Summary and General discussion

The studies described in this thesis cover four main themes. First, we addressed the assessment of gender identity disorder (GID)/gender dysphoria. Second, we examined three potential determinants of GID in childhood. Third, we investigated the (social) consequences of having a GID in childhood. Fourth, we studied the long-term psychosexual outcome of gender-referred children.

Psychometric research

In **chapter 2** we reported on a cross-national, cross-clinic comparative analysis of an instrument, called the Gender Identity Interview for Children (GIIC). The GIIC was administered to 376 gender-referred children from a gender identity clinic in Toronto, Canada, 228 gender-referred children from our own clinic, and 180 control children from Toronto (*M* age: 7.65 yrs). Factor analysis identified a strong one-factor solution that contained all 12 items on the GIIC, accounting for 32.4% of the total variance. Probands from both clinics had a significantly higher deviant score than the controls, with effect sizes of *d* = 1.72 for the Canadian probands and *d* =2.98 for the Dutch probands. The Dutch probands had significantly higher deviant scores than the Canadian gender probands. As expected, probands in both clinics who met complete *DSM*[1] criteria for GID had a significantly higher deviant score than probands sub-threshold for the diagnosis. Using cutoff scores of 3+ or 4+ deviant responses yielded specificity rates of 86.1% and 92.8%, respectively, for the controls. Sensitivity rates were higher for the Dutch probands than for the Toronto probands. This study was the first to report on the discriminant validity of the GIIC in a sample of children outside of North America.

Chapter 3 reported on results of a cross-national, cross-clinic comparative analysis of a quantitative and standardized parent-report measure of gender identity and gender role behavior named the Gender Identity Questionnaire for Children (GIQC). Data of 338 gender-referred children from Toronto were compared with data of 156 gender-referred children from Utrecht/Amsterdam (the Utrecht clinic was transferred to Amsterdam in 2002). First of all, the probands from both clinics had higher cross-gender scores than the controls, providing evidence for the validity of the instrument. The percentages of children in the two clinics who met complete *DSM*[1] criteria of GID were comparable. There were also differences between the clinics. The gender-referred boys from Utrecht/Amsterdam had a significantly lower total score (indicating more cross-gender behavior) than the gender-referred boys from Toronto, but there was no significant difference for girls. In the Toronto sample, the gender-referred girls had a significantly higher total score than the gender-referred boys, but there was no significant sex difference in the Utrecht/Amsterdam sample. Across both clinics, the GIQC total score was significantly lower for the gender-referred children who met the complete *DSM*[1] criteria for GID, than the gender-referred children who were sub-threshold for GID (Cohen's *d* = 1.08). This result provides evidence for the validity of the GID diagnosis and is the first to demonstrate this in a cross-national, cross-clinic comparative context. The results also provide some support for cross-clinic consistency in clinician-based diagnosis of GID.

Potential determinants of GID

In **chapter 4** we reported on a study assessing anxiety and stress in 25 children with GID and 25 control children by measuring their cortisol, heart rate (HR) and skin conductance levels (SCL), and asking them to report their moods and experience of control. By using an established psychological challenge involving provocation and frustration, we investigated whether children with GID as compared to controls without GID reacted in a more anxious way. The gender dysphoric children reported more negative emotions than the controls and had a tonically elevated SCL. There were no differences between the groups in cortisol and HR. This study lends some support to the idea that children with GID have a more anxious nature as compared to controls.

Chapter 5 concerns the prevalence and type of co-morbidity in gender dysphoric children, examined with the Diagnostic Interview Schedule for Children- Parent version (DISC-P). We assessed psychopathology according to the *DSM*[1] in two groups of children. The first group consisted of 120 Dutch children (age range: 4 -11) who were referred to our Gender Identity Clinic (GID group), and the second group consisted of 47 Dutch children who were referred to an ADHD clinic (ADHD group). We found that 52% of the children diagnosed with GID had one or more diagnoses other than GID. As expected, more internalizing (37%) than externalizing (23%) psychopathology was present in both boys and girls. Furthermore, the odds of having internalizing or externalizing co-morbidity were higher in the clinical comparison group (ADHD group) than in the GID group (odds ratios were 1.28 and 1.39, respectively). Finally, 31% of the children with GID suffered from an anxiety disorder. From the results of this categorical diagnostic study we concluded that children with GID are at risk for developing co-occurring problems, that internalizing disorders were not indicative for children with GID, and that, as 69% of the children did not suffer from an anxiety disorder, a full-blown anxiety disorder does not seem to be a necessary condition for the development of GID.

Chapter 6 addressed parental characteristics to test Zucker and Bradley's[2] hypotheses about the role of parents in the development of GID. We examined psychological problems in parents of gender dysphoric boys and girls, and compared these results with results from two control groups in order to examine parental psychopathology as a potentially contributing factor in GID. Furthermore, we examined parent-child interaction style of these parents to test Zucker and Bradley's hypothesis that parents of gender dysphoric children lack the ability to set limits on their children's behavior, cross-gender behavior included. In this study, three groups of parents were compared with respect to psychological functioning and parent-child interaction style. The first group (GID group) consisted of parents of 120 children (85 boys and 35 girls) who were referred to our Gender Identity Clinic, the second group was a clinical control group (CC group) consisting of parents of 25 children (18 boys and 7 girls) who were referred to two child psychiatric outpatient clinics, and the third group was a non-referred control group (NC group) consisting of parents of 35 non-referred boys and 27 non-referred girls (total $n = 62$). Parental functioning was measured with the Symptom Checklist 90-R, the Beck Depression Inventory and with a Dutch questionnaire

that assesses personality disorders ('Vragenlijst Kenmerken Persoonlijkheid' or VKP). Parent-child interaction was measured with a Dutch questionnaire (the 'Ouder-Kind Interactie Vragenlijst-Revised' or OKIV-R). Except for some anxiety symptoms in a subgroup of mothers of boys with GID, parents of children with GID generally did not report more psychological problems than parents of non-referred children. Also, parents of children with GID had a constructive parent-child interaction style. We concluded that parental psychological functioning as such is not a major risk factor for GID development.

In **Chapter 7** we reported on a study testing the most prominently assumed biological determinant of GID: prenatal brain exposure to testosterone. We used an indirect method for investigating the effects of prenatal exposure to testosterone: the 2D:4D finger ratio--the relative lengths of the 2nd ("index") finger and the 4th ("ring") finger. This marker is assumed to reflect prenatal brain exposure to testosterone and has been intensively studied in relation to postnatal behavior and sexual orientation (for a meta-analytic study, see[3]). In our study finger ratios of 85 children with GID were compared to finger ratios of 137 control children. Furthermore, we compared the 2D:4D ratios of 96 male and 51 female adult individuals with GID to that of heterosexual male and female adult controls. In the sample of adults with GID, we classified their sexual orientation as either homosexual or non-homosexual (in relation to their birth sex) in order to examine whether or not there were any within-group differences as a function of sexual orientation. We found, as expected, for both hands a normative sex difference in the finger ratio: boys and men had significantly lower finger ratios than girls and females. However, there were no significant differences between the children with GID and their controls and we also found no evidence for an altered 2D:4D ratio in adult males with GID (in both homosexual and non-homosexual patients). We did, however, find a significantly masculinized 2D:4D ratio in adult females with GID (with a co-occurring homosexual orientation). Our own study, together with two other studies, found some support for a different finger ratio pattern in adults with GID.

Social consequences

In **chapter 8** we reported on a study examining the social position of children referred to our clinic because of gender dysphoria and investigated whether they are victimized at school. Using a peer nomination technique, we examined whether classmates perceive the gender dysphoric child as a victim of bullying and/or as their friend. Twenty-eight gender dysphoric children (14 boys and 14 girls) and their classmates ($n = 495$) were included (mean age: 10.5 years). We found that gender-referred children did have friends at school, but hardly any same-sex friends. With regard to social acceptance, we found a sex difference: male classmates rejected gender dysphoric boys, whereas female classmates did not reject gender dysphoric girls. However, neither gender dysphoric boys nor girls were bullied at school. From our study it seems that homophobic bullying is not very prevalent at Dutch schools, and that gender dysphoric children are socially quite well accepted.

Psychosexual outcome

Chapter 9 reports on the psychosexual outcomes of gender-referred children who were assessed in childhood. At the time of the study, they were 16 years of age or older. This was also the first study that prospectively examined whether childhood characteristics were related to psychosexual outcome. We assessed gender dysphoria, sexual orientation and psychological functioning in 54 children (mean age: 18.9; age range at the time of the study: 16–28 years) who had been referred to the Gender Identity Clinic in childhood (mean age: 8.4; age range at first assessment 5-12). Twenty-three other children (Non-responders group), who had been referred in the same period, were not traceable. We found that 27% ($n = 21$) of the total group of 77 children were still gender dysphoric (Persistence group) and 43% percent of the children ($n = 33$; Desistence group) were no longer gender dysphoric in adolescence or young adulthood. Children in the Persistence group had more severe GID symptoms in childhood than the children in the other two groups. At follow-up, nearly all participants in the Persistence group reported having a homosexual or bisexual preference, whereas in the Desistence group only half had a homosexual or bisexual preference. Our study indicated that, despite the fairly high percentage of GID persistence, the majority will desist. Furthermore, the children with more extreme forms of gender dysphoria in childhood were more likely to persist than children with less extreme forms. With regard to sexual orientation, the most likely outcome was homosexuality or bisexuality.

General discussion

Diagnosis of childhood GID

Over the years a variety of measurement approaches have been developed to assess the sex-typed behaviors in children referred clinically for gender dysphoria. In two studies[4-5] the reliability and - discriminant - validity of two instruments were demonstrated: the Gender Identity Interview for Children (GIIC) and the Gender Identity Questionnaire for Children (GIQC). However, in both studies only Canadian populations were used. The properties of these instruments when used for Dutch populations were unknown. We therefore carried out two cross-national studies. In both studies we found that the good instrument properties were also observed when the instruments were used in a Dutch population.

Apart from assessing the psychometric properties of the two instruments, both studies also gave information about cross-national and cross-clinic differences in the clinical populations. A striking difference in both studies was that the Dutch probands were more cross-gendered in their behavior and feelings than the Canadian probands. We believe that cultural factors may account for these differences in the sense that Dutch culture is more tolerant with regard to gender atypicality than North-American culture. Two cross-cultural studies[6-7] indeed showed that different cultures have different attitudes towards same-sex sexuality. In these studies, the most accepting attitude with respect to homosexuality was observed in the Netherlands. It is, therefore, possible that the threshold for referral is lower in Canada than it is in the Netherlands, and that Canadian children need to display less extreme cross-gender behavior for a parent to seek clinical evaluation than is the case in the Netherlands (see also[8]). This explanation is supported by a study showing that Canadian gender dysphoric children are seen at significantly younger ages than Dutch children[9] and by the same study and one from the UK[10] showing that, in these countries, higher rates of boys are seen than in the Netherlands. Both results may reflect greater homophobic anxiety, as gender atypical behavior is generally less accepted in boys than in girls. Another explanation for the differences between the clinically referred groups might be related to a relative inhibition vs. openness in reporting gender atypicality. Perhaps families from the Canadian clinic were more guarded than their Dutch counterparts in acknowledging such behavior and feelings in their children. This would imply that the referred children are in fact equally gender atypical in both countries, but that Canadian children and their parents are less likely to report on these behaviors than Dutch children. In order to gain more insight into the causes of these cultural differences, future research should investigate the motives of parents seeking clinical attention for their children in the two clinics, perhaps using more qualitative methods as well as measures of defensiveness or social desirability.

Potential determinants of GID
Anxiety and co-morbid problems

Zucker and Bradley[2] formulated a two-stage model that explained the dynamics between predisposing, provoking and perpetuating risk factors for GID development. In the first stage, general child and environmental factors need to be present to set the stage for the development of a GID (predisposing factors). These factors make the child vulnerable to other, more specific, influences. In the second stage, these specific factors (child-related and/or environmental provoking and perpetuating factors) for GID development have to be present during a sensitive period in which formation and consolidation of a child's gender identity normally takes place.

Zucker and Bradley[2] hypothesized that GID development may originate with predisposing child factors, such as an anxious temperament and/or sensitivity to parental affect. Empirical evidence for an anxious temperament in children with GID comes from studies[2,9] that used the Child Behavior Checklist (CBCL: a parent-report questionnaire), and from two studies[11-12] that examined the prevalence rate of separation anxiety disorder in children with GID. The CBCL studies[2,10] showed a predominance of internalizing problems in children with GID, and the Coates and Person's study[11] showed that a large proportion (60%) of their patients had *DSM*-III-R criteria for separation anxiety disorder.[13] However, Zucker et al.[12] found no significant association between GID and a conservative definition of separation anxiety. A more liberal definition of separation anxiety disorder showed that it occurred significantly more often in boys with GID than in gender-referred boys who did not meet the complete criteria for GID.[12]

The above findings show that gender dysphoric children likely have other psychological problems. In the CBCL[2,9] studies there was a wide range of psychopathology, with some children exhibiting little problematic behavior and others a great deal. It was, however, unclear how severe the co-occurring problems of the gender dysphoric were, and whether and what type of anxiety disorders (except for separation anxiety disorder) were prevalent among these children. We, therefore, conducted a study in which we assessed psychopathology according to the DSM.

As Zucker and Bradley[2] also proposed that the anxious nature of the child results from an innate vulnerability to elevated arousal in response to stressful or challenging situations, we further chose to expose gender dysphoric children to a challenging situation, and examined whether they reacted in a more anxious way than control children. We measured their physiological anxiety levels [cortisol levels as indicators of the hypothalamic-pituitary-adrenal axis (HPA) response, heart rate (HR), and skin conductance levels (SCL)], and we asked them to report their moods and experience of control during stressful tasks.

Our physiological study pointed to a discrepancy between the physiological and psychological measurements as a result of stress induction. Although, the gender dysphoric children were not different from matched control children with respect to HPA axis functioning and autonomic nervous system activity when exposed to stress, they did report stronger negative moods and felt more out of control during stress as compared to control children. It seems that the gender dysphoric children underestimate their ability to cope with the stress situation. Earlier research showed that

high levels of anxiety in children was accompanied by high levels of self-reported negative feelings and cognitions.[14] Because gender dysphoric children experienced more negative feelings, we believe, in line with the Muris et al. study,[14] that this reflects a more anxious nature in gender dysphoric children. This is also in accordance with our finding of a tonically elevated skin conductance level in gender dysphoric children, which did not seem to be a response to stress, but to indicate an anxious temperament. The part of Zucker and Bradley's theory[2] that proposed such an anxious temperament as general vulnerability to developing psychological problems was thus supported by our findings.

More support for the hypothesis of general vulnerability in gender dysphoric children comes from our DISC study. Here we found that more than half of the children had co-morbid disorders, and that the pattern of co-occurring internalizing and externalizing disorders in both the gender dysphoric and the clinically referred group was similar. These results give reason to believe that gender dysphoric children are at risk for developing co-occurring psychiatric problems. Having a psychiatric condition of one kind seems to be more often than not accompanied by disorders in the internalizing or the externalizing spectrum. This result is also in line with the studies measuring emotional and behavioral problems in a dimensional way.[2,9] Studies with the Child Behavior Checklist (CBCL)[2,10] showed that gender-referred children had, on average, significantly more emotional and behavior problems than their siblings and non-referred children, and that demographically matched clinical controls (without gender dysphoria) had comparable levels of emotional and behavior problems. However, when we looked specifically at the percentage of gender-referred children with anxiety disorders, we found that the prevalence rates of anxiety disorders were not higher in the GID group than in the clinical control group. This implies that gender dysphoric children are somewhat more anxious than other children. This may be related to GID development, but these children do not fulfill the criteria for anxiety disorder.

It is difficult to ascertain the relationship between psychopathology and gender dysphoria. If co-morbid conditions represent distinct disorders, one wonders whether one condition increases the risk for another condition, or whether the conditions are caused by distinct or overlapping factors.[15] One often proposed explanation for the relationship between co-morbid problems and GID is that the co-morbid problems are only a consequence of the gender dysphoria. It has been suggested that the gender dysphoric children's gender atypical behavior gives them a deviant social position, resulting in poor peer relations and victimization by peers.[16-17] It is has been argued[18-19] that it is their deviant social status and/or victimization that results in co-morbid psychiatric condition,[20-21] probably through a mechanism of minority stress.[22] Our findings, however, give no reason to assume that minority stress is present in all gender dysphoric children. In our study on the social status of gender-referred children, we did not find that they were victimized at school. Furthermore, considering the fact that more than half of the gender dysphoric children had co-morbid conditions in our DISC study, we find it unlikely that this diversity of co-morbid problems was solely the result of psychosocial stress. Considering our data on anxiety, we believe it is more

likely that the general vulnerability that seems to be present in many gender dysphoric children may also cause the co-morbid problems.

Parental psychological functioning

In the etiological literature, the influence of parents on GID development is often considered to be extremely important.[23-24] Earlier studies gave some information about the psychological states of mothers of gender dysphoric children. However, they did not provide sufficient evidence to conclude that parents of gender dysphoric children were truly different regarding their emotional states, or that these parental problems actually influenced GID development. Our study was the first one assessing parental functioning of mothers and fathers of both boys and girls in a categorical and dimensional way, including large sample sizes, and using two control groups. Generally, we did not find parents of gender dysphoric children to have more psychological problems than parents of non-referred children. However, a subgroup of mothers of gender dysphoric boys did report somewhat more anxiety than control mothers. It may be that, in this subgroup, the mothers' emotional state did play an etiological role in their children's GID. Another possibility is that this subgroup of mothers is less able than the other mothers of gender dysphoric children to handle the stress that comes from having a son who is not accepted by peers and/or has co-morbid problems.[25] In this case the mothers' psychological problems would be the result rather than cause of their children's GID. Considering our data on anxiety in gender dysphoric children, another explanation could be that anxiety runs more in families of gender dysphoric children than in other families.

Another finding on parent-child interaction style of parents of gender dysphoric children, led us to believe that this parental characteristic is not a major risk factor for GID development. Although we found a subgroup of mothers of gender dysphoric children to be more anxious than control mothers, the results taken together do not support the assumptions about the importance of parental psychological functioning in the development of GID.[2,26-27] This, of course, does not mean that parents do not play a role in the process. Generally, parents use multiple strategies to raise their children, and the total effect of a particular type of parenting behavior will be a function of the entire repertoire of correlated behaviors used by the parents.[28] Therefore, it is still possible that parental characteristics other than the ones we studied influence the gender development of children. Another limitation of the study is that we focused on the current family situation. Parental factors that operated only in the children's first years of life, may have contributed to their gender dysphoria. Finally, we used self-report measurements and it is, therefore, possible that parents responded in a socially desirable way. One would, however, expect that this would also apply to the parents in the CC group, but in this group a number of differences with the other groups of parents were indeed found. Taken together, our results give no reason to believe that parental psychological functioning is a major risk factor for GID development in children.

Prenatal testosterone exposure

Apart from the possibility of a genetic influence on GID[29], the most often assumed biological determinant of GID development concerns prenatal brain exposure to atypical levels of sex hormones.[30-31] It has been proposed that atypical prenatal testosterone levels are responsible for differentiation of gender identity,[32] gender role,[33] and sexual orientation.[34-36] However, studies determining prenatal hormonal levels postnatally in gender dysphoric children are hard to conduct. GID becomes manifest long after such brain exposure and it is virtually impossible to conduct prospective studies. Because of the rarity of the condition, the testing of very large numbers of pregnant mothers would be required, and the follow-up would take about two decades. This implies that, at present, there is no direct evidence of atypical prenatal sex steroid exposure in gender dysphoric children.

One of the indirect measures of prenatal testosterone exposure is the 2D:4D finger ratio. In our study we did not find a difference between the gender dysphoric children and their controls, nor did we find evidence for an altered 2D:4D ratio in adult males with GID (neither in males who were sexually attracted to men, nor in males who were not sexually attracted to men). We did, however, find a significantly masculinized 2D:4D ratio in adult females with GID (with a co-occurring homosexual sexual orientation). From a methodological point of view, it should be noted that, in our control samples, significant sex differences in 2D:4D were obtained, a pattern that is fully consistent with the now large normative literature on such differences.[37] This affords some confidence in offering interpretations of the null effect.

Given the positive findings for adult females with GID, it is reasonable to ask why there was a clear null finding for the girls with GID. An explanation for this can lie in the fact that GID is not homogeneous in all children and adults with GID. It has been frequently proposed that adults with GID can be divided into two categories that differ in their developmental routes. One category is often referred to as early-onset (before puberty), core, primary, 'homosexual' (attracted to persons of the same biological sex). The other category is called late-onset (after puberty), non-core, secondary, 'non-homosexual' (not attracted to persons of the same biological sex). The early onset group has been found to show several characteristics and a developmental pattern which is clearly different from that of the late onset group. The early onset group, for instance, has been shown to present earlier for assessment, to report more childhood masculine or feminine identification, to show better social gender reorientation and to show less postoperative regret than the late onset group.[38-41] It is therefore possible that biological etiological factors play a more important role in the early than in the late onset group. Indeed, in our 2D:4D study we found evidence for a biological etiology in early onset female adults with GID.

For girls with GID, our follow-up study indicated that these girls could be classified into two subgroups, the persisters or pre-transsexuals, and the desisters who will 'lose' their gender dysphoric feelings by adolescence. In our group, the persisting girls were significantly more gender dysphoric than the other girls. For adult 'homosexual' female-to-male transsexuals it has been found that they had more pervasive cross-gender behavior and feelings in childhood than the non-homosexual female-to-male transsexuals[38-39] and thus it seems that the pre-transsexual girls have more in

common with these adult females than with other gender-referred girls. However, for the 2D:4D study it was not yet possible to make comparisons between the different subgroups of children, because classification on the basis of psychosexual outcome can only be made retrospectively. The heterogeneity of the group of gender dysphoric girls may account for the absence of 2D:4D findings in this group.

Why there was a null finding in male adults with GID and boys with GID is unclear. It is possible that associations and interactions between early hormonal events, brain anatomy and (psycho) sexual outcome are different for the sexes[42] and/or that estrogens are more involved in sexual brain differentiation than has long been suspected.[42] Studies that examined assumed prenatal hormonal effects on sex-dimorphic cognitive functions in adults with GID[44-45] indeed found that the results in female-to-male transsexuals do not simply mirror those in male-to-female transsexuals. That is, these studies give reason to believe that the relationship between prenatal exposure to sex steroids and psychosexual differentiation is different between males and females with GID.

Relation between childhood and adult GID

Some critics have expressed concerns that the *DSM[1]* criteria may not adequately differentiate children with GID from children who show healthy gender nonconforming behavior and that, as a consequence, children who should not be classified as having a psychiatric disorder would be treated.[47-48] Assuming that the 'true' cases of GID are the children with persisting GID, it would be important to find a way to discriminate the extreme cases from the milder ones. Two of our dimensional instruments (GIIC and GIQC) seem to be helpful in this respect, although a diagnosis made on such instruments alone would, of course, not be sufficient.

In our cross-clinic studies, 'caseness' was defined based on clinician diagnoses of GID (threshold vs. sub-threshold). Our follow-up study showed that a childhood DSM[1] diagnosis does not perfectly predict the outcome of the children. That is, all persisting children were given a complete diagnosis of GID in childhood, whereas, in the desisting group, 65% were also given a complete diagnosis. Apparently the DSM[1] criteria, as they are currently formulated, are not sharp enough to distinguish children who will have persistent GID from healthy gender nonconforming children. On the other hand, it is well known that various psychiatric disorders in childhood do not show complete persistence into adulthood, but result in remission by adolescence or adulthood. For example, the vast majority of children with oppositional defiant disorder and the majority of children with conduct disorder will not be diagnosed with antisocial personality disorder in adulthood.[48-49] It is therefore possible that, even with more strict criteria, a certain percentage of children with GID will desist. However, we believe that the percentage of desisters could be much lower than it is now. It is beyond the scope of this thesis to propose an entire set of new *DSM* criteria, but on the base of our follow-up study, we conclude that it would be useful if indicators of extremeness or intensity of gender dysphoria would be incorporated more explicitly into the next version of the DSM.

Table 1. Diagnostic and Statistical Manual-IV diagnostic criteria for gender identity disorder

A. A strong and persistent cross-gender identification (not merely a desire for any perceived cultural advantages of being the other sex)

<u>The disturbance is manifested by at least four (or more) of the following:</u>

1. Repeatedly stated desire to be, or insistence that she or he is, the other sex
2. In boys, preferences for cross-dressing or simulating female attire; in girls, insistence on wearing only stereotypical masculine clothing
3. Strong and persistent preferences for cross-sex roles, in make-believe play or persistent fantasies of being the other sex
4. Intense desire to participate in the stereotypical games and pastimes of the other sex.
5. Strong preference for playmates of the other sex

B. Persistent discomfort with his or her sex or sense of inappropriateness in the gender role of that sex

<u>The disturbance is manifested by any of the following:</u>

In boys, assertion that his penis or testes are disgusting or will disappear or assertion that it would be better not to have a penis, or aversion towards rough-and tumble play and rejection of male stereotypical toys, games, and activities.

In girls, rejection of urinating in a sitting position, assertion that she has or will grow a penis, or assertion that she does not want to grow breasts or menstruate, or marked aversion towards normative feminine clothing.

C. The disturbance is not concurrent with physical intersex condition

D. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning

General conclusions

From our studies it seems that some aspects of Zucker and Bradley's theory were supported, whereas others were not. Gender-referred children do seem to have a general vulnerability (anxious temperament), comparable to other children with psychiatric conditions. Clinicians and parents should be aware that these children are at risk for developing co-morbid psychiatric disorders, internalizing problems in particular.

For the other potential determinants of GID - parental psychopathology and parent-child interaction style - we did not find clear supporting evidence. Nor with regard to the role of prenatal exposure to abnormal sex steroid levels, did we find evidence either for the entire gender referred group.

In a – relatively – accepting environment, gender dysphoric children seem to do quite well in their relationships. For their mental health, it seems to be more important that they have friends, than that these friends belong to their own sex. Gender dysphoric boys seem to be more at risk for social rejection (especially by other boys) than girls. Knowing that many are already somewhat vulnerable because of their anxious temperament, it might be good for parents and schools to pay specific attention to their social competence and to stimulate and support them in making friends.

If gender dysphoric children appear to belong to the subgroup of persisters, which seems to happen to the more extremely cross-gendered children, a timely treatment with GnRH analogs to suppress puberty is beneficial.[50] The number of children who are desisters, however, is much larger than the number of persisters. This makes a complete social role change before puberty not advisable.

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