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Gender dysphoria in children and adolescents: a review of recent research

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Abstract

Purpose of review: With the advent of medical treatments like puberty suppression and cross-sex hormones in gender dysphoric minors there has been a debate around questions of gender identity and brain development. This review aimed to identify recent empirical studies that addressed this controversial topic.

Recent findings: Epidemiological data from several countries indicate that gender dysphoria in children and adolescents is far more common than initially anticipated. This is in line with the currently observed steady increase in referrals to gender clinics. Minors with gender dysphoria are a vulnerable population as they may face a high psychopathological burden. Recently published data on the long-term outcome of puberty suppression and subsequent hormonal and surgical treatment indicate that young people with gender dysphoria may benefit substantially with regard to psychosocial outcomes. Brain development studied by neuroimaging methods seems not to be disturbed by puberty suppression.

Summary: The first reports about long-term outcome in adolescents having undergone puberty suppression have shown promising results. However, in a substantial part of gender dysphoric minors puberty suppression is not indicated so far due to psychiatric comorbidity and long-term follow-up data from these patients is still scarce.

Keywords: gender dysphoria, gender incongruence, gender identity disorder, transsexualism, transsexual, gender variance, childhood, adolescence

Keypoints:

1. Gender dysphoric minors have a high burden of psychiatric comorbidities
2. Number of referrals to gender clinics of children and adolescents with gender dysphoria especially of natal females are ever increasing

3. A recently published long-term study on puberty suppression and subsequent cross sex hormones in gender dysphoric minors highlights positive effects on psychosocial outcomes
4. Brain development and function regarding executive functioning seems not to be disturbed by puberty suppression.
5. Hopefully this review will encourage researchers and clinicians to perform further research, especially long-term follow up studies, with gender dysphoric minors.

Introduction

When preparing for our “a year in review”-lectures at the first biennial conference of the European Professional Association for Transgender Health (EPATH) in Ghent (Belgium) 2015, we (JF and MKA) were puzzled about the increasing variety and number of research in the field of gender dysphoria. While some research topics are relevant for gender dysphoric people of all ages there are also issues that vary profoundly across the lifespan. One of the most controversial and timely question in the field is the care for gender dysphoric minors. Recent research may help to tailor treatment to the needs and difficulties of gender dysphoric minors. In the present article, we thus review recent studies that investigated aspects of gender dysphoria in children and adolescents. We will use the term gender dysphoria from the DSM-5 for the present review. The database PubMed was searched for empirical studies that were published between May 2014 and May 2015. To detect all relevant studies we used the following search term: ((transgender OR transsexuality OR gender dysphoria OR gender incongruence OR gender identity disorder)) AND ("2014/05/01"[Date - Publication] : "2015/05/01"[Date - Publication]) and found 555 studies with a potential relevance for the present review. Out of these, we reviewed all studies that addressed the mental health of gender dysphoric minors.

Epidemiological data and comorbidity

The prevalence of gender dysphoria in general and particularly in child and adolescent samples varies considerably across different countries. To date representative studies are extremely scarce. In 2014, Clark and colleagues [1*] presented for the first time data from a nationally representative survey (Youth ’12 in New Zealand; n = 8166) on the prevalence of *transgenderism* in adolescents. Transgender is an umbrella term for gender dysphoric people and those with an incongruence of natal sex and gender identity. From more than 8000 secondary school students, 1.2% indicated to identify as transgender, while 2.5% were not sure about their gender. From those that identified as transgender, roughly 40% were not exclusively opposite-sex attracted, which is comparable to adult samples [2]. Interestingly, identifying as transgender was also associated with a significantly higher burden of weekly school bullying (20%), current

depressive symptoms (40%) and suicide attempts within the last 12 months (20%). However, it is still a causality dilemma if the mental health burden was a sequela of being stigmatized as transgender or mental disorder a risk factor that increased the likelihood of becoming transgender or both. There has been a move towards the first explanation (distress because of discrimination, stigmatization and prejudice) and away from *psycho*-pathologizing gender dysphoric people *per se*. Nevertheless, there is still a debate around this question because it very much affects the clinical decision making of how to organize mental health care for gender dysphoric youth and adults in the first place.

Two recent studies from the UK [3] and US [4] demonstrated in line with the study from New Zealand that the most prevalent associated problems of gender dysphoric adolescents were bullying, depression, suicide attempts and self-harm. All of these may well be understood as sequelae of encountering gender dysphoria. In adolescents with gender dysphoria in the UK, natal females presented significantly more often with self-harm and natal males with autism spectrum disorder. A relation between autism spectrum disorder and gender dysphoria was also scrutinized by VanderLaan and colleagues [5] who reported an elevation of obsessional interests in gender dysphoric children. It was suggested that kids with autism spectrum disorder "may hold more rigid views of what it is to be male or female" [3] and thus be more at risk towards developing gender dysphoria if they don't feel fit within their binary categories of girls and boys. Another explanation was that cross-sex obsessional interests may rather be a symptom of gender dysphoria and only superficially autism-like [5] and that especially the fragility of identity experiences in gender dysphoric minors leads to a more rigid fixation on gender-based stereotypes. It was further speculated that prenatal exposure to high testosterone levels or high birth weight may be involved in the simultaneous development of gender dysphoria and autism spectrum disorder [6,7].

In contrast to these reports that predominantly described comorbid psychopathology without indicating if gender dysphoria preceded or resulted from it, Kaltiala-Heino and colleagues [6*] published a retrospective analysis of all minors that were treated in their gender clinic in Tampere/Finland within a two-year period. They concluded from their data that severe

psychopathology was preceding the onset of gender dysphoria. Although natal girls were overrepresented and the prevalence of autism spectrum disorder is generally lower in natal girls, the comorbid prevalence for autism spectrum disorder was as high as 26% in their sample. They also found that bullying was a severe problem but reported that in two thirds of the cases it had already started before the onset of gender dysphoria and was not targeted on gender or sexual behavior. Most of their young patients needed additional care from a child and adolescent psychiatrist due to psychiatric problems (other than gender dysphoria) and the authors concluded that "comorbid disorders were thus severe and could seldom be considered secondary to gender dysphoria." This report contradicted the findings in other countries where comorbid psychopathology was less prevalent and rather a result of difficulties associated with gender dysphoria [8]. To date it is still unclear why different researchers in different countries find such different results concerning the mental health of gender dysphoric minors. Are there previous assumptions or assessment methods responsible for these differences? Is it that gender dysphoric minors in Finland (and other countries) are really on average more psychiatrically disordered than for example in the Netherlands? And if so, which social and biological factors drive this difference? A higher mental health burden for affective disorders in gender dysphoric adultsfor example has been described in Germany and Norway compared to the Netherlands and Belgium [9]. To answer the abovementioned questions we need more multi-center studies that include different countries in the next years. Thus we will learn to what extend and in what form gender dysphoric children and adolescents need psychiatric care or psychotherapeutic interventions by mental health professionals (also approaches that are sometimes critically compared to reparative or conversion therapy in homosexual individuals need to have an evidence base if they are applied, especially since they are highly disputed and were banned in the United States recently [10]).

Puberty suppression

Importantly, the adolescents from the above-mentioned studies were not treated with puberty suppression, yet and Holt and colleagues observed that "many of the difficulties increased with

age" (without puberty suppression) [3]. The studies were thus not able to differentiate if the psychosocial burden was higher or lower after their wish for transitioning was fulfilled. Another crucial question is, in which adolescents gender dysphoria will persist (persisters) and in whom it will remit (desisters) and how this relates to long-term mental health. Follow-up studies indicate a decrease of gender dysphoria during puberty in 60 - 80% of adolescents [25]. Both, those with persisting and with remitting gender dysphoria indicate that they considered the period between 10 - 13 years of age to be crucial for long-term gender identity [25]. In consequence, hormonal treatment in adolescents with persisting gender dysphoria may help to reduce mental health burden.

After its first description in the 1990s, [11] puberty suppression in gender dysphoric youth with gonadotropin-releasing hormone analogues (GnRHa) has become one form of treatment in many specialized centers around the world. The rationale is to give youth more time to explore their gender identity by inhibiting the onset of permanent bodily changes through puberty. The so-called "Dutch protocol" [16] recommends to treat gender dysphoric minors after an extensive psychological evaluation (to exclude "desisters") with puberty suppression at the age of 12 years and after the young people have reached the first stages of puberty (Tanner stage 2 - 3). Later they become eligible for cross-sex hormones and sex-reassignement surgery at the age of 16 and 18, respectively. This protocol dramatically changed the treatment of gender dysphoric minors and has been a guideline for many clinicians. Of note, minor changes to this protocol have been suggested (e.g. young patients receive puberty suppression sometimes even earlier than at the age of 12 years if they reach Tanner stage 2 – 3 at earlier age and since GnRHa treatment is not recommended to expand 2 years in order to avoid a disturbed bone development, cross-sex hormones may be prescribed well before the age of 14 years [12]). To evaluate the "Dutch protocol", de Vries and colleagues published the first long-term results in 2014 [13**]. They assessed the psychological functioning (GD, body image, global functioning, depression, anxiety, emotional and behavioral problems), the objective (social and educational/professional functioning) and subjective (quality of life, satisfaction with life and happiness) well-being of 55 young transgender adolescents before the onset of puberty suppression (T0), when cross-sex

hormones started (T1) and 1 year after sex-reassignment surgery (T2). They found that after surgery the psychological functioning and well-being had steadily improved and were similar or better than in same-age young adults from the general population. As expected, gender dysphoria and problems with the body image persisted through puberty suppression and remitted only after cross-sex hormones and surgery. Body image difficulties are a core feature of gender dysphoria and are also present in young adult patients [14]. The majority of the 55 young adults indicated that they experienced the social transition as easy and none of them reported regret concerning the medical interventions. Moreover intriguing is that none of the natal females had received a phalloplasty yet and nevertheless reported a good quality of life. This study impressively demonstrated that psychiatric problems in gender dysphoric youth improved through medical treatment with a combination of puberty suppression and cross-sex hormones and surgery in minors. However, the "Dutch protocol" demands the "absence of psychiatric comorbidity" [15] and thus minors that are psychologically unstable and suffer from psychiatric comorbidity are excluded from participation in such studies [16]. One reason to exclude those minors is that puberty suppression had been an experimental therapy approach without a sound evidence-base. This situation has however changed after publication of the de Vries study [13**]. As Kaltiala-Heino and colleagues demonstrated [6*] a substantial part of minors that present with gender dysphoria in Finland have a severe psychiatric comorbidity. It is therefore important to gain more insight into long-term follow-up of these minors. Also evidence to define factors that exclude minors from puberty suppression is needed (and also to identify "desisters" beforehand). There seems to be a certain threshold of psychiatric comorbidity that is acceptable for clinicians to indicate puberty suppression. What defines this threshold and what defines psychological stability? Is only mild comorbid psychopathology reduced by medical treatments? And if not, is it ethical to exclude gender dysphoric minors from medical treatment just because they have a psychiatric comorbidity? These questions highlight that longitudinal studies in gender dysphoric minors addressing outcomes in relation to particular comorbidities (like autism spectrum disorder) are needed urgently. Such research

may help to tone down the extremely emotional debate about treatment and diagnosis of children and adolescents with gender dysphoria.

From clinical practice we know that sometimes adult gender dysphoric patients have severe comorbid psychopathology (e.g. recurrent depression or borderline personality disorder) and nevertheless experience a dramatic improvement in mental health through transitioning and transition-related care. A recent long-term follow-up evaluation (> 10 years) points to the same conclusion [17]. However, some people do not experience a complete remission from psychopathology and need an ongoing psycho- or pharmacotherapy even after transitioning [17]. Especially the study by Kaltiala-Heino and colleagues emphasizes that we need to be very clear about which kids we need to treat by which protocol because we have fewer time for decision making with the looming onset of puberty and its irreversible bodily changes. We are not in a situation in which we can easily postpone a decision about transitioning into adulthood and refer to ethical statements in medicine like "in dubio abstine" or "primum non nocere" because either way - by suppressing or not-suppressing puberty - we may harm. Some patients that due to psychiatric comorbidity were not eligible for treatment before the age of 18 years at the VU clinic in Amsterdam (where the "Dutch protocol" was established) persisted in their wish for transition [15]. For these children and adolescents we need evidence whether medical interventions despite comorbid mental disorders are indicated or not.

Neuroimaging and predictive measures

A fear that was associated with puberty suppression in minors was that brain development during puberty might be disturbed by hormonal suppression. Especially the prefrontal cortex (PFC) undergoes profound plastic changes during puberty and early adolescence [18]. Therefore, Staphorsius and colleagues [19**] studied executive functioning – which is highly dependent on the PFC and improves with age until adulthood – in gender dysphoric adolescents that were treated with puberty suppression. Using the *Tower of London*-fMRI paradigm, they found that puberty suppression had neither an effect on executive functioning in gender dysphoric boys nor in girls. However, they found that natal sex affected neural activation during

the task in controls and puberty suppressed gender dysphoric adolescents. In contrast, unsuppressed adolescents with gender dysphoria exhibited no sex difference in neural activation. Thus, the authors concluded that "puberty suppression even seemed to make some aspects of brain functioning more in accordance with the natal sex". This study was to our knowledge the first to investigate how puberty suppression affects brain development and to indicate that puberty suppression does not disturb brain development during puberty in gender dysphoric adolescents. From adult people with gender dysphoria we know that cross-sex hormones have a profound effect on brain plasticity markers like cortical thickness and brain-derived neurotrophic factor [20,21] and thus would expect long-term effects of puberty suppression and cross-sex hormones on brain plasticity in minors.

There is also an ongoing debate about the diagnosis of gender identity disorder or gender incongruence in childhood. Some advocacy groups claim that the diagnosis pathologizes gender variant behavior of kids that do not have a stable gender identity yet but merely explore the gender boundaries. Using implicit and explicit measures, a recent study [22] investigated the gender cognition of gender dysphoric children. Of note, the population of the Olson study was highly selected: all children in this study were supported by their families to live according to their identified gender in the United States. Olson and colleagues found on all measures that responses of gender dysphoric children were indistinguishable from controls, when matched by gender identity. They stressed that gender dysphoric "children are not confused, delayed, showing gender-atypical responding, pretending or oppositional – they instead show responses entirely typical and expected for children with their gender identity." They even went further and suggested to test for the predictive value of the investigated measures in future research to possibly use them in clinical settings to identify those kids that remain stable in their gender identity in later life. In light of the abovementioned findings concerning puberty suppression predictive measures may indeed be helpful in clinical decision making, especially for those kids with psychiatric comorbidity and add to other factors that were described earlier [23].

Conclusion

In conclusion, more longitudinal research with gender dysphoric children and adolescents is needed to compare different strategies of care and to see long-term results especially in those minors with comorbid psychiatric disorders. The lack of evidence is even more pressing considering a recent study in which the dramatically increasing number of referrals to gender clinics was reported [24]. Particularly the number of referred natal females is increasing [24]. To date it is unclear what cultural and biological underpinnings are the driving forces behind this increase in gender dysphoria and how we should face it.

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