

Psychosexual Outcome of Gender-Dysphoric Children

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ABSTRACT

Objective: To establish the psychosexual outcome of gender-dysphoric children at 16 years or older and to examine childhood characteristics related to psychosexual outcome. **Method:** We studied 77 children who had been referred in childhood to our clinic because of gender dysphoria (59 boys, 18 girls; mean age 8.4 years, age range 5–12 years). In childhood, we measured the children's cross-gender identification and discomfort with their own sex and gender roles. At follow-up 10.4 ± 3.4 years later, 54 children (mean age 18.9 years, age range 16–28 years) agreed to participate. In this group, we assessed gender dysphoria and sexual orientation. **Results:** At follow-up, 30% of the 77 participants (19 boys and 4 girls) did not respond to our recruiting letter or were not traceable; 27% (12 boys and 9 girls) were still gender dysphoric (persistence group), and 43% (desistance group: 28 boys and 5 girls) were no longer gender dysphoric. Both boys and girls in the persistence group were more extremely cross-gendered in behavior and feelings and were more likely to fulfill gender identity disorder (GID) criteria in childhood than the children in the other two groups. At follow-up, nearly all male and female participants in the persistence group reported having a homosexual or bisexual sexual orientation. In the desistance group, all of the girls and half of the boys reported having a heterosexual orientation. The other half of the boys in the desistance group had a homosexual or bisexual sexual orientation. **Conclusions:** Most children with gender dysphoria will not remain gender dysphoric after puberty. Children with persistent GID are characterized by more extreme gender dysphoria in childhood than children with desisting gender dysphoria. With regard to sexual orientation, the most likely outcome of childhood GID is homosexuality or bisexuality. *J. Am. Acad. Child and Adolesc. Psychiatry*, 2008;47(12):1413–1423. **Key Words:** gender identity disorder, gender dysphoria, pubertal outcome, psychosexual differentiation, sexual orientation.

Children diagnosed with gender identity disorder (GID) have a strong cross-gender identification and a persistent discomfort with their biological sex or gender role associated with that sex (gender dysphoria). Initial studies have shown that most children with GID will no longer be gender dysphoric later in life.^{1–7} However, a

few more recent articles^{8,9} indicated that the psychosexual differentiation of children with GID is more variable than what the early studies suggested and that, in a substantial proportion of the children (20%), the gender-dysphoric feelings persist into adolescence.

With *DSM-V* on the horizon, an important diagnostic issue concerns the relation between childhood and adolescent/adult GID. Some critics have expressed concerns that the *DSM*^{10,11} criteria do not adequately differentiate the children with “true” (and probably persistent) GID from those who show merely gender-nonconforming behavior¹² and that, as a consequence, children who should not be classified as having a psychiatric disorder would be treated with various psychological interventions. Clinically, it is also important to be able to discriminate between persisters and desisters before the start of puberty. If one was certain that a child belongs to the persisting group, interventions with gonadotropin-releasing hormone (GnRH) analogs to delay puberty could even start before puberty

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This article is the subject of an editorial by Dr. Kenneth Zucker in this issue.

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rather than after the first pubertal stages, as now often happens.¹³ The possibility of identifying the persisters in childhood would also be helpful, if treatments would be available to prevent the intensive and drastic hormonal and surgical treatments these children face in adolescence or adulthood.

Another issue regarding the psychosexual outcome of children with GID is the relation between the child's gender atypicality and sexual orientation in adulthood. Early prospective follow-up studies indicated that a high rate (60%–100%) of children (mostly boys) with gender dysphoria had a homosexual or bisexual sexual orientation in adolescence or adulthood and no longer experienced gender-dysphoric feelings.^{1–8} In a prospective follow-up study by Green,³ sexual orientation and gender identity in adulthood were assessed in 44 feminine boys and 30 control boys. Of these 44 feminine boys, only one youth was gender dysphoric at the age of 18, whereas none of the control boys reported gender dysphoria at follow-up. Sexual orientation in fantasy and behavior was assessed by means of a semi-structured interview. Green found that, on the behavior dimension, 80% of the feminine boys were either homosexual or bisexual, and, on the fantasy dimension, 75% of the feminine boys had a homosexual or a bisexual sexual orientation at follow-up. Among the control boys, the ratings were 4% for behavior and 0% for fantasy. Green and colleagues¹⁴ also found that sexual orientation was associated with childhood doll play and female role playing. The results of Green and others^{1–7} are in accordance with retrospective studies among adult homosexuals, who recalled more childhood cross-gender behavior than heterosexuals.¹⁵

The earlier follow-up studies^{1–9} indicated that the percentages of gender-dysphoric boys and girls who had a later bisexual/homosexual orientation were much higher than the base rates of bisexuality or homosexuality in general surveys and in epidemiological studies of adolescents and young adults. The reported percentages are lower in the study by Zucker and Bradley⁸ on (mostly) gender-dysphoric boys (31% of the 41 participants who had sexual fantasies had either a bisexual or homosexual sexual orientation in fantasy; for 58%, no data on sexual behavior were available) and in a study by Drummond et al.¹⁶ among 25 gender-dysphoric girls (32% of the girls reported having bisexual or homosexual fantasies; there were no data on sexual behavior for 32% of the girls), but in both studies, the proportion of

participants with a homosexual and bisexual sexual orientation was still substantially higher than the base rates in the general population.

Because a gender-dysphoric outcome was not common in the above studies, the studies^{1–9} focused more on the sexual orientation outcome of the gender-dysphoric children than on the relation between childhood gender dysphoria and later GID. Therefore, these reports do not give information on whether participants with distinct gender identity outcomes differ from each other in childhood. It has been argued that there is plasticity in gender identity differentiation that occurs in early development and narrows considerably by adolescence,¹⁶ but the precise factor or set of factors influencing psychosexual development is still unknown. It is likely that only the children with extreme gender dysphoria are future sex reassignment applicants, whereas the children with less persistent and intense gender dysphoria are future homosexuals or heterosexuals without GID. However, none of the follow-up studies have as yet provided evidence for this supposition.

In this study, we first assessed the psychosexual outcome of gender-dysphoric boys and girls in terms of gender identity and sexual orientation. Second, we investigated which childhood measures of gender behavior and feelings were related to GID persistence or desistance. Based on our clinical experience, we expected the more extreme gender-dysphoric children to be persisters.

METHOD

Participants

Between 1989 and 2005, 200 children (144 boys and 56 girls) were referred to the Gender Identity Clinic of the Department of Child and Adolescent Psychiatry at the University Medical Center Utrecht (which moved to the Department of Medical Psychology of the VU University Medical Center in Amsterdam in 2002). To be included in the follow-up study, participants had to be at least 16 years of age. Using this cutoff, we identified 77 children (59 boys and 18 girls, who were between 5 and 12 years of age at first assessment). All 77 children were contacted for participation.

Table 1 provides participant characteristics at childhood assessment (T₀) and follow-up assessment (T₁). At T₀, 75% of the 77 potential participants who were contacted had met complete diagnostic criteria for GID, according to the *DSM-III-R*,²⁰ whereas 25% were subthreshold for the diagnosis (GID not otherwise specified [NOS]).²⁰

At T₁, 23 of the 77 potential participants (30%; 19 boys and 4 girls) did not respond or were not traceable (nonresponder group); the other 54 (40 boys and 14 girls) were included in our study.

TABLE 1
Demographic Characteristics, IQ, and DSM Diagnosis of GID at T₀ and T₁

Variables	All (N = 77)		Persistence (n = 21)		Desistance (n = 23)		Parent (n = 10)		Nonresponders (n = 23)	
	Boys (n = 59)	Girls (n = 18)	Boys (n = 12)	Girls (n = 9)	Boys (n = 19)	Girls (n = 4)	Boys (n = 9)	Girls (n = 1)	Boys (n = 19)	Girls (n = 4)
Age at childhood assessment										
Mean	8.3	8.6	8.6	8.8	8.7	8.3	8.1	9	7.9	8.5
SD	2.0	1.5	1.4	1.8	2.4	1.9	2.3	0	1.8	1.8
Range	5-12	6-11	6-11	6-11	5-12	7-11	5-12	0	5-11	7-9
Age at follow-up assessment										
Mean	19.4	18.7	19.1	17.8	19.8	18.3	17.8	25	19.8	19.8
SD	3.4	2.7	2.9	2.5	3.3	1.3	1.4	0	4.3	2.2
Range	16-28	16-25	16-24	16-24	16-28	17-2	16-20	0	16-24	17-22
Interval, y ^a	10.4	10.1	10.5	9.0	9.9	10.0	8.8	16	11.6	11.3
SD	3.4	3.8	3.7	4.3	3.2	4.3	3.1	0	3.4	2.8
Marital status ^b										
Two parents, n	42	11	9	8	15	2	7	0	11	1
Other family/institution, n	12	5	3	1	4	2	0	0	5	2
Total IQ ^c										
Mean	96.7	103.2	92.2	101	101.8	107.3	99.3	122	92.5	91.7
SD	16.1	23.4	14.2	20.2	13.4	31.4	20.3	0	17.1	28.0
Range	67-131	61-129	67-114	74-128	79-129	61-129	70-131	0	68-129	74-124
Nationality										
Dutch, n	50	16	10	8	15	4	9	1	16	3
Other, n	9	2	2	1	4	0	0	0	3	1
Childhood GID diagnosis, n	44	14	12	9	12	3	5	1	15	1
Childhood GID NOS diagnosis, n	15	4	0	0	7	1	4	0	4	3

Note: GID = gender identity disorder; NOS = not otherwise specified.

^aInterval denotes the time between childhood assessment and follow-up assessment.

^bFor marital status, we asked whether the children were living with two parents or had another family composition. For seven children, there were no data on marital status.

^cIQ was assessed with Dutch versions of the Wechsler Preschool and Primary Scale of Intelligence¹⁷ or the WISC.^{18,19} For five boys and two girls, there were no IQ data.

Twenty-one participants (27%; 9 girls and 12 boys) were still gender dysphoric at follow-up (persistence group). All of these persisters had met the complete diagnostic criteria for GID according to the *DSM-IV*¹⁰ or the *DSM-IV-TR*¹¹ at follow-up and had applied for sex reassignment at the Gender Identity Clinic before the age of 16. They had subsequently followed a standardized diagnostic protocol. This implies that information is obtained from the adolescents and their parents or caretakers on various aspects of their general and psychosexual development since the last contact with the clinic and on their current functioning. The procedure also includes a psychodiagnostic assessment, a child psychiatric evaluation (by a different clinician than the diagnostician), and often a family evaluation (for more information on the clinical procedure, see Reference 21). In this group, we found a significant sex difference ($\chi^2_1 = 5.129, p < .05$): 50% of the girls and 20% of the boys had persisting gender dysphoria (Table 1). Because of this significant sex difference, we analyzed our data separately by sex.

Twenty-three participants (30%; 19 boys, 4 girls) were visited at home because they had no longer been seen at the clinic after childhood (desistance group). Ten participants (13%) did not want to participate themselves, but they allowed their parents to fill out a questionnaire. This parent group consisted of 9 boys and 1 girl. Because there were no significant differences between the desistance group and the parent group for all background variables (marital status: $\chi^2_3 = 4.41, p > .05$); diagnoses in childhood ($\chi^2_1 = 0.676, p > .05$); nationality: ($\chi^2_4 = 2.56, p > .05$); full-scale IQ ($z = -0.27, p = .80$); and psychological functioning, as measured by the Child Behavior Checklist (CBCL; total T scores [$z = -0.88, p > .05$], internalizing T scores [$z = -0.84, p > .05$], or externalizing T scores [$z = -1.17, p > .05$]), the participants in the parent group were included in the desistance group. Therefore, the desistance group consisted of 33 participants (28 boys and 5 girls).

Table 1 shows the background data and age for the children at T_0 and for the four different groups at T_1 . There were no data on marital status for 7 participants because three parents of adolescents (parent group) did not provide this information, and for four children from the nonresponder group, we had no childhood data on marital status. Furthermore, we had no total IQ scores for 5 boys and 2 girls because their intelligence had not been assessed in childhood. Three of these boys belonged to the nonresponder group, one boy to the persistence group, and one boy belonged to the desistance group. One of the two girls belonged to the persistence group, and the other to the desistance group. No significant age differences were found between the groups.

Because there were no differences between the nonresponder and the desistance group, or between the nonresponder and the parent group on all scales of the CBCL and on background variables, the desistance group seems to be representative of all subjects who did not seek sex reassignment after puberty.

Measures

Background Measures and DSM Diagnosis. Diagnoses and five background measures were obtained from the medical charts at childhood assessment: age at assessment, sex, parents' marital status, total IQ, and nationality. Information provided by the parents (clinical interviews on gender development and current gender role behavior, Gender Identity Questionnaire for Children [GIQC; for a description of the GIQC, see below]), the child (clinical interviews on current and past peer and play preferences, gender role behavior and identity status, Gender Identity Interview for Children [GIIC; for a description, see below], a standardized play observation, and the

Draw-a-Person test), and teachers (by means of a self-developed teacher questionnaire and the Teacher's Report Form, a teacher version of the CBCL²²), during a standardized clinical assessment procedure, was used to determine whether a child met the *DSM* criteria for GID^{10,11} (for a detailed description of the clinical procedure and instruments, see Reference 21). The diagnosis was made by either a clinical child psychologist or a child and adolescent psychiatrist. IQ was assessed with Dutch versions of the Wechsler Preschool and Primary Scales of Intelligence¹⁷ or one of two versions of WISC.^{18,19}

Gender Identity/Gender Dysphoria. Table 2 provides the study design. At T_0 , a Dutch translation of the semistructured GIIC of Zucker et al.²³ was used. This child informant instrument consists of 12 items and measures two factors: affective gender confusion and cognitive gender confusion. Higher scores reflect more gender-atypical responses. Each question is scored on a three-point scale ranging from 0 to 2. A score of 0 is assigned if the child answers a factual question correctly (e.g., "Are you a boy or a girl?") or gives a putatively normal or stereotypic response (e.g., "no" to the question, "In your mind, do you ever think that you would like to be a [opposite sex]?"). A score of 1 is assigned if the child provides an ambiguous or intermediate response (e.g., "I don't know" to the question, "Do you think it is better to be a boy or a girl?"; "sometimes" to the question, "In your mind, do you ever think that you would like to be a [opposite sex]?"). A score of 2 is assigned to responses that are putatively atypical and without ambiguity (e.g., "yes" to the question, "In your mind, do you ever think that you would like to be a [opposite sex]?"). The GIIC strongly discriminated gender-referred children from controls, with a large effect size, using Cohen d of 1.72 for Canadian probands and of 2.98 for Dutch probands (M.S.C. Wallien, unpublished data, 2007).

At T_1 , a Dutch translation of the semistructured Gender Identity Interview for Adolescents and Adults (GIIAA) was used.²⁴ This interview has 27 items measuring gender identity and gender

TABLE 2
Study Design

Time	Group	Age, y	Instruments	Variable
T_0	All ($N = 77$)	5–12	GIIC	Gender
			GIQC	Gender
			CBCL	Psychological functioning
T_1	Persistence group ($n = 21$)	16–24	UGS	Gender
			BIS	Body satisfaction
T_1	Desistance group ($n = 23$)	16–28	Sexual orientation questionnaire	Sexual orientation
			GIIAA	Gender
			UGS	Gender
			BIS	Body satisfaction
T_1	Parent group ($n = 10$)	16–25	Parent questionnaire	Gender and sexual orientation

Note: GIIC = Gender Identity Interview for Children; GIQC = Gender Identity Questionnaire for Children; CBCL = Child Behavior Checklist; UGS = Utrecht Gender Dysphoria Scale; BIS = Body Image Scale; GIIAA = Gender Identity Interview for Adolescents and Adults.

dysphoria in adolescents and adults. Responses, rated on a five-point scale, are based on a time frame of the past 12 months. Lower scores reflect more gender-atypical responses. The GIIAA score is calculated by summing scores on the completed items and dividing by the number of marked responses. Deogracias et al.²⁴ reported a Cronbach α of .97 and found that people with GID reported significantly more gender dysphoria than both heterosexual and nonheterosexual non-gender-dysphoric individuals, indicating good discriminant validity. Using a cutoff score of 3.00, they found that the sensitivity was 90.4% for the gender-dysphoric group and the specificity was 99.7% for the controls.

Gender Identity Questionnaire for Children. The GIQC is a one-factor, 14-item parent-report questionnaire covering a range of sex-typed behaviors that correspond to various features of the core phenomenology of the GID diagnosis. Each item is rated on a five-point scale for frequency of occurrence, with lower scores reflecting more cross-gendered behavior.²⁵ A GIQC score is calculated by summing the 14 items and then dividing the sum by 14. Johnson et al.²⁵ reported that a one-factor solution best fit the data, accounting for 43% of the variance, and that 14 of the 16 items have factor loadings 0.30 or greater. The GIQC strongly discriminated gender-referred children from controls, with a large effect size, using Cohen d of 3.70. With a specificity set at 95% for the controls, the sensitivity for the probands was 86.8%.

Utrecht Gender Dysphoria Scale (UGS). The UGS measures the degree of gender dysphoria in adolescents or adults.²⁶ Reported Cronbach α 's are .61 and .81 for male and female controls, .80 and .92 for males with gender dysphoria, and .78 and .80 for females with gender dysphoria. The scale showed good discriminant validity in a sample of individuals with and without GID and in gender-dysphoric individuals who were accepted and rejected for sex reassignment.²⁷ The scale consists of 12 items; scores range from 1 to 5, with higher scores reflecting more gender dysphoria.

Body Image Scale (BIS). The BIS,²⁸ used in a Dutch translation,²⁹ measures body satisfaction. On a five-point scale, one has to indicate satisfaction on 30 body parts and features (e.g., "neutral" body parts, such as hands or nose, and various primary and secondary sex characteristics). A score of 1 indicates the highest satisfaction regarding the specific body part; a score of 5 indicates the highest dissatisfaction.

Sexual Orientation. To assess sexual orientation, we used a questionnaire with nine items. The Sexual Orientation Questionnaire can be found in the supplemental digital content (online-only) materials at <http://links.lww.com/A569>. We assessed sexual orientation in four domains: sexual identity, sexual behavior (experience), sexual fantasy, and sexual attraction. In each of the domains, the questions were rated on a seven-point scale ranging from exclusively heterosexual (0) to exclusively homosexual (6).³⁰ Items 1 and 2 were used to rate sexual attraction, items 3 and 4 were used for the assessment of sexual fantasy, items 5 to 8 assessed sexual behavior, and item 9 pertained to sexual identity.

Psychological Functioning. To assess whether the desistance group was representative of all children who do not seek sex reassignment, and to check whether the parent group and desistance group were comparable with regard to psychological functioning, we used the Dutch translation of the CBCL.^{31,32} This instrument measures behavioral and emotional problems. Parents (or other caregivers) have to rate the child/young adult using a three-point scale: 0 = not true, 1 = somewhat or sometimes true, and 2 = very true or often true. Depending on age group and sex, Cronbach α 's for the internalizing, externalizing, and total score scales range from .78 to .93.

Psychosexual Outcome (Parent Report). This questionnaire consists of nine questions covering gender identity and sexual orientation of the participant, as observed by the parent. This instrument was used only if participants were not available for assessment at follow-up.

Procedure

Childhood Assessment (T_0). Childhood measures were collected as part of the child's clinical assessment at the Gender Identity Clinic. Four of the obtained measures were used: the CBCL, total IQ, the GIQC, and the GIIA. Background information was also collected during clinical assessment.

Follow-up (T_1). All children in the persistence group had applied for sex reassignment at the Gender Identity Clinic before the age of 16 and had followed the clinic's standardized diagnostic procedure.²¹ The assessment of the persisters took place during this procedure. All had subsequently been treated with GnRH analogs to suppress puberty and with cross-sex hormones after the age of 16 years. At our clinic, GnRH analogs are used as an aide in the diagnostic procedure (for a description of the eligibility criteria, see Reference 13).

The other adolescents received a letter in which the purpose of the study was explained. Although many participants were older than 18 years, we contacted the parents first and asked their permission to contact their child. We did so because the last clinical contact had been with them rather than with the child, and we did not want to approach their children without their consent. If the parents gave their permission, and the adolescent wanted to participate, we visited the participants at home. If the adolescent did not want to participate, we asked if they would allow their parents to fill out a questionnaire, the Parent Questionnaire on Psychosexual Outcome.

Two measures, UGS and BIS, were obtained from both the adolescents who were visited at home and the adolescents who were seen at the clinic because of their persistent gender dysphoria. In addition, the GIIAA and the sexual orientation questionnaire were administered to the participants who were seen at home. Information on sexual orientation of the participants who applied for sex reassignment was gathered during the clinical procedure. Questions were part of a semistructured clinical interview.

The ethical committees of the University Medical Center Utrecht and VU University Medical Center approved the study.

RESULTS

T_0 : Childhood Gender Dysphoria

The percentages of *DSM* GID or GID NOS diagnoses were significantly different between the persistence and the desistance groups ($\chi^2_2 = 10.90, p = .004$) and between the persistence and the nonresponder groups ($\chi^2_1 = 7.6, p = .006$). All participants in the persistence group were given a diagnosis of GID. This was not the case in the other two groups (Table 1). When all nonpersisting groups were taken together, 69% had a GID diagnosis.

For the boys, the percentages of *DSM* GID or GID NOS diagnoses were also significantly different between the persistence and the desistance groups ($\chi^2_2 = 6.50, p = .011$). There were no significant differences between

TABLE 3
Mean Scores on the Gender Identity Interview for Children and the Gender Identity Questionnaire at T₀

Scale	Persistence, Mean (SD)		Desistance, Mean (SD)		Nonresponders, Mean (SD)		Desistance- Persistence, <i>p</i>		Desistance- Nonresponders, <i>p</i>		Nonresponders- Persistence, <i>p</i>	
	Boys (<i>n</i> = 12)	Girls (<i>n</i> = 9)	Boys (<i>n</i> = 19)	Girls (<i>n</i> = 4)	Boys (<i>n</i> = 19)	Girls (<i>n</i> = 4)	Boys	Girls	Boys	Girls	Boys	Girls
	GIIC	<i>n</i> = 9 11.6 (4.6)	<i>n</i> = 8 12.9 (1.8)	<i>n</i> = 19 7.2 (4.7)	<i>n</i> = 3 11.3 (5.5)	<i>n</i> = 18 9.3 (5.4)	<i>n</i> = 3 6.7 (4.5)	.02	NS	NS	NS	NS
GIQC	<i>n</i> = 11 2.1 (0.4)	<i>n</i> = 7 2.2 (0.6)	<i>n</i> = 19 2.6 (0.6)	<i>n</i> = 4 2.9 (0.4)	<i>n</i> = 16 2.6 (0.7)	<i>n</i> = 3 3.2 (0.4)	.008	NS	NS	NS	0.02	.03

Note: GIIC = Gender Identity Interview for Children; GIQC = Gender Identity Questionnaire for Children; NS = not statistically significant.

the desistance and the nonresponder groups, or between the persistence and the nonresponder groups. Among the girls, the percentages of *DSM* diagnoses of *GID* or *GID NOS* were significantly different between the persisting and the nonresponding girls ($\chi^2_1 = 8.775, p = .003$), but not between the persisting and desisting girls (Table 1).

With regard to the scores on the *GIIC* and *GIQC*, persisters generally showed more cross-gender behavior than the other groups. The persistence group had a significantly higher mean *GIIC* score (mean 12.2) than the desistance group (mean 7.6; $z = -2.35, p = .02$) and the nonresponder group (mean 8.9; $z = -2.01, p = .04$). This indicates more cross-gender identification in the total persistence group than in the desistance group (Table 3). The persisters had a significantly lower mean *GIQC* score than the desisters ($z = -2.782, p = .005$) and the nonresponders ($z = -2.82, p = .005$), again reflecting more cross-gender identification in childhood

in the persistence group than in the desistance and the nonresponder groups.

Among the boys, the scores on both the *GIIC* and the *GIQC* indicated that the persisting subgroup had a more cross-gender identification and that the persisters showed a more cross-gender behavior in childhood than the desisting boys. Among the girls, the scores on both the *GIIC* and the *GIQC* indicated that the persisting girls had a more cross-gender identification and showed more cross-gender behavior than the nonresponding girls but not the desisting girls (Table 3).

T₁: Gender Dysphoria

At T₁, all participants in the persistence group had been given a *DSM* diagnosis of *GID*. The desistance group did not have a second clinical assessment, but their mean *GIIAA* scores (1.1) and their *UGS* scores indicated that they no longer had gender-dysphoric

TABLE 4
Mean Scores on the Gender Identity Interview for Adolescents and Adults and on the Utrecht Gender Dysphoria Scale and the Body Image Scale at T₁

Scale	Persistence			Desistance			Persistence- Desistance, <i>p</i>		
	All	Boys	Girls	All	Boys	Girls	All	Boys	Girls
<i>GIIAA</i>					<i>n</i> = 17	<i>n</i> = 3			
Divided score, mean (SD)					1.2 (0.2)	1.1 (0.2)			
Total score, mean (SD)					31.8 (4.8)	30.1 (6.4)			
<i>UGS</i>	<i>n</i> = 12	<i>n</i> = 5	<i>n</i> = 7	<i>n</i> = 1	<i>n</i> = 19	<i>n</i> = 2			
Total score, mean (SD)	53.5 (7.4)	50.6 (10.6)	55.6 (3.8)	13.6 (3.0)	13.6 (3.1)	13.0 (1.4)	.001	.001	.004
<i>BIS</i>	<i>n</i> = 16	<i>n</i> = 9	<i>n</i> = 7	<i>n</i> = 17	<i>n</i> = 14	<i>n</i> = 3			
Total score, mean (SD)	3.1 (0.4)	3.1 (0.4)	3.1 (0.5)	2.5 (0.5)	2.4 (0.3)	2.5 (1.0)	.001	.001	NS

Note: Desistance group consists of children who had not applied for sex reassignment when approached by us at 16 years or older. Persistence group consists of children who were still gender dysphoric at 16 years or older. Values are cited in italics. *GIIAA* = Gender Identity Interview for Adolescents and Adults; *UGS* = Utrecht Gender Dysphoria Scale; *BIS* = Body Image Scale; NS = not statistically significant.

feelings at follow-up (Table 4). With regard to the UGS, it was found that the persistence group had significantly more gender dysphoria than the desistance group ($z = -4.81, p = .001$; Table 4). This was also found when separately analyzed for boys and girls (boys: $z = -3.51, p = .001$; girls: $z = -2.06, p = .004$).

As expected, the persistence group also reported significantly more body dissatisfaction on the BIS ($z = -3.62, p = .001$; Table 4) than the participants in the desistance group. The desistance group reported, on average, dissatisfaction with four body parts, and the participants in the persistence group reported, on average, dissatisfaction with nine body parts. Most participants in the persistence group were dissatisfied with their primary and secondary sex characteristics and height. Most of the subjects in the desistance group were dissatisfied with “sex neutral” body characteristics such as nose, shoulders, or feet, and they were satisfied with their primary sex characteristics. Analyzed separately for the sexes, the persisting boys reported more body dissatisfaction than the desisting boys ($z = -3.5, p = .001$), whereas this was not found for the girls.

T₁: Sexual Orientation

Table 5 shows the data on sexual orientation at follow-up. Participants were classified in the following way, according to their scores on sexual fantasy, sexual

attraction, and sexual behavior: heterosexual (Kinsey rating 0–1), bisexual (Kinsey rating 2–4), and homosexual (Kinsey rating 5–6).³⁰ The participants also rated their sexual identity as heterosexual, bisexual, or homosexual. In the parent group, only the parents’ ideas about their children’s sexual attraction feelings could be asked for. We therefore have more participants who are rated on the sexual attraction dimension than on the other sexual orientation dimensions.

On the sexual attraction dimension, about half of the boys ($n = 25$) in the desistance group were attracted to men ($n = 14$), and the others ($n = 11$) were attracted to women. Almost all natal boys in the persistence group ($n = 11$) were attracted to men; only one natal boy reported to be attracted to women. All persisting girls were attracted to women, and all desisting girls were attracted to men.

On the sexual identity dimension, half of the boys in the desistance group reported having a homosexual identity, three boys reported a bisexual identity, and one-third reported a heterosexual identity. All desisting girls reported having a heterosexual identity. Because we classified sexual orientation in relation to birth sex, all natal boys and almost all natal girls in the persistence group reported a homosexual identity. Only one natal girl in the persistence group classified herself as bisexual, although she reported that she was attracted to girls.

TABLE 5
Percentage Participants Who Rated Themselves on Three Dimensions of Sexual Orientation and on Sexual Identity

Group	Attraction		Behavior		Fantasy		Sexual Identity	
	Boys	Girls	Boys	Girls	Boys	Girls	Boys	Girls
Desistance	$n = 25$	$n = 3$	$n = 13$	$n = 2$	$n = 16$	$n = 1$	$n = 18$	$n = 3$
Heterosexual	44	100	23	100	19	100	27	100
Bisexual	0	0	23	0	25	0	17	0
Homosexual	56	0	54	0	56	0	56	0
Persistence	$n = 12$	$n = 7$	$n = 6$	$n = 3$	$n = 5$	$n = 2$	$n = 9$	$n = 8$
Heterosexual	8	0	17	0	17	0	0	0
Bisexual	0	0	0	0	0	0	0	12
Homosexual	92	100	83	100	83	100	100	88
Combined group of gender-dysphoric children	$n = 37$	$n = 10$	$n = 19$	$n = 5$	$n = 21$	$n = 3$	$n = 27$	$n = 11$
Heterosexual	32	30	21	40	19	0	19	18
Bisexual	0	0	16	0	19	33	19	9
Homosexual	68	70	63	60	62	66	62	73
Normative study	$n = 1,628$	$n = 1,676$	$n = 1,618$	$n = 1,670$	$n = 1,624$	$n = 1,674$		
Heterosexual	96	98	94	83	91	76		
Homosexual	3	1	6	17	9	24		

Note: The percentages are in relation to birth sex. In the combined group, the percentages of children in the Persistence and the Desistance groups are combined. The normative data are from a study by de Graaf et al.³³

We also compared our sexual orientation findings with prevalence estimates from a large Dutch study among 3,304 adolescents and young adults (age range 12–25 years).³³ Table 5 shows that, in all our groups, there were considerably more adolescents with a nonheterosexual sexual orientation than in the non-referred Dutch adolescents. In our study group, the overall odds of reporting same-sex or bisexual attraction was 2.1 (32 of the 47 children reported same-sex attraction, and 15 were attracted to the opposite sex: $32/15 = 2.1$; for the natal males, it was 2.1; for the natal females, 2.3). This percentage would even be higher if one assumes that most nonresponders may also have a homosexual sexual orientation. Adult individuals with childhood gender dysphoria are thus much more likely to have a nonheterosexual sexual orientation than a heterosexual sexual orientation. In the normative study, the odds of same-sex or bisexual attraction was 0.02 (68 of the 3,268 children reported same-sex or bisexual attraction; for the males, it was 0.03; for the females, 0.04). This implies that it is about 100 times more likely that someone with childhood gender dysphoria is attracted to partners of the same sex or to both sexes than someone without a gender-dysphoric history.

Participants (both persisters and desisters) who were rated differently on the Kinsey dimensions did not differ in age at T_0 or at T_1 . There was one significant difference between the GIQC score of the participants with same-sex or bisexual attraction and the participants with a heterosexual attraction ($z = -2.53, p = .01$). The participants with same-sex or bisexual attraction had a lower score (mean 2.26) than the participants with a heterosexual attraction (mean 2.78). This indicates more parent-reported gender atypicality in childhood in participants with same-sex or bisexual attraction than in participants with a heterosexual attraction. However, when we analyzed the GIQC scores of participants in the desistance group only, we found no significant differences between the participants with same-sex or bisexual attraction and the participants with heterosexual attraction. Therefore, the more extreme scores of the persisters were responsible for the total group difference on the GIQC.

DISCUSSION

This study investigated the psychosexual outcome among gender-dysphoric children and determined

whether childhood characteristics gave an indication of later GID. We found that 27% of our total group of gender-dysphoric children was still gender dysphoric in adolescence. In the Netherlands, treatment is covered by insurance and easily available, but only in the Amsterdam clinic. It therefore seems unlikely that some nonresponders are, in fact, persisters, and that the observed persistence rate of 27% differs much from the actual persistence rate.

For boys, our percentage of persisting gender dysphoria was similar to what Zucker and Bradley⁸ reported: one of five boys was still gender dysphoric in adolescence/young adulthood. For girls, we found a much higher percentage of persisters than was found in the only follow-up study on girls by Drummond et al.¹⁶ In our study, 50% of the gender-dysphoric girls seemed to be persisters, whereas Drummond et al.¹⁶ found that only 12% of gender-dysphoric girls seemed to have persistent gender dysphoria. Our higher rate of persisting girls could perhaps be explained by differences in childhood cross-gender behavior between the Canadian and Dutch referred children. Although no direct comparison between the girls in the Drummond et al.¹⁶ study and our follow-up study could be made with respect to their scores on the GIIC, a study comparing 376 Canadian and 228 Dutch gender-referred children from both centers reported that the Dutch girls scored significantly higher on the GIIC than the Canadian girls (M.S.C. Wallien, unpublished data, 2007). However, the percentages of girls fulfilling the childhood GID criteria in the study of Drummond et al. (64%) and our study (77%) were not significantly different. In another study, it was found that Dutch children are, on average, referred for gender problems at an older age than Canadian children.³⁴ It may thus be that a combination of a relatively late age at referral and severity of gender-dysphoria accounts for the differences between the rates of female persisters in the two studies. Because these are reports from only two studies with relatively small numbers of female participants, it is, of course, possible that the percentages of females with persisting gender dysphoria will change when larger samples are studied.

We also found that both boys and girls with more extreme gender dysphoria were more likely to develop adolescent/adult GID, whereas children with less extreme gender dysphoria seemed to have overcome their gender dysphoria. For example, all participants in

the persistence group were given a complete GID diagnosis in childhood, whereas half of the group of desisting children was subthreshold for the diagnosis (Table 1). The diagnoses were partly based on a number of parent and child measures (GIIC and GIQC scores), and scores on these instruments also fairly consistently indicated that the persisters showed more childhood gender atypicality than the desisters. Comparing the scores separately for the sexes, similar results were found, although not all comparisons were significant. However, this may have been due to the sometimes small numbers in the various subgroups. Taking all results together, it seems that certain childhood gender identity and gender role measures may give an indication of gender dysphoria persistence after puberty. Clinicians should therefore take child and parent reports of cross-gender identification and behavior seriously, to address them in a timely manner when the subjects enter adolescence. It is conceivable that, in the future, persisting children will be identified and treated with GnRH analogs, even before the actual beginning of puberty. However, at the moment, their reaction to the first physical signs of puberty is still used diagnostically. Clearly, many more studies are needed before one can make any evidence-based recommendations about hormonal interventions in prepubertal children.

With regard to sexual orientation, almost all persisters seemed to be attracted to someone of the same biological sex at follow-up, whereas in the desistance group, this was found for only about half of the participants. In total (persistence and desistance groups together), two-thirds of the participants reported having a same-sex or bisexual attraction. This high percentage of nonheterosexuality is similar to what has been reported in other follow-up studies.¹⁻⁸ Compared with sexual orientation rates from a Dutch normative study, both our boys and girls were far more likely to have a bisexual or homosexual sexual orientation. Childhood gender dysphoria thus seems to be associated with a high rate of later same-sex or bisexual sexual orientation. In clinical practice, gender-dysphoric children and their parents should be made aware of such an outcome and, if this would create problems, be adequately counseled.

Because almost all persisters reported having same-sex sexual attractions, there were no sex differences in this group. However, in the desistance group, half of the boys reported a homosexual or bisexual sexual orienta-

tion, whereas none of the desisting girls did. In contrast to our findings, Drummond et al.¹⁶ found much higher rates of desisting girls with either a homosexual or bisexual sexual orientation. Their rates for either a homosexual or bisexual sexual orientation in fantasy and behavior were 30% (6 of 20) and 26% (4 of 15). This difference can probably be attributed to the fact that our sample size of desisting girls was small ($n = 3$) and that two of our desisting girls (16 years of age) mentioned that they were still questioning their sexuality. If one of the two would, at an older age, seem to be homosexual, the numbers would be much more comparable. All of the desisting homosexual/bisexual girls in the study of Drummond et al.¹⁶ were older than 23. Thus, it is possible that these girls were more "crystallized" with respect to their sexual identities. A study by Diamond³⁵ showed that it is not uncommon for nonheterosexual adolescent girls to change their sexual orientation over time. In her 2-year follow-up study of 80 lesbian, bisexual, and "unlabeled" women, first interviewed at 16 to 23 years of age, half of the women seemed to change their sexual identities more than once, and one-third changed their sexual identity since the first interview. Changes in sexual attraction were small but were larger among bisexuals and "unlabeled" females. Considering this, it is possible that the apparent differences between our results and those of Drummond et al.¹⁶ are, in fact, nonexistent.

Research on the sexual identity development of lesbian, gay, and bisexual youths has shown that the sexual orientation, especially for bisexual youths, may change over time.^{36,37} Our results on sexual orientation also suggest that some male participants were still in an experimentation phase, as the percentage of participants reporting a heterosexual or bisexual orientation differs between the three dimensions of sexual orientation. Furthermore, social desirability is a key validity issue in the assessment of sexual orientation during the adolescent years. One limitation of this study is that we did not measure the participants' propensity to give socially desirable responses, because we did not want to lose cooperation by making the follow-up session unnecessarily long and tedious. Therefore, it is possible that some of our "heterosexual" adolescents were, in fact, attracted to people of the same sex. Even if this were not true, the prevalence rates of same-sex attraction in our study are still substantially higher than in the general population.

Carver et al.³⁸ assumed that gender atypicality may precede the development of a homosexual identity as such. Drummond et al.¹⁶ indeed found that the participants with a bisexual or homosexual orientation recalled more cross-gender behavior during childhood than the participants with a heterosexual or asexual sexual orientation. Although our persisting and desisting participants taken together with a homosexual or bisexual sexual orientation were more cross-gendered in childhood than the participants with a heterosexual sexual orientation, we did not find any significant differences on the childhood measurements between the desisting participants with different sexual orientation outcomes. It is, however, possible that our results did not reach statistical significance because of the small sample sizes. Conversely, in retrospective reports, there is always a risk of memory distortion. It is clear that long-term prospective follow-up studies, in which gender nonconformity is measured in large normative samples of young children, and psychosexual outcome in adolescence or adulthood, are needed to gain more insight in the relationship between childhood gender nonconformity and sexual orientation.

In response to our question at what point in time the desisting participants noticed that their cross-gender preferences and feelings had decreased or disappeared, most answered that the change took place upon entry into secondary school. Only few answered that it took place during the first stages of puberty. It is understandable that an intensification or moderation of the gender dysphoria is closely related to the development of the physical markers of maleness and femaleness. Why most participants reported entrance into secondary school as a “turning point” is less clear. It may be that secondary school entrance is better remembered than the start of puberty because puberty concerns a more gradual transition. More systematic follow-up every few years, especially around critical developmental time points (i.e., school entry, pubescent milestones such as menarche or first ejaculation), is needed to know better exactly when and how GID persistence or desistance takes place.³⁹

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REFERENCES

1. Bakwin H. Deviant gender-role behavior in children: relation to homosexuality. *Pediatrics*. 1968;41:620–629.

2. Davenport CW. A follow-up study of 10 feminine boys. *Arch Sex Behav*. 1986;15:511–517.
3. Green R. *The “Sissy Boy Syndrome” and the Development of Homosexuality*. New Haven, CT: Yale University Press; 1987.
4. Kosky RJ. Gender-disordered children: does inpatient treatment help? *Med J Aust*. 1987;146:565–569.
5. Lebovitz PS. Feminine behavior in boys: aspects of its outcome. *Am J Psychiatry*. 1972;128:1283–1289.
6. Money J, Russo AJ. Homosexual outcome of discordant gender identity/role in childhood: longitudinal follow-up. *J Pediatr Psychol*. 1979;4:29–41.
7. Zuger B. Early effeminate behavior in boys: outcome and significance for homosexuality. *J Nerv Ment Dis*. 1984;172:90–97.
8. Zucker KJ, Bradley SJ. *Gender Identity Disorder and Psychosexual Problems in Children and Adolescents*. New York: Guilford Press; 1995.
9. Cohen-Kettenis PT. Letter to the editor: gender identity disorder in the DSM? *J Am Acad Child Adolesc Psychiatry*. 2001;40:391.
10. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, 4th ed*. Washington, DC: American Psychiatric Association; 1994.
11. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, 4th ed, Revised Text*. Washington, DC: American Psychiatric Association; 2001.
12. Hill DB, Rozanski C, Carfagnini J, et al. Gender identity disorders in childhood and adolescence: a critical inquiry. *Int J Sex Health*. 2007;19:57–75.
13. Delemarre-van de Waal HA, Cohen-Kettenis PT. Clinical management of gender identity disorder in adolescents: a protocol on psychological and pediatric endocrinology aspects. *Eur J Endocrinol*. 2006;155: S131–S137.
14. Green R, Roberts CW, Williams K, Goodman M, Mixon A. Specific cross-gender behaviour in boyhood and later homosexual orientation. *Br J Psychiatry*. 1987;15:84–88.
15. Bailey JM, Zucker KJ. Childhood sex-typed behavior and sexual orientation: a conceptual analysis and quantitative review. *Dev Psychol*. 1995;31:43–55.
16. Drummond KD, Bradley SJ, Peterson-Badali M, Zucker KJ. A follow-up study of girls with gender identity disorder. *Dev Psychol*. 2008;44:34–45.
17. Wechsler D. *Wechsler Preschool and Primary Scales of Intelligence (WPPSI-R)*. 1997. Flemish-Dutch translation by G. Vandersteene and A. Bos.
18. Wechsler D. *Wechsler Intelligence Scale for Children: Manual*, 3rd ed. San Antonio, TX: The Psychological Corporation; 1991.
19. Wechsler D. *Wechsler Intelligence Scale for Children: Manual*, 3rd ed. Dutch translation by W. Kort, M. Schittekatte, P.H. Dekker, P. Verhaeghe, E.L. Compaan, lic. M. Bosmans, lic. G. Vermeir; 2005.
20. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition*. Washington, DC: American Psychiatric Association; 1987.
21. Cohen-Kettenis PT. Gender identity disorder. In: Gillberg C, Harrington R, Steinhausen HC, eds. *A Clinician’s Handbook of Child and Adolescent Psychiatry*. Cambridge: Cambridge University Press; 2006:695–725.
22. Verhulst FC, Van der Ende J, Koot HM. *Manual for the Teacher’s Report Form (TRF)*. Rotterdam: Erasmus University/Department of Child and Adolescent Psychiatry, Sophia Children’s Hospital; 1997.
23. Zucker KJ, Bradley SJ, Lowry Sullivan CB, Kuksis M, Birkenfeld-Adams A, Mitchell JN. A gender identity interview for children. *J Pers Assess*. 1993;61:443–456.
24. Deogracias JJ, Johnson LL, Meyer-Bahlburg HFL, Kessler SJ, Schober JM, Zucker KJ. The gender identity/gender dysphoria questionnaire for adolescents and adults. *J Sex Res*. 2007;4:370–379.
25. Johnson LL, Bradley SJ, Birkenfeld-Adams AS, et al. A parent-report gender identity questionnaire for children. *Arch Sex Behav*. 2004;33: 105–116.
26. Doorn CD, Kuiper AL, Verschoor AM, Cohen-Kettenis PT. Het verloop van de geslachtsaanpassing: een 5-jarige prospectieve studie [The course of sex reassignment: a 5-year prospective study]. Report for the Dutch National Health Council; 1996.
27. Cohen-Kettenis PT, van Goozen SHM. Sex reassignment of adolescent

- transsexuals: a follow-up study. *J Am Acad Child Adolesc Psychiatry*. 1997;36:263–271.
28. Lindgren TW, Pauly IB. A Body Image Scale for evaluating transsexuals. *Arch Sex Behav*. 1975;4:639–656.
 29. Kuiper AJ. *Transseksualiteit: Evaluatie van de Geslachtsaanpassende Behandeling [Transsexuality; Evaluation of Sex-Reassignment]*. Amsterdam: VU University Press; 1991.
 30. Kinsey AC, Pomeroy WB, Martin CE. *Sexual Behavior in the Human Male*. Philadelphia: WB Saunders; 1948.
 31. Achenbach TM. *Manual for the Child Behavior Checklist and 1991 Profile*. Burlington: University of Vermont Department of Psychiatry; 1991.
 32. Verhulst FC, van der Ende J, Koot H. *Handleiding voor de CBCL/4-18*. Rotterdam: University Press; 1996.
 33. de Graaf H, Meijer S, Poelman J, Vanwesenbeeck I. *Seks onder je 25e: Seksuele gezondheid van jongeren in Nederland anno 2005 [Sex Under 25: Sexual Health of Youth in the Netherlands Anno 2005]*. Delft: Eburon; 2005.
 34. Cohen-Kettenis PT, Owen A, Kaijser VG, Bradley SJ, Zucker KJ. Demographic characteristics, social competence, and behavior problems in children with gender identity disorder: a cross-national, cross-clinic comparative analysis. *J Abnorm Child Psychol*. 2003;31:41–53.
 35. Diamond LM. Sexual identity, attraction, and behavior among young sexual-minority women over a 2-year period. *Dev Psychol*. 2000;36:241–250.
 36. Rosario M, Schrimshaw EW, Hunter J, Braun L. Sexual identity development among lesbian, gay, and bisexual youths: consistency and change over time. *J Sex Res*. 2006;43:46–58.
 37. Stokes JP, Damon W, McKirnan DJ. Predictors of movement towards homosexuality: a longitudinal study of bisexual men. *J Sex Res*. 1997;34:304–312.
 38. Carver PR, Egan SK, Perry DG. Children who question their heterosexuality. *Dev Psychol*. 2004;40:43–53.
 39. Wallien MSC, Cohen-Kettenis PT, Lambert SL, Owen-Anderson A, Bradley SJ, Zucker KJ. Cross-National Replication of the Gender Identity Interview for Children, submitted.

Prospective Effects of Attention-Deficit/Hyperactivity Disorder, Conduct Disorder, and Sex on Adolescent Substance Use and Abuse Elkins IJ, McGue M, Iacono WG

Context: Attention-deficit/hyperactivity disorder (ADHD), an early manifestation of externalizing behavior, may identify children at high risk for later substance abuse. However, the ADHD-substance abuse relationship often disappears when co-occurring conduct disorder (CD) is considered. **Objective:** To determine whether there is a prospective relationship between ADHD and the initiation of substance use and disorders, and whether this relationship depends on the ADHD subtype (hyperactive/impulsive or inattentive), CD, or sex. **Design, Setting, and Participants:** Dimensional and categorical measures of ADHD and CD were examined via logistic regression analyses in relation to subsequent initiation of tobacco, alcohol, and illicit drug use by 14 years of age and onset of substance use disorders by 18 years of age in a population-based sample of 11-year-old twins (760 female and 752 male twins) from the Minnesota Twin Family Study. **Main Outcome Measures:** Structured interviews were administered to adolescents and their mothers regarding substance use and to generate diagnoses. **Results:** For boys and girls, hyperactivity/impulsivity predicted initiation of all types of substance use, nicotine dependence, and cannabis abuse/dependence (for all, $p < .05$), even when controlling for CD at 2 time points. By contrast, relationships between inattention and substance outcomes disappeared when hyperactivity/impulsivity and CD were controlled for, with the possible exception of nicotine dependence. A categorical diagnosis of ADHD significantly predicted tobacco and illicit drug use only (adjusted odds ratios, 2.01 and 2.82, respectively). A diagnosis of CD between 11 and 14 years of age was a powerful predictor of substance disorders by 18 years of age (all odds ratios, 94.27). **Conclusions:** Hyperactivity/impulsivity predicts later substance problems, even after growth in later-emerging CD is considered, whereas inattention alone poses less risk. Even a single symptom of ADHD or CD is associated with increased risk. Failure in previous research to consistently observe relationships between ADHD and substance use and abuse outcomes could be due to reliance on less-sensitive categorical diagnoses. Reproduced with permission from *Archives of General Psychiatry*, 2007;64(10): 1145–1152. Copyright © 2007, American Medical Association. All rights reserved.