

Psychiatric comorbidity in gender dysphoric adolescents

Annelou L.C. de Vries,¹ Theo A.H. Doreleijers,¹ Thomas D. Steensma,² and Peggy T. Cohen-Kettenis²

Departments of ¹Child and Adolescent Psychiatry; and ²Medical Psychology, VU University Medical Center, Amsterdam, The Netherlands

Background: This study examined psychiatric comorbidity in adolescents with a gender identity disorder (GID). We focused on its relation to gender, type of GID diagnosis and eligibility for medical interventions (puberty suppression and cross-sex hormones). **Methods:** To ascertain DSM-IV diagnoses, the Diagnostic Interview Schedule for Children (DISC) was administered to parents of 105 gender dysphoric adolescents. **Results:** 67.6% had no concurrent psychiatric disorder. Anxiety disorders occurred in 21%, mood disorders in 12.4% and disruptive disorders in 11.4% of the adolescents. Compared with natal females ($n = 52$), natal males ($n = 53$) suffered more often from two or more comorbid diagnoses (22.6% vs. 7.7%, $p = .03$), mood disorders (20.8% vs. 3.8%, $p = .008$) and social anxiety disorder (15.1% vs. 3.8%, $p = .049$). Adolescents with GID considered to be 'delayed eligible' for medical treatment were older [15.6 years ($SD = 1.6$) vs. 14.1 years ($SD = 2.2$), $p = .001$], their intelligence was lower [91.6 ($SD = 12.4$) vs. 99.1 ($SD = 12.8$), $p = .011$] and a lower percentage was living with both parents (23% vs. 64%, $p < .001$). Although the two groups did not differ in the prevalence of psychiatric comorbidity, the respective odds ratios ('delayed eligible' adolescents vs. 'immediately eligible' adolescents) were >1.0 for all psychiatric diagnoses except specific phobia. **Conclusions:** Despite the suffering resulting from the incongruence between experienced and assigned gender at the start of puberty, the majority of gender dysphoric adolescents do not have co-occurring psychiatric problems. Delayed eligibility for medical interventions is associated with psychiatric comorbidity although other factors are of importance as well. **Keywords:** Gender identity disorder, gender dysphoria, adolescents, psychiatric comorbidity, puberty suppression, cross-sex hormones.

Introduction

Adolescents diagnosed with gender identity disorder (GID) exhibit a deeply felt discomfort with their assigned gender and a strong identification with the opposite gender (American Psychiatric Association, 2000). Adolescents with GID are of current interest, as increasing numbers of adolescents with GID are reported to be attending specialized gender identity clinics around the world (Zucker, Bradley, Owen-Anderson, Kibblewhite, & Cantor, 2008), and the age of applying for gender reassignment has dropped considerably (Cohen-Kettenis, Delemarre-van de Waal, & Gooren, 2008). Compared with studies on children and adults with GID, research on gender dysphoric adolescents is lagging behind and little is known about psychological functioning of adolescents with GID as a group. However, assessing psychiatric comorbidity of gender dysphoric adolescents is considered essential, especially when making a decision on clinical management that may include medical interventions (Cohen-Kettenis et al., 2008).

Whereas gender dysphoria will remit in the majority of prepubertal children (Drummond, Bradley, Peterson-Badali, & Zucker, 2008; Wallien & Cohen-Kettenis, 2008), in most gender dysphoric

adolescents it will not (Cohen-Kettenis & Pfäfflin, 2003). In recent years, after careful psychological evaluation, medical interventions for adolescents have become available. Cross-sex hormone treatment may be prescribed to a selected group of gender dysphoric adolescents between the ages of 16 and 18 years, and suppression of puberty by means of gonadotropin-releasing hormone analogs can start in 12–16-year olds. Puberty suppression is fully reversible. The gender dysphoric adolescents therefore 'buy time' to explore their gender dysphoria without physical changes that cannot be undone before making a more definite decision on treatment of gender reassignment. It is meant to prevent the distress and emotional problems that may stem from further development of secondary sex characteristics (Cohen-Kettenis et al., 2008).

Studies on psychological functioning of adolescents with GID who were accepted for cross-sex hormones as the first step of gender reassignment between the ages of 16 and 18 years show diverse results. Using the Dutch short Minnesota Multiphasic Personality Inventory (MMPI), psychological functioning appeared to be within the normal range before medical treatment had started (Cohen-Kettenis & van Goozen, 1997). On the Dutch version of the Symptom Checklist 90, however, adolescents with GID had a total score that was in the high range

Conflict of interest statement: No conflicts declared.

compared with the Dutch normative sample (Smith, van Goozen, & Cohen-Kettenis, 2001). In a retrospective analysis at a specialized gender identity clinic of medical chart notes on 69 adolescents aged 12 years and over, various problem behaviors were observed (Di Ceglie, Freedman, McPherson, & Richardson, 2002). For example, aggressive behavior was found in 32% and depression in 52% of the cases. One problem in comparing gender dysphoric adolescents across clinics is that gender identity clinics do not always use the same measures. There is one cross-national study comparing prepubertal children with GID using the parent-reported Child Behavior Checklist (CBCL; Cohen-Kettenis, Owen, Kaijser, Bradley, & Zucker, 2003; Zucker & Bradley, 1995). No such comparative studies have been performed yet in gender dysphoric adolescents. However, there are studies of the same Dutch and Canadian clinics that have both used the CBCL. For example, 84% in gender dysphoric adolescents who were recommended for puberty suppression in a Toronto gender identity clinic (Zucker et al., 2011) had a total sum CBCL score that fell in the clinical range, whereas this was the case in only 44% of the adolescents with GID eligible for puberty suppression at the Amsterdam gender identity clinic (de Vries, Steensma, Doreleijers, & Cohen-Kettenis, 2010b). From these reports, it can be deemed that a subgroup of adolescents who present at gender identity clinics have psychological problems other than gender dysphoria. The percentage of applicants with psychopathology, however, seems to differ widely between clinics. One explanation for these differences is that the experienced psychosocial adversity as a result of the GID, which might contribute to elevated rates of psychopathology, varies between countries (Clements-Nolle, Marx, & Katz, 2006; Grossman & D'Augelli, 2007; Widmer, Treas, & Newcomb, 1998). The presence of psychiatric comorbidity could also be related to family factors, for example, how families cope with their gender dysphoric adolescent might be of influence (Wren, 2002). High levels of psychiatric comorbidity in gender dysphoric adolescents might also be expected secondary to the distress associated with GID, as the incongruence between experienced and desired gender becomes more salient (e.g., Cohen-Kettenis et al., 2008).

In prepubertal children with GID, only one study used a categorical approach on psychiatric comorbidity (Wallien, Swaab, & Cohen-Kettenis, 2007). Fifty-two percent of the children had one co-occurring psychiatric diagnosis, and 29% had multiple comorbid diagnoses. Emotional disorders (31% anxiety disorders, 7% mood disorders) were more prevalent than disruptive disorders (23% attention deficit hyperactivity disorder (ADHD) and oppositional defiant disorder). To our knowledge, no such study has been conducted on adolescents with GID, despite the importance of insight into associated

psychopathology of adolescents with GID for assessment and treatment planning. Therefore, we conducted a study focusing on gender dysphoric adolescents aged 12–17 years attending the Amsterdam Gender Identity Clinic. Assuming that a subgroup of adolescents have psychological problems other than gender dysphoria, we first investigated prevalence rates and types of co-occurring psychiatric disorders in all referred adolescents. Second, we compared adolescents who met the complete criteria of GID with gender dysphoric adolescents who were subthreshold for GID. We hypothesized that adolescents with subthreshold GID have specific types of comorbid psychopathology. For example, the incidence of an autism spectrum disorder was almost sixfold higher in adolescents with GID-NOS (not otherwise specified) than in adolescents with complete GID in another study by the Amsterdam Gender Identity Clinic (de Vries, Noens, Cohen-Kettenis, van Berckelaer-Onnes, & Doreleijers, 2010a). Finally, within the group of adolescents diagnosed with GID, we compared psychiatric comorbidity of those who were considered immediately eligible for puberty suppression with that of adolescents whose diagnostic procedure took longer before they were considered eligible for puberty suppression. We expected more co-occurring psychiatric problems in adolescents with longer diagnostic procedures as one of the criteria for puberty suppression eligibility is the absence of pervasive psychiatric comorbidity that might interfere with the diagnostic work-up (Cohen-Kettenis et al., 2008).

Methods

Participants and procedure

Between April 2002 and December 2009, 201 adolescents were consecutively referred to the Gender Identity Clinic of the VU University Medical Center (VUmc) in Amsterdam. This is the only clinic in the Netherlands with a multidisciplinary team treating gender dysphoric adolescents. Seventeen adolescents dropped out of the diagnostic procedure, often after just one session and mostly because it had become evident that gender dysphoria was not the main problem. It might be possible that these 17 drop-outs had higher rates of psychiatric problems, somewhat suppressing the prevalence rates in this study. The remaining 184 adolescents underwent a standardized clinical assessment (for a complete description of the procedure, see Cohen-Kettenis et al., 2008). Eighteen parents who had previously participated in the earlier study on psychiatric comorbidity when their then prepubertal children were assessed (see Wallien et al., 2007) were not again invited to be interviewed. The parents of the remaining 166 adolescents were invited to have a standardized Diagnostic Interview Schedule for Children (DISC) interview (see later for a description of the instrument). Preferably, the appointment was combined with the psychological assessment of their son or daughter.

Table 1 General characteristics of 105 gender dysphoric adolescents

Variable	All (<i>N</i> = 105)	Natal males (<i>N</i> = 53)	Natal females (<i>N</i> = 52)	<i>t</i> or χ^2	<i>p</i>
Age in years (<i>N</i>)	105	53	52	-0.22	.59
<i>M</i> (<i>SD</i>)	14.6 (2.2)	14.5 (2.2)	14.6 (2.2)		
Range	10.5–18.0	10.5–17.7	10.7–18.0		
Full-scale IQ (<i>N</i>)	100	49	51	-1.4	.45
<i>M</i> (<i>SD</i>)	97.4 (14.2)	95.4 (13.1)	99.5 (15.0)		
Living arrangements, ^a <i>N</i> (%)	103	52	51	1.6	.20
Both parents	53 (51.5)	30 (56.6)	23 (43.3)		
Other	50 (48.5)	22 (44.0)	28 (56.0)		
Parents' educational level, ^b <i>N</i> (%)	103	52	51	1.57	.53
High	16 (15.5)	6 (11.5)	10 (19.6)		
Middle	70 (68.0)	37 (71.2)	33 (64.7)		
Low	17 (16.5)	9 (17.3)	8 (15.7)		

^aFor living arrangements, the category 'other' included living with one biological parent, adopted, living in a group home and the like.

^bParents' educational level was measured on a 5-point scale: 1 = completed or some elementary school; 2 = junior general secondary school; 3 = senior secondary or vocational school; 4 = college or higher professional education; 5 = university. Education level was divided into three groups: 1, 2 = low; 3, 4 = middle; 5 = high.

When this was not possible a separate appointment was made. In most cases, the mother was the interviewed caregiver. Caregivers of 61 adolescents were not able to come to the clinic, even after repeated invitations, or declined to participate. The primary reason was that the regular visits necessary for the clinical assessment of the adolescent were already a great burden for the family, as some families had to travel long distances.

Participants were parents of the remaining 105 gender dysphoric adolescents, whose general demographic characteristics are presented in Table 1. The study was approved by the Medical Ethics Committee of the VUmc in Amsterdam. All adolescents and their parents gave informed consent.

Measures

Intelligence. Full-scale intelligence was measured by Dutch versions of the Wechsler Intelligence Scale for Children (WISC) or the Wechsler Adult Intelligence Scale (WAIS), depending on the age of the assessed adolescent (Wechsler, 1997; Wechsler et al., 2002; WISC-R Project group et al., 1986).

Behavior problems. Overall problem behavior was assessed by the mean total *T* score of the CBCL (Achenbach, 1991; Verhulst, van der Ende, & Koot, 1996), a widely used parent report questionnaire to assess behavioral problems in children and youths.

Living arrangements and educational level of the parents. For living arrangements of the adolescents, they were coded as living with either both biological parents, or as having other living conditions (e.g., one biological parent, foster care, adopted). Parents' educational level was measured on a 5-point scale, where 1 = completed or some elementary school, 2 = junior general secondary school, 3 = senior secondary or vocational school, 4 = college or higher professional education and 5 = university. Educational level was divided into three groups: 1 and 2 = low, 3 and 4 = middle and 5 = high. When data on both parents were available, a mean score was derived.

GID diagnosis. Either a GID or GID subthreshold diagnosis was made after an extensive diagnostic procedure over a prolonged period of time (usually 6–12 months) according to the criteria of the DSM-IV-TR (American Psychiatric Association, 2000). Adolescents received a GID diagnosis when they fulfilled all GID criteria (*n* = 89). Adolescents who reported gender problems but did not fulfill all GID criteria, were considered to be 'subthreshold' for GID (*n* = 16).

Eligibility. All adolescents with GID were considered eligible for puberty suppression. For puberty suppression, eligible adolescents were divided into two groups: *immediately eligible* adolescents (*n* = 63) when the interval from the start of diagnostic procedures to the start of puberty suppression took less than 1.5 years and *delayed eligible* adolescents (*n* = 26), when this interval took 1.5 years or more (for a complete description of the eligibility criteria, see Cohen-Kettenis et al., 2008). The mean time between their first attendance at the clinic and the start of puberty suppression in the *immediately eligible* group was 0.78 year (*SD* = 0.54). Of the 26 *delayed eligible* adolescents with GID, most often referral to and treatment at a mental health clinic were requested before they were eligible for medical interventions. Of the 26, 23 had started hormone treatment at the time of the analyses of this study. The mean time between their first attendance at the clinic and the start of any medical intervention was 1.86 years (*SD* = 0.14). The three other adolescents with GID had not yet fulfilled the eligibility criteria at the time of the analyses of this study, 1.5 years after the last DISC data were collected.

Psychiatric comorbidity. Psychopathology was assessed by using the Dutch translation of the DISC-IV (Ferdinand & van der Ende, 1998; Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000). The DISC is a highly structured, respondent-based psychiatric interview assessing all common DSM-IV Axis I mental disorders in children and adolescents. The DISC is designed for use by nonclinicians. The child version of the DISC has been designed for administration to

children between the ages of 9 and 17 years; the parent version of the DISC can be administered to parents of children aged 6–17 years (Shaffer et al., 2000). We chose to use the parent version for this study, as the adolescents already had taken a large battery of tests for their clinical assessment and the DISC interview takes around 2 hr. Trained lay interviewers administered the DISC to the parents or caregivers of the adolescents. Interviewers were medical or psychology students who chose to fulfill their research training at the gender identity clinic. Each trainee received personal feedback on the style and adequacy of the interview and the accuracy of scoring.

The DISC-IV interview covers more than 30 DSM-IV diagnoses and is organized into six diagnostic sections: anxiety disorders (social phobia, separation anxiety, specific phobias, agoraphobia, panic disorder, generalized anxiety disorder, post-traumatic stress disorder, obsessive compulsive disorder), mood disorders (major depression, dysthymic disorder, mania, hypomania), disruptive disorders (conduct disorder, oppositional defiant disorder, attention deficit hyperactivity disorders), substance use disorders, schizophrenia and miscellaneous disorders (anorexia nervosa, bulimia nervosa, enuresis, encopresis, tic disorders, pica, trichotillomania). Our measure of the presence of any DSM diagnosis concerned the previous 12 months.

Analyses

To determine whether the 105 participating adolescents were representative of all 184 adolescents assessed between 2002 and 2009, between group analyses were performed. There were no significant differences

between the 105 participating adolescents and the 79 nonparticipating adolescents with regard to gender distribution, mean full-scale intelligence, marital status and educational level of the parents, mean total problem *T*-score on the CBCL, GID diagnosis (GID or subthreshold GID) or eligibility (eligible, not eligible or delayed eligible) for a medical intervention. Only age at assessment was significantly older in the participating adolescents (14.4 years, *SD* = 2.2) compared with the nonparticipating group (13.9 years, *SD* = 2.2, *p* < .05). Our study sample was thus, in many relevant ways, representative of our whole patient group.

Gender differences, differences between adolescents with GID and subthreshold GID, and differences between eligible and delayed eligible adolescents with GID with regard to age, full-scale IQ, parental marital status and educational level of the parents were analyzed using *t*-tests or chi-squared tests when applicable.

First, prevalence rates of past year DSM diagnoses were estimated. Second, differences in prevalence rates and odds ratios (ORs) were ascertained between the various groups (natal males vs. natal females, GID vs. subthreshold GID and 'delayed eligible' vs. 'immediately eligible').

Results

All gender dysphoric adolescents

General characteristics of the adolescents are presented in Table 1. No gender differences were observed with regard to age at assessment, full-scale IQ, parental marital status or educational level of the parents.

Table 2 Prevalence estimates and gender differences of DSM-IV diagnoses in gender dysphoric adolescents

Diagnosis ^a (past year)	All (<i>N</i> = 105) Percent (no.)	Natal males (<i>N</i> = 53) Percent (no.)	Natal females (<i>N</i> = 52) Percent (no.)	<i>p</i> ^b	OR ^c
Any anxiety	21 (22)	24.5 (13)	17.3 (9)	.25	0.64
Specific phobia	7.6 (8)	4.5 (4)	4.5 (4)	.63	1.0
Social phobia	9.5 (10)	15.1 (8)	3.8 (2)	.049	0.26
Agoraphobia	1.0 (1)	1.1 (1)	0	.51	
Separation anxiety	3.8 (4)	1.9 (1)	5.8 (3)	.36	3.2
Generalized anxiety	1.0 (1)	0	1.9 (1)	.50	
Any mood	12.4 (13)	20.8 (11)	3.8 (2)	.008	0.15
Major depression	8.6 (9)	13.2 (7)	3.8 (2)	.09	0.26
Dysthymia	3.8 (4)	7.5 (4)	0	.06	
Any disruptive	11.4 (12)	15.1 (8)	7.7 (4)	.19	0.47
ADHD ^d combined	2.9 (3)	1.9 (1)	3.8 (2)	.50	2.1
ADHD inattentive	1.9 (2)	1.9 (1)	1.9 (1)	.75	1.0
ADHD hyperactive	1.0 (1)	1.9 (1)	0	.50	
Oppositional defiant	8.6 (9)	11.3 (6)	5.8 (3)	.18	0.48
Any substance use ^c	1.0 (1)	1.9 (1)	0	.50	
One or more DSM-IV diagnoses	32.4 (34)	39.6 (21)	25 (13)	.08	0.51
Two or more DSM-IV diagnoses	15.2 (16)	22.6 (12)	7.7 (4)	.03	0.29
Three or more DSM-IV diagnoses	2.9 (3)	3.8 (2)	1.9 (1)	.51	0.50

Significant results are printed in bold.

^aPrevalence rates of panic disorder (with and without agoraphobia), selective mutism, obsessive compulsive disorder, post-traumatic stress disorder, anorexia nervosa, bulimia nervosa, enuresis, encopresis, any tic disorder, pica, trichotillomania, manic episode, hypomanic episode, schizophrenia and conduct disorder were 0%.

^bFisher's exact test.

^cOR, odds ratio, ratio of odds of psychiatric comorbidity natal males versus females.

^dADHD, attention deficit hyperactivity disorder. One adolescent had a marijuana dependency; no other substance use disorders were reported.

Table 2 shows that 67.6% of the 105 assessed adolescents referred to the gender identity clinic had no concurrent psychiatric disorder, 32.4% had at least one and 15.2% had two or more comorbid diagnoses. The most common disorders were social anxiety disorder (9.5%), major depression (8.6%), oppositional defiant disorder (8.6%) and specific phobia (7.6%). With a prevalence of 21%, anxiety disorders were most common. A mood disorder occurred in 12.4% and a disruptive disorder in 11.4% of the adolescents. Panic disorder (with and without agoraphobia), selective mutism, obsessive compulsive disorder, post-traumatic stress disorder, anorexia nervosa, bulimia nervosa, enuresis, encopresis, tic disorders, pica, trichotillomania, manic episode, hypomanic episode, schizophrenia and conduct disorder were not observed. Substance use disorders had a prevalence of 1% with one marijuana-dependent adolescent.

There were significant gender differences. Compared with natal females, natal males suffered more often from two or more comorbid diagnoses [22.2% vs. 7.7%, $p = .03$, OR = 0.29, 95% confidence interval (CI): 0.09–0.95], mood disorders (20.8% vs. 3.8%, $p = .008$, OR = 0.15, 95% CI: 0.03–0.73) and social anxiety disorder (15.1% vs. 3.8%, $p = .049$, OR = 0.26, 95% CI: 0.05–1.19).

Adolescents with GID versus adolescents subthreshold for GID

No differences between adolescents with a complete GID and adolescents with subthreshold GID were observed with regard to age at assessment, full-scale IQ, parental marital status or educational level of the parents. With respect to the prevalence of comorbid psychiatric diagnoses, adolescents with a complete and subthreshold GID only differed with respect to the prevalence of specific phobia (4.5% with a com-

plete GID vs. 25%, $p = .02$, OR = 0.80, 95% CI: 0.08–8.01).

Adolescents with GID

In adolescents with a GID diagnosis, differences in general characteristics were observed between adolescents considered immediately eligible compared with adolescents considered delayed eligible for medical interventions (see Table 3). The delayed eligible group was, when attending the clinic, significantly older [15.6 years ($SD = 1.6$) vs. 14.1 years ($SD = 2.2$), $t(64.3) = -3.4$, $p = .001$] than the immediately eligible group, and their IQs were significantly lower [91.6 ($SD = 12.4$) vs. 99.1 ($SD = 12.8$), $t(84) = 2.5$, $p = .011$]. In addition, significantly fewer delayed eligible adolescents were living with both biological parents compared with immediately eligible adolescents [23.1% vs. 63.9%, $\chi^2(1) = 11.8$, $p < .001$], but no difference in educational level of the parents was observed between both groups.

Although there were higher percentages of psychiatric comorbidity in delayed eligible adolescents than in immediately eligible adolescents with GID (Table 4), this difference was not statistically significant. The odds of having a comorbid psychiatric disorder are higher in delayed eligible adolescents, except specific phobia (ORs are shown in Table 4).

Discussion

More than two third (68%) of the gender dysphoric adolescents in the current study had no psychiatric comorbidity. When comparing this rate with results of studies that were conducted with the same instrument (the DISC) and in the same age group (adolescents), the 32% that met DSM-IV criteria for one or more co-occurring psychiatric disorders, is, on average, more than in the general population but

Table 3 General characteristics of 89 adolescents with gender identity disorder (GID), immediately eligible and delayed eligible

Variable	All GID ($N = 89$)	Immediately eligible ($N = 63$)	Delayed eligible ($N = 26$)	t or χ^2	p
Age in years (N)	89	63	26	-3.43	.001
M (SD)	14.5 (2.2)	14.1 (2.2)	15.6 (1.6)		
Range	10.5–17.9	10.5–17.75	12.0–17.9		
Full-scale IQ (N)	86	61	25	2.50	.011
M (SD)	96.9 (13.1)	99.1 (12.8)	91.6 (12.4)		
Living arrangements, N (%)	87	61	26	12.2	<.001
Both parents	45 (51.7)	39 (63.9)	6 (23.1)		
Other ^a	42 (48.3)	22 (36.1)	20 (76.9)		
Parents' educational level, ^b N (%)	87	63	24	0.07	.96
High	11 (12.6)	12 (19.0)	4 (16.7)		
Middle	60 (69.0)	43 (68.3)	17 (70.8)		
Low	16 (18.4)	8 (12.7)	3 (12.5)		

Significant results are printed in bold.

^aFor living arrangements, the category 'other' included living with one biological parent, adopted, living in a group home and the like.

^bParents' educational level was measured on a 5-point scale: 1 = completed or some elementary school; 2 = junior general secondary school; 3 = senior secondary or vocational school; 4 = college or higher professional education; 5 = university. Education level was divided into three groups: 1, 2 = low; 3, 4 = middle; 5 = high.

Table 4 Prevalence estimates of DSM-IV diagnoses in gender identity disorder (GID) adolescents, immediately eligible and delayed eligible

Diagnosis (past year)	GID (<i>N</i> = 89) Percent (no.)	Eligible (<i>N</i> = 63) Percent (no.)	Delayed eligible (<i>N</i> = 26) Percent (no.)	<i>p</i> ^a	OR ^b
Any anxiety	20.2 (18)	17.5 (11)	26.9 (7)	.23	1.7
Specific phobia	4.5 (4)	4.8 (3)	3.8 (1)	.67	0.80
Social phobia	11.2 (10)	7.9 (5)	19.2 (5)	.12	2.8
Agoraphobia	1.1 (1)	1.6 (1)	0	.71	
Separation anxiety	3.4 (3)	3.2 (2)	3.8 (1)	.65	1.2
Generalized anxiety	1.1 (1)	1.6 (1)	0	.71	
Any mood	12.4 (11)	11.1 (7)	15.4 (4)	.41	1.5
Major depression	9.0 (8)	7.9 (5)	11.5 (3)	.43	1.5
Dysthymia	3.4 (3)	3.2 (2)	3.8 (1)	.65	1.2
Any disruptive	10.1 (9)	6.3 (4)	19.2 (5)	.08	3.5
ADHD ^c combined	3.4 (3)	3.2 (2)	3.8 (1)	.65	1.2
ADHD inattentive	2.2 (2)	1.6 (1)	3.8 (1)	.50	2.5
ADHD hyperactive	1.1 (1)	0	3.8 (1)	.29	
Oppositional defiant	6.7 (6)	3.2 (2)	15.4 (4)	.06	5.5
One or more DSM-IV diagnoses	31.5 (28)	28.6 (18)	38.5 (10)	.25	1.6
Two or more DSM-IV diagnoses	13.5 (12)	9.5 (6)	23.1 (6)	.09	2.9
Three or more DSM-IV diagnoses	2.2 (2)	0	7.7 (2)	.08	

^aFisher's exact test.

^bRatio of odds of psychiatric comorbidity 'eligible' versus 'delayed eligible'.

^cOR, odds ratio; ADHD, attention deficit hyperactivity disorder.

less than in youth receiving mental health care. For example, 21% of a national sample of Dutch adolescents met criteria for one or more DSM-III-R diagnoses (Verhulst, van der Ende, Ferdinand, & Kasius, 1997). When using DSM-IV diagnoses, this was true for 17% of adolescents in a large North American metropolitan area (Roberts, Roberts, & Xing, 2007), whereas in youth attending mental health services a 60% estimate was found (Garland et al., 2001).

Most prevalent in our study were emotional disorders, with a nearly 10% prevalence of social phobia; studies in the general adolescent population reveal a prevalence of 1.65%–6.5% (Roberts et al., 2007; Verhulst et al., 1997). Disruptive disorders were also observed. Clearly, many gender dysphoric youth are in despair, as reflected by their depression, anxiety and oppositional behavior. Other studies in adolescents with GID, however, show higher rates of associated problems, including aggression, depression, suicidal thoughts and attempted suicide (Di Ceglie et al., 2002; Grossman & D'Augelli, 2007). The 10% prevalence of social phobia may indicate that the development of gender variant adolescents' peer relations is at stake in a non-negligible subgroup. Indeed, in a study comparing gender dysphoric children with adolescents, the latter showed poorer peer relations, which were in turn the strongest predictor of CBCL psychopathology (Zucker, Owen, Bradley, & Ameeriar, 2002).

The prevalence rate of 32% of adolescents in the current study was low compared with prepubertal gender dysphoric children in the same clinic, with an observed 52% prevalence rate of one or more psychiatric disorders (Wallien et al., 2007). Our findings

are thus in contrast to other studies showing more problem behavior in adolescents compared with children (Di Ceglie et al., 2002; Zucker et al., 2002). However, in these studies, puberty suppression was not an option at the time that the studies were conducted. In our study, the trust adolescents felt that puberty suppression would be available by the time they would need it, may have relieved the acute distress accompanying their gender dysphoria and contributed to the fact that we found lower rates of comorbidity.

In our sample, gender dysphoric natal males had higher odds than natal females of having a mood disorder or social phobia whereas gender dysphoric natal females had lower odds than natal males of disruptive disorders. It is interesting that in the general population the rates of anxiety and depression are generally higher in female than male adolescents and the prevalence rate of disruptive disorders is lower in females compared with males (Garland et al., 2001; Roberts et al., 2007; Verhulst et al., 1997). Apparently, adolescents with GID show types of psychopathology that are usually associated with the desired gender.

Contrary to our expectations, co-occurring psychopathology was not associated with the type of GID diagnosis (GID or subthreshold GID) an adolescent had. Likewise, prepubertal children with subthreshold GID did not have significantly more or different comorbid psychiatric problems than children with complete GID (Wallien et al., 2007). Both studies, however, did not assess autism spectrum disorders. Presumably, the sixfold higher odds of a co-occurring autism spectrum disorder in adolescents with GID-NOS compared with youth fulfilling the complete criteria of GID in another study by the

Amsterdam Gender Identity Clinic, is an exception in this regard (de Vries et al., 2010a).

Although prevalence rates were not significantly different, delayed eligible adolescents had higher odds of having psychiatric comorbidity, especially of an oppositional defiant disorder, social phobia or more than three DSM diagnoses. These conditions can easily disturb the necessary long-term therapeutic relationship with the pediatric endocrinologist and the psychologist or psychiatrist of the gender identity clinic when adolescents' puberty is suppressed. Furthermore, delayed eligible adolescents differed on important general demographic characteristics from immediately eligible adolescents with GID; they were older when attending the gender identity clinic, had a lower intelligence and they were less often living with both biological parents. This may indicate that a constellation of these factors was deemed clinically important when making a decision to delay puberty suppression, and not psychiatric comorbidity only.

Several limitations in this study warrant comment. First, the size of the overall sample is moderate and the high rate of caregivers who were not able or declined to participate is problematic. However, to assess a potential selection bias in this subsample, we found that in many relevant ways, including total problem scores on the CBCL (Achenbach & Rescorla, 2001), the study group was representative of the complete patient group. Second, the small number of adolescents with subthreshold GID limits the power to examine differences with adolescents meeting all criteria for GID. Third, we used only parent informants. It is possible that this underestimated the number of some diagnoses, such as substance use, which parents are not always informed about. Many studies have reported that children's and parents' reports on psychiatric problems often do not overlap and that combining both informants to determine 'cases' may yield higher rates than true prevalence (Jensen et al., 1999). In a Dutch prevalence study on DSM diagnoses in adolescents, there was only moderate overlap between DISC-C and DISC-P diagnoses, although prevalence rates of any disorder based on parent information were quite similar to that based on adolescent information (Verhulst et al., 1997). Therefore, the prevalence estimates of

our study are most probably not very much biased by the use of the parent as the only informant, despite the necessity of both adolescent and parent information for individual clinical decisions.

Finally, this study was limited by the use of the DISC-IV, which does not include autism spectrum disorders. If that would have been the case, the rate of co-occurring psychiatric problems in gender dysphoric adolescents would have been higher, as the previously mentioned study at the same gender identity clinic revealed that 9.4% of the referred adolescents suffered from an autistic spectrum disorder (de Vries et al., 2010a).

In conclusion, this study showed that the majority of gender dysphoric adolescents do not have any comorbid psychiatric disorder, despite their increased suffering from the incongruence between experienced and assigned gender at the start of puberty. However, a significant minority of gender dysphoric adolescents is in need of specific care for mood, anxiety and oppositional disorders. Gender dysphoric natal males appear to require more mental health support than gender dysphoric females. The results further revealed that all adolescents with a GID diagnosis may be considered eligible for medical interventions, despite possible co-occurring psychopathology. However, clinicians need more time to make such a decision when there is psychiatric comorbidity. Finally, other factors might extend and complicate clinical assessment, such as age, intelligence and living arrangements of parents might complicate decisions.

Acknowledgements

This study was supported by a personal grant awarded to the first author by the Netherlands Organization for Health Research and Development (ZonMw). The authors would like to thank the adolescents and their parents who participated in this study.

Correspondence to

Annelou L.C. de Vries, VU University Medical Center, PO Box 7057, 1007 MB Amsterdam, The Netherlands; Tel: +31 20 4440861; Fax: +31 20 4440851; Email: alc.devries@vumc.nl

Key points

- In adolescents with GID, psychiatric comorbidity is reported to occur frequently, but empirical studies are limited and none have used a categorical approach.
- We studied the extent and type of psychiatric comorbidity and the implications for clinical management.
- The majority of gender dysphoric youth (68%) had no concurrent comorbid psychiatric diagnoses.
- When comorbid psychiatric diagnoses occurred, emotional disorders were most prevalent. Natal males had higher odds of co-occurring psychopathology than natal females.
- Adolescents considered delayed eligible for medical interventions had higher odds of having comorbidity, but other factors were of relevance as well (intelligence, age and living arrangements).

References

- Achenbach, T.M. (1991). *Manual for the youth self-report*. Burlington, VT: Department of Psychiatry, University of Vermont.
- Achenbach, T.M., & Rescorla, L.A. (2001). *Manual for the ASEBA school-age forms and profiles*. Burlington, VT: University of Vermont, Research Centre for Children, Youth and Families.
- American Psychiatric Association (2000). *Diagnostic and statistical manual of mental disorders, fourth edition, text revision* (4th edn). Washington, DC: Author.
- Clements-Nolle, K., Marx, R., & Katz, M. (2006). Attempted suicide among transgender persons: The influence of gender-based discrimination and victimization. *Journal of Homosexuality, 51*, 53–69.
- Cohen-Kettenis, P.T., Delemarre-van de Waal, H.A., & Gooren, L.J. (2008). The treatment of adolescent transsexuals: Changing insights. *Journal of Sexual Medicine, 5*, 1892–1897.
- Cohen-Kettenis, P.T., Owen, A., Kaijser, V.G., Bradley, S.J., & Zucker, K.J. (2003). Demographic characteristics, social competence, and behavior problems in children with gender identity disorder: A cross-national, cross-clinic comparative analysis. *Journal of Abnormal Child Psychology, 31*, 41–53.
- Cohen-Kettenis, P.T., & Pfäfflin, F. (2003). *Transgenderism and intersexuality in childhood and adolescence* (vol. 46). Thousand Oaks, London, New Delhi: Sage.
- Cohen-Kettenis, P.T., & van Goozen, S.H. (1997). Sex reassignment of adolescent transsexuals: A follow-up study. *Journal of the American Academy of Child and Adolescent Psychiatry, 36*, 263–271.
- Di Ceglie, D., Freedman, D., McPherson, S., & Richardson, P. (2002). Children and adolescents referred to a specialist gender identity development service: Clinical features and demographic characteristics. *International Journal of Transgenderism, 6*, http://www.symposium.com/ijt/ijtvo06no01_01.htm.
- Drummond, K.D., Bradley, S.J., Peterson-Badali, M., & Zucker, K.J. (2008). A follow-up study of girls with gender identity disorder. *Developmental Psychology, 44*, 34–45.
- Ferdinand, R.F., & van der Ende, J. (1998). *Diagnostic Interview Schedule for Children IV Parent-Version*. Rotterdam, The Netherlands: Department of Child and Adolescent Psychiatry, Erasmus University Rotterdam.
- Garland, A.F., Hough, R.L., McCabe, K.M., Yeh, M., Wood, P.A., & Aarons, G.A. (2001). Prevalence of psychiatric disorders in youths across five sectors of care. *Journal of the American Academy of Child and Adolescent Psychiatry, 40*, 409–418.
- Grossman, A.H., & D'Augelli, A.R. (2007). Transgender youth and life-threatening behaviors. *Suicide and Life-Threatening Behavior, 37*, 527–537.
- Jensen, P.S., Rubio-Stipec, M., Canino, G., Bird, H.R., Dulcan, M.K., Schwab-Stone, M.E., & Lahey, B.B. (1999). Parent and child contributions to diagnosis of mental disorder: Are both informants always necessary? *Journal of the American Academy of Child and Adolescent Psychiatry, 38*, 1569–1579.
- Roberts, R.E., Roberts, C.R., & Xing, Y. (2007). Rates of DSM-IV psychiatric disorders among adolescents in a large metropolitan area. *Journal of Psychiatric Research, 41*, 959–967.
- Shaffer, D., Fisher, P., Lucas, C.P., Dulcan, M.K., & Schwab-Stone, M.E. (2000). NIMH Diagnostic Interview Schedule for Children Version IV (NIMH DISC-IV): Description, differences from previous versions, and reliability of some common diagnoses. *Journal of the American Academy of Child and Adolescent Psychiatry, 39*, 28–38.
- Smith, Y.L., van Goozen, S.H., & Cohen-Kettenis, P.T. (2001). Adolescents with gender identity disorder who were accepted or rejected for sex reassignment surgery: A prospective follow-up study. *Journal of the American Academy of Child and Adolescent Psychiatry, 40*, 472–481.
- Verhulst, F.C., van der Ende, J., Ferdinand, R.F., & Kasius, M.C. (1997). The prevalence of DSM-III-R diagnoses in a national sample of Dutch adolescents. *Archives of General Psychiatry, 54*, 329–336.
- Verhulst, F.C., van der Ende, J., & Koot, H.M. (1996). *Handleiding voor de CBCL 4-18 (Manual for the Child Behavior Checklist and Revised Child Behavior Profile)*. Rotterdam, The Netherlands: Sophia Kinderziekenhuis/Academisch Ziekenhuis Rotterdam/Erasmus Universiteit.
- de Vries, A.L., Noens, I.L., Cohen-Kettenis, P.T., van Berckelaer-Onnes, I.A., & Doreleijers, T.A. (2010a). Autism spectrum disorders in gender dysphoric children and adolescents. *Journal of Autism and Developmental Disorders, 40*, 930–936.
- de Vries, A.L., Steensma, T.D., Doreleijers, T.A., & Cohen-Kettenis, P.T. (2010b). Puberty suppression in adolescents with gender identity disorder: A prospective follow-up study. *Journal of Sexual Medicine*, doi: 10.1111/j.1793-6109.2010.01943.x.
- Wallien, M.S., & Cohen-Kettenis, P.T. (2008). Psychosexual outcome of gender-dysphoric children. *Journal of the American Academy of Child and Adolescent Psychiatry, 47*, 1413–1423.
- Wallien, M.S., Swaab, H., & Cohen-Kettenis, P.T. (2007). Psychiatric comorbidity among children with gender identity disorder. *Journal of the American Academy of Child and Adolescent Psychiatry, 46*, 1307–1314.
- Wechsler, D. (1997). *Wechsler Adult Intelligence Scale-Third Edition (WAIS-III), Dutch Version* (3rd edn). Lisse, The Netherlands: Swets and Zeitlinger.
- Wechsler, D., Kort, W., Compaan, E.L., Bleichrodt, N., Resing, W.C.M., & Schittkatte, M. (2002). *Wechsler Intelligence Scale for Children-Third Edition (WISC-III)* (3rd edn). Lisse, The Netherlands: Swets and Zeitlinger.
- Widmer, E.D., Treas, J., & Newcomb, R. (1998). Attitudes toward nonmarital sex in 24 countries. *Journal of Sex Research, 35*, 349–358.
- WISC-R Project group, (1986). *WISC-R, Wechsler Intelligence Scale for Children-Revised, Nederlandse uitgave*. [Dutch version] Lisse, The Netherlands: Swets & Zeitlinger.
- Wren, B. (2002). 'I can accept my child is transsexual but if I ever see him in a dress I'll hit him': Dilemmas in parenting a transgendered adolescent. *Clinical Child Psychology and Psychiatry. Special Issue: Sexual Identity and Gender Identity, 7*, 377–397.
- Zucker, K.J., & Bradley, S. (1995). *Gender identity disorder and psychosexual problems in children and adolescents*. New York: Guilford.
- Zucker, K.J., Bradley, S.J., Owen-Anderson, A., Kibblewhite, S.J., & Cantor, J.M. (2008). Is gender identity disorder in adolescents coming out of the closet (Letter to the editor)? *Journal of Sex and Marital Therapy, 34*, 287–290.
- Zucker, K.J., Bradley, S.J., Owen-Anderson, A., Singh, D., Blanchard, R., & Bain, J. (2011). Puberty-blocking hormonal therapy for adolescents with gender identity disorder: A descriptive clinical study. *Journal of Gay and Lesbian Mental Health, 15*, 58–82.
- Zucker, K.J., Owen, A., Bradley, S.J., & Ameeriar, L. (2002). Gender-dysphoric children and adolescents: A comparative analysis of demographic characteristics and behavioral problems. *Clinical Child Psychology and Psychiatry, 7*, 398–411.

Accepted for publication: 3 May 2011

Published online: 14 June 2011