyeung et al., 2009), according to the EMB theory, prenatal testosterone levels and autistic traits are linked (Auyeung et al., 2009).
for endocrine disruptors, especially phthalates. Phthalates are included in plastic and their increase in the environment has been recorded. Although not further tested, Bejerot rationalized that they might contribute to elevated fetal testosterone exposure, and therefore not only increase the risk for ASD, but also for GD and the co-occurrence between the two conditions.

One study investigated several other ASD-related risk factors in 49 children with GD in relation to autistic symptoms (Vanderlaan et al., 2015). A relationship between gender nonconformity and autistic symptoms was found with increased birth weight, but not with sibling sex ratio and parental age at birth, which were other risk factors proposed for ASD (Vanderlaan et al., 2015). As high birth weight is negatively correlated with testosterone exposure in utero, high birth weight could be a physical marker for low prenatal testosterone exposure (Carlsen et al., 2006). Low birth weight and therefore less masculinization of certain regions of the brain might be associated with female sexual dimorphism and associated behaviour in birth-assigned boys with GD (Carlsen et al., 2006). In birth-assigned girls, higher birth weight and masculinized features are correlated, which would also lend some support to this notion (Avidime et al., 2011).

Social factors

The poor understanding of social relationships which is characteristic of individuals with ASD, led Landen and Rasmussen (1997) to suggest that GD could develop as a consequence of this difficulty in social interactions. A boy with ASD who had been bullied by other boys might have developed a feeling of belonging to the female sex out of aversion to the male gender (Tateno et al., 2008). Indeed, this was mentioned by one adolescent in a sample of individuals with co-occurring GD and ASD who stated that he had always had the feeling of being different from his peers – which he attributed to GD (de Vries et al., 2010). Parkinson (2014) also described two birth-assigned men who had feelings of being different and interpreted these feelings as GD and therefore requested gender reassignment therapies. Caution was warranted, however, as these feelings turned out not to belong to a true GD but more likely to ASD.

It has also been suggested that ASD relates to deficits in social communication which can lead to people missing social cues about a child’s gender presentation which, in turn, might increase the likelihood of the child developing GD (Strang et al., 2014). In line with this hypothesis, Shumer et al. (2015) found an increase in autistic symptoms as measured by the Social Responsiveness Scale (SRS) in mothers with children who show higher degrees of gender nonconformity. Shumer suggested that one factor involved in a child’s gender expression is the maternal social responsiveness, however, no relation between paternal SRS and gender nonconformity was found.

Whereas the authors above suggested that ASD characteristics make one susceptible for GD, Skagerberg et al. (2015) suggested that the increased rate of autistic features in a sample of children and adolescents with GD (as compared to the general population) in their study might have stemmed from the GD itself and did not reflect true autism. In this conception, GD may cause social difficulties by, for example, people with GD being subject to a high level of bullying (Holt et al., 2014). However, Skagerberg et al. (2015) found it was unclear whether these autistic features deserve a separate diagnosis or are part of GD.

Psychological factors

Pre-occupations and obsessive–compulsive disorder. Several authors have suggested a link between GD and unusual interests, pre-occupations, or obsessive–compulsive disorder (OCD). Williams et al. (1996) were the first authors who described two boys with ASD with pre-occupations with feminine dresses, activities and objects. They considered these interests as unusual pre-occupations that had resulted from the need for sensory input belonging to the ASD diagnosis. In the same line, Tateno et al. (2008) hypothesized that the pre-occupation with, for example, specific clothes in individuals with ASD might resemble symptoms of GD while they are actually part of the ASD. Likewise, Mukaddes (2002) interpreted co-occurring cross-gender behaviour as unusual interests that are characteristic of ASD instead of a true GD. He described two boys with ASD and persistent cross-gender behaviour despite eclectic treatment and follow-up.

Landen and Rasmussen (1997) were the first to hypothesize that GD may be seen not only as pre-occupations related to ASD but as OCD stemming from ASD. Perera (2003) also stated that in the patient they described, features of GD might represent OCD; and Gallucci et al. (2005) proposed that OCD might be the link between GD and ASD. It was also suggested that if both the diagnoses of GD and OCD are given in ASD, the primary diagnosis is more likely OCD than GD (Perera, 2003). Parkinson (2014) has described that in two men with ASD feelings of GD were transient and cautioned that GD might be a temporary pre-occupation and therefore treatment of GD in these cases is unadvisable (see also the treatment section below).
Apart from the case reports mentioned above, there is only one quantitative study which investigated intense or obsessional interests in children referred for GD (Vanderlaan et al., 2014). These children showed elevated symptoms of obsessions and compulsions compared to non-referred controls. The reported intense or obsessional interests more often involved gender-related themes in gender-referred boys than in non-referred controls. However, in gender-referred girls there were no differences with non-referred controls. Three possible explanations were proposed in the article (Vanderlaan et al., 2015). First, children with GD might have intense interests and obsessions about cross-gender activities or objects (e.g. long hair in birth-assigned boys with GD) which might lead to symptoms of ASD but are in fact a manifestation of GD. Second, children with ASD might inversely express symptoms of GD by showing cross-gender interests. Third, it was argued that one or more underlying additional variables may influence both GD and ASD.

**Developmental rigidity.** As part of normative gender development, children between the ages of three and five show more rigid gender-stereotypical beliefs as compared to older children (Ruble et al., 2007), which then decreases after the age of five. It is hypothesized that individuals with ASD may not reach this level of flexibility in their gender development, due to their general rigidity and are therefore prone to develop GD (de Vries et al., 2010). For example, Lemaire et al. (2014) described a case of a 23-year old woman in which the rigid thinking of ASD might have contributed to GD, or at least increased the difficulty in coping with GD. Further, Jacobs et al. (2014) pointed out that the social gender role transition in individuals with co-occurring GD and ASD might involve a difficult interim period as being in between two genders during this transition from stereotypically male to stereotypically female could be experienced as awkward and difficult to tolerate for rigid-thinking individuals with ASD. He suggested that it might even ‘push’ them into the direction of more extreme GD (Jacobs et al., 2014).

**Theory of mind.** Baron-Cohen (1991) defined theory of mind (ToM) as the ability of the child’s developing mind to create a picture of the emotional state of mind of another child. Indeed, ToM might also influence the development of gender identity (Jacobs et al., 2014). Pasterski et al. (2014) hypothesized that children with ASD may experience a different sense of self which could lead to a different sense of gender identity compared to other non-ASD individuals. Whether ToM is also altered in children with GD has not been investigated yet, but cases with impairment in ToM are described (Jacobs et al., 2014).

**Sexual orientation.** In the study of de Vries et al. (2010) the majority of the adolescents with co-occurring GD and ASD (5 out of 9) were not sexually attracted to individuals of their birth-assigned gender (sometimes referred to as the non-homosexual subtype of GD (although individuals with GD identify themselves as homosexual (Lawrence, 2010)). This was in contrast to most non-ASD adolescents with GD at their clinic who are sexually attracted to their birth-assigned gender (homosexual subtype of GD (Smith et al., 2005)). In Pasterski et al. (2014) adults with GD who reported a sexual attraction to individuals of their experienced gender had significantly more autistic symptoms than those who reported a sexual attraction to their birth-assigned gender. The study of Jones et al. (2012) partly supported these results. They found that non-homosexual birth-assigned men with GD reported more autistic symptoms compared to those with a homosexual sexual orientation, but they found no differences for birth-assigned women with GD with regard to sexual orientation and autistic symptoms. There is some evidence in adults with GD that a sexual attraction to the experienced gender may be accompanied by more psychological problems compared to sexual attraction to the birth-assigned gender (Smith et al., 2005; Lawrence, 2010).

**Gender identity development.** Although Abelson (1981), who questioned the ability of people with ASD to develop a gender identity, confirmed that children with ASD had the potential to develop this identity, according to van Schalkwyk et al. (2015) the development of gender identity in children with ASD might follow a different pattern compared to gender development in children without ASD. The timeline of a framework followed in this development might vary. Tateno et al. (2008) suggested that confusion in the development of gender identity, or an altered development of gender identity, might increase feelings of GD in children with ASD.

**Implications for diagnosing GD**

Although all case reports included showed complex issues concerning diagnostics, none of the authors described ASD as an exclusion criterion for diagnosing GD. Consequently, in every article it was eventually possible to assess whether or not a diagnosis of GD was applicable.

However, several challenges in the diagnostic process were mentioned. One is the possible poor compliance
with attending clinical appointments (Perera, 2003). Another is the difficulty that individuals with ASD may have with acquiring sufficient linguistic ability to express themselves and to develop a self-concept (Mukaddes, 2002; Tateno et al., 2002). Verbal expression of gender disappointment is needed to properly diagnose children with ASD and co-occurring GD.

Another frequently mentioned challenge is that the clinical picture of GD is sometimes complicated by (symptoms of) ASD (Perera, 2003). Indeed, Williams et al. (1996) cautioned against diagnosing their cases as GD and preferred to evaluate the cases in the context of ASD. In all the cases of GD and ASD described by de Vries et al. (2010) the diagnostic procedure was extended because it was difficult to disentangle a diagnosis of GD from a feeling of being different from others or from a cross-gender obsession. They proposed an individual approach for diagnosis and treatment of every clinical case where rigidity and concrete thinking should be taken into consideration. Van Schalkwyk et al. (2015) suggested that in diagnosing possible GD and ASD, one should take clear notice of the development of gender identity. The study of van der Miesen et al. (in preparation, a) found that, not one, but all subdomains of ASD were increased in children with feelings of GD. Consequently a diagnosis of GD must be seen from different perspectives, not only from the perspective of GD or ASD but also from an individual psychosocial developmental perspective, including the complete GD and ASD spectrum.

**Diagnosis and follow-up**

Developmentally, most pre-pubescent children with GD, but without ASD, will desist (‘desisters’) when they reach the age of puberty; Whereas in gender dysphoric adolescents the wish to be of the other gender most often persists (‘persisters’; e.g. Wallen & Cohen-Kettenis, 2008). In the current narrative review both categories are described below. Mukaddes (2002), for example, described two cases of boys (7 years and 10 years old respectively) with ASD followed for 4 years, who showed persistent cross-gender behaviour. In another study no differences were found between children and adolescents with GD and ASD, and with GD alone with respect to the persistence of GD feelings (de Vries et al., 2010). However, Parkinson (2014) described two men with ASD and initial strong symptoms of GD who, after several years had elapsed, reported that their feelings of GD had abated along with their wish for both hormonal and surgical treatment. Parkinson cautioned that the irreversible treatments should therefore only be started if it is clear that there is true GD and not a transient obsession. Consequently the real life experience, or social gender role transition in the experienced gender, is considered an important element before making decisions on medical treatment (Parkinson, 2014). If follow-up time is sufficient, diagnosing persistent GD is thought to be possible (Tateno et al., 2008).

**Implications for treatment**

Three of the case reports (Jacobs et al., 2014; Kraemer et al., 2005; Lemaire et al., 2014) described gender reassignement treatment being provided for individuals with ASD. Kraemer et al. (2005) concluded that treatment recommendation is not altered depending on whether GD and ASD are two different conditions; or that one of the conditions is the (evolutionary and dynamic) underlying condition. Vanderlaan et al. (2015) mentioned that if a common neurodevelopmental pathway started in utero, symptoms of ASD might have no influence on co-occurring GD and treatment of ASD may not be necessary. We therefore suggest that treatment decisions should be made based upon the amount of psychological and social distress rather than upon possible underlying hypotheses. Such treatment options described in the literature included pharmacological, psychological and surgical gender reassignment treatment.

**Pharmacological treatment**

Because Landen & Rasmussen (1997) viewed GD as OCD, they prescribed clomipramine as treatment. However, while symptoms of OCD decreased, symptoms of GD increased. Indeed, in the case described by Perera (2003) of GD in a girl with ASD and OCD, clomipramine was also used. Similarly, in this case the symptoms of OCD improved, but distress about her gender remained. Based on these cases, clomipramine seems not to affect GD.

**Psychological treatment**

All the individuals included in this review received at least some form of psychological treatment or support ranging from psycho-education and behaviour modification (Mukaddes, 2002), special education (Williams et al., 1996) to psycho-dynamic psychotherapy (Lemaire et al., 2014; Parkinson, 2014) which improved, for example, communication skills (Williams et al., 1996) but not (feelings) of GD (see also Table 1). It therefore appears to be important to provide psychological support throughout the changes that occur if gender reassignment treatment is started, including helping to
integrate these changes into the client’s sense of self (Jacobs et al., 2014).

**Gender reassignment treatment**

Hormonal treatment was provided in some of the case reports (Jacobs et al., 2014; Kraemer et al., 2005; Lemaire et al., 2014), was mentioned as a possible option in another case description (Tateno et al., 2008), and was further prescribed in two of the systematic studies (de Vries et al., 2010; Pasterski et al., 2014). However, hormonal treatment was withheld in two cases described by Parkinson (2014) because of the transient nature of the reported feelings of GD. Gender reassignment surgery was mentioned in only one original data study (de Vries et al., 2010) but until now there has been no gender reassignment treatment outcome published on individuals with co-occurring GD and ASD.

In summary, although the literature reports on individuals with ASD that are diagnosed with GD and receive gender reassignment treatment, no conclusions could be drawn about the optimal diagnostic procedure, treatment protocol and treatment outcomes in gender dysphoric individuals with co-occurring ASD. Consequently, small and evolving steps seem to be advisable, with extra psychological support – including psycho-education – while taking into account not only the frequent obsessions, but also rigidity and other symptoms of the ASD spectrum.

**Discussion: future directions**

From this literature review we can conclude that knowledge on the co-occurrence of GD and ASD is far from complete. When considering future steps, the current literature points in three important directions.

First, as almost all aetiological factors are speculative, more research is needed to find out which factors are important in this co-occurrence. We therefore suggest that, in line with van Schalkwyk et al. (2015), a longitudinal controlled study on larger samples is needed to analyse the development of gender identity from an early age in general, and in ASD in particular.

Second, as it is unclear whether available diagnostic and treatment outcomes in individuals with GD alone are generalizable to populations with GD and ASD (symptoms), follow-up studies in these populations are necessary. Indeed, a specific diagnostic and treatment protocol should be developed and tested for this population. An individualized protocol could help to overcome the above-mentioned challenges in diagnosis and treatment. This treatment protocol should be specifically based on the features of ASD and should help to differentiate between a diagnosis of GD and symptoms of the broader autistic spectrum.

Finally, to ensure that these vulnerable patients receive optimal care, educational programmes concerning the co-occurrence of GD and ASD are needed for all caregivers involved with these patients, which should be based on the features of ASD and not on the knowledge of GD only.

**Conclusion**

Despite the limited current literature on GD and ASD, there is now some replicated evidence of an over-representation of co-occurring GD and ASD compared to what would be expected by chance based on the estimated prevalence in the general population of both conditions. As up to around 20% of gender identity clinic-assessed individuals reported clinical range features of ASD, we can cautiously conclude that co-occurring GD and ASD is frequent. The variability of percentages may be due to differences in diagnostic criteria and different manners of sample selection.

At present, there is no evidence for specific risk factors that might be involved for either GD or ASD and the aetiological factors that are suggested are speculative. It is plausible that not only one hypothesis but multiple suggested hypotheses may play a role in the GD–ASD co-occurrence. This conclusion is further complicated by the different perspectives of the restricted view of an ASD diagnosis compared to the broader view of the autism phenotype (van Schalkwyk et al., 2015). It is unclear whether these different perspectives play a different role in the underlying aetiology.

The papers reviewed above concluded that diagnosis of GD and gender reassignment treatment when there is co-occurring ASD is possible, but that the diagnostic phase should be extended because of the difficulty of differentiation between both conditions. Clinicians and caregivers need specific support in diagnosis and treatment, and a specific protocol for these individuals seems also to be advisable. Currently, therefore, an individualized approach seems to be the best practice.

In conclusion, as there is no agreement on aetiological factors and on diagnosis and treatment of co-occurring GD and ASD, research is needed to help our understanding of the phenomenon and to provide evidence for optimal care in this unique population.

**References**

Abelson, A.G. (1981). The development of gender identity in the autistic child. *Child care health and development*, 7, 347–356.
Aitken, M., Steensma, T.D., Blanchard, R., VanderLaan, D.P., Wood, H., Fuentes, A., . . . Zucker, K.J. (2014). Evidence for an Altered Seks Ratio in Clinic-Referral Adolescents with Gender Dysphoria. J. Sexual Med., 12, 765–763.

American Psychiatric Association. (1980). Diagnostic and statistical manual of mental disorders (3rd ed.). Washington, DC: Author.

American Psychiatric Association. (2000). Diagnostic and statistical manual of mental disorders (4th ed., text revision). Washington, DC: Author.

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Washington, DC: Author.

Asperger, H. (1944). Die ‘Autistischen Psychopathen’ im Kindesalter [The Autistic Psychopaths]. Archiv fur Psychiatrie und Nervenkrankheiten, 117, 76–136.

Auyeung, B., Wheelwright, S., Alisson, C., Atkinson, M., Samarawickrema, N. & Baron-Cohen, S. (2009). The children’s Empathy Quotient and Systemizing Quotient: sex differences in typical development and in autism spectrum conditions. Journal of Autism and Developmental Disorders, 39, 1509–1521.

Bejerot, S., Humble, M.B. & Gardner, A. (2011). Endocrine disruptors, the increase of autism spectrum disorder and its comorbidity with gender identity disorder—a hypothetical association. Int J Androl, 34(5 Pt 2):e350.

Bejerot, S., Humble, M.B. & Gardner, A. (2011). Endocrine disruptors, the increase of autism spectrum disorder and its comorbidity with gender identity disorder—a hypothetical association. Int J Androl, 34(5 Pt 2):e350.

Baron-Cohen, S. (2002). The extreme male brain theory of autism. Trend Cogn Sci, 6, 248–254.

Baron-Cohen, S. (2009). Autism: the empathizing-systemizing (E-S) theory. Ann NY Acad Sci, 1156, 60–80.

Baron-Cohen, S. (1991). The development of a theory of mind in autism: deviance and delay? Psychiatr Clin North Am, 14, 33–51.

Baron-Cohen, S. (2002). The extreme male brain theory of autism. Trends Cogn Sci, 6, 248–254.

Baron-Cohen, S. (2009). Autism: the empathizing-systemizing (E-S) theory. Ann NY Acad Sci, 1156, 60–80.

Bejerot, S., Humble, M.B. & Gardner, A. (2011). Endocrine disruptors, the increase of autism spectrum disorder and its comorbidity with gender identity disorder—a hypothetical association. Int J Androl, 34(5 Pt 2):e350.

Carlsen, S.M., Jacobsen, G. & Romundstad, P. (2006). Maternal testosterone levels during pregnancy are associated with offspring sex at birth. European Journal of Endocrinology, 155, 365–370.

de Vries, A.L.C., Noens, I.L.J., Cohen-Kettenis, P.T., van Berckelaer-Onnes, I.A. & Doreleijers, T.A.H. (2010). Autism spectrum disorders in gender dysphoric children and adolescents. J Autism Dev Disord, 40, 930–936.

de Vries, A.L.C., Kreukels, B.P.C., Steensma, T.D. & McGuire, J. (2014). Gender Identity Development: A Biopsychosocial Perspective. In: B.P.C. Kreukels, T.D. Steensma & A.L.C. de Vries (Eds), Gender Dysphoria and Disorders of Sex Development Focus on Sexuality Research (pp53–58). New York: Springer.

Dewinter, J., Vermeiren, R., Vanwesenbeeck, I. & van Nieuwenhuizen, C. (2013). Autism and normative sexual development: a narrative review. J Clin Nurs, 22, 3467–3483.

Di Ceglie, D., Skagerberg, E., Baron-Cohen, S. & Auyeung, B. (2014). Empathizing and systemizing in adolescents with Gender Dysphoria. Opticon1826, 6, 1–8.

Fombonne, E. (2005). Epidemiology of autistic disorder and other pervasive developmental disorders. J Clin Psychiatry, 66, 3–8.

Gallucci, G., Hackerman, F. & Schmidt, C.W. (2005). Gender Identity Disorder in an Adult Male with Asperger’s Syndrome. Sex Disabil, 23, 35–40.

Holt, V., Skagerberg, E. & Dunsford, M. (2014). Young people with features of gender dysphoria: Demographics and associated difficulties. Clin Child Psychol Psychiatry, doi:10.1177/1359104514558431.

Jacobs, L.A., Rachlin, K., Erickson-Schroth, L. & Janssen, A. (2014). Gender Dysphoria and Co-Occurring Autism Spectrum Disorders: Review, Case Examples, and Treatment Considerations. LGBT Health, 1, 271–282.

Jones, R.M., Wheelwright, S., Farrell, K., Martin E., Green, R., Di Ceglie, D. & Baron-Cohen, S. (2012). Brief report: female-to-male transsexual people and autistic traits. J Autism Dev Disord, 42, 301–306.

Kanner, L. (1943). Autistic disturbances of affective contact. Nerv Child, 2, 217–250.

Kraemer, B., Delsignore, A., Gundelfinger, R., Schnyder, U. & Hepp, U. (2005). Comorbidity of Asperger syndrome and gender identity disorder. European Child Adolescent Psychiatry, 14, 292–296.

Lai, M., Lombardo, M.V. & Baron-Cohen, S. (2014). Autism. Lancet, 383, 896–910.

Landen, M. & Rasmussen, P. (1997). Gender identity disorder in a girl with autism—a case report. European Child Adolescent Psychiatry, 6, 170–173.

Lawrence, A.A. (2010). Sexual orientation versus age of onset as bases for typologies (subtypes) for gender identity disorder in adolescents and adults. Arch Sexual Behav, 39, 514–545.

Lemaire, M., Thomazeau, B. & Bonnet-Brilhault, F. (2014). Gender Identity Disorder and Autism Spectrum Disorder in a 23-Year-Old Female. Arch Sexual Behav, 43, 395–398.

Mukaddes, N.M. (2002). Gender identity problems in autistic children. Child Care Health Dev, 28, 529–532.

Parkinson, J. (2014). Gender dysphoria in Asperger’s syndrome: a caution. Australas Psychiatry, 22, 84–85.

Pasterski, V., Gilligan, L. & Curtis, R. (2014). Traits of Autism Spectrum Disorders in Adults with Gender Dysphoria. Arch Sex Behav, 43, 387–393.

Perera, H. (2003). Gender identity disorder presenting in a girl with Asperger’s disorder and obsessive compulsive disorder. Ceylon Med J, 48, 57–58.

Pohl, A., Cassidy, S., Auyeung, B., & Baron-Cohen, S. (2014). Uncovering steroidopathy in women with autism: a latent class analysis. Mol Autism, 5, 27–27.

Ruble, D.N., Taylor, L.J., Cyphers, L., Greulich, F.K., Lurye, L.E., & Shрут, P.E. (2007). The role of gender constancy in early gender development. Child Dev, 78, 1121–1136.

van Schalkwyk, G.L., Klingensmith, K. & Volkmar, F.R. (2015). Gender Identity and Autism Spectrum Disorders. Yale journal of biology and medicine, 88, 81–83.

Shumer, D.E., Roberts, A.L., Reisner, S.L., Lyall, K. & Austin, S.B. (2015). Brief Report: Autistic Traits in Mothers and Children Associated with Child’s Gender Nonconformity. Journal of Autism Developmental Disorders, 45, 1489–1494.

Skagerberg, E., Di Ceglie, D. & Carmichael, P. (2015). Brief Report: Autistic Features in Children and Adolescents with Gender Dysphoria. J Autism Dev Disord. doi: 10.1007/s10803-015-2413-x.
Smith, Y.L., van Goozen, S.H., Kuiper, A.J. & Cohen-Kettenis, P.T. (2005). Transsexual subtypes: Clinical and theoretical significance. *Psychiatr Res*, 137, 151–160.

Strang, J.F., Kenworthy, L., Dominska, A., Sokoloff, J., Kenealy, L.E., Berl, M., ... Wallace, G.L. (2014). Increased Gender Variance in Autism Spectrum Disorders and Attention Deficit Hyperactivity Disorder. *Arch Sexual Behav*, 43, 1525–1533.

Tateno, M., Tateno, Y. & Saito, T. (2008). Comorbid childhood gender identity disorder in a boy with Asperger syndrome. *Psychiatr Clin Neurosci*, 62, 238.

Tateno, M., Teo, A.R. & Tateno, Y. (2015). Eleven-year follow up of boy with Asperger’s syndrome and comorbid gender identity disorder of childhood. *Psychiatr Clin Neurosci*. doi:10.1111/pcn.12328.

Vanderlaan, D.P., Postema, L., Wood, H., Singh, D., Fantus, S., Hyun, J., ... Zucker, K.J. (2014). Do Children with Gender Dysphoria Have Intense/Obsessional Interests? *J Sex Res*, 52, 213–219.

Vanderlaan, D.P., Leef, J.H., Wood, H., Hughes, S.K. & Zucker, K.J. (2015). Autism Spectrum Disorder Risk Factors and Autistic Traits in Gender Dysphoric Children. *J Autism Dev Disord*, 46, 1742–1750.

Wallen, M.S. & Cohen-Kettenis P.T. (2008). Psychosexual outcome of gender-dysphoric children. *J Am Acad Child Adolesc Psychiatr*, 47, 1413–1423.

Williams, P.G., P.L. Allard, A.M. & Sears, L. (1996). Case study: Cross-gender preoccupations with two male children with autism. *J Autism Dev Disord*, 26, 635–642.

Wood, E. & Halder, N. (2014). Gender disorders in learning disability- a systematic review. *Tizard Learn Disabil Rev*, 19, 158–165.

Zucker, K.J. & Lawrence, A.A. (2009). Epidemiology of gender identity disorder: Recommendations for the standards of care of the world professional association for transgender health. *Int J Transgender*, 11, 8–18.