Chapter 9 Summary and General Discussion

Summary

Children may show variability in their gender role behaviors, interests and preferences and/or their experienced gender identity (their experience to be male, female or a different gender). Within the male-female¹ continuum of gender role expressions and gender identity three groups can be distinguished. First, the gender normative children: Their gender role and gender identity are congruent with their natal sex. Second, the gender variant children: These children show (mild) cross-gender behaviors, interests and preferences, and may experience a gender identity which is congruent with their natal sex to a lesser extent than is the case in gender normative children. And third, the *gender dysphoric* children: These children show extreme and enduring forms of cross-gender role expressions, experience a crossgender identity and fulfill the criteria of a DSM-IV-TR diagnosis of Gender Identity Disorder (GID) (American Psychiatric Association 2000). In contrast to most of the gender variant children, gender dysphoric children may need clinical attention as a result of significant distress or a significant risk of distress, and/or impairment in important areas of functioning. Knowledge about the future development, the trajectories and possible associated factors of gender non-normative children (both gender variant and gender dysphoric) is however limited.

The studies described in this thesis aimed to enhance our understanding of the development of gender variant and gender dysphoric children and adolescents, and to identify factors associated with the persistence and desistence of gender dysphoria.

In **chapter 2**, we provided an overview of what is currently known about the trajectories and contributing factors to gender identity development, particularly during adolescence in the general population and in gender variant / gender dysphoric youth. Compared to what is known from gender identity development in gender variant or gender dysphoric children, studies of normative gender identity development during adolescence in the general population are lacking behind.

With regard to the factors contributing to non-normative gender identity development, earlier studies mainly focused on the role of psychosocial factors. Factors such as elevated levels of psychopathology in the parents, increased anxiety of the child, and a lack of parental limit setting have been put forward as possible determinants. However, the evidence from these

¹ Although it is conceivable that children have an identity outside the male-female continuum, thus far we did not come across children identifying as gender queer in our studies or in our clinical work.

studies showed to be equivocal and it is unclear whether the factors that were associated with a non-normative gender identity development were the cause of this development or a consequence of the gender variance or gender dysphoria. More recently, research has focused on the role of biological factors on a non-normative gender identity development. Studies of individuals with a Disorder of Sex Development (DSD), congenital conditions in which the development of chromosomal, gonadal and/or anatomical sex is atypical (Hughes et al. 2006), point to the role of prenatal exposure to gonadal hormones and their effects on gender role behavior and possibly on gender identity development. From post mortem, neuropsychological, and brain imaging studies of individuals with gender dysphoria, differences between gender dysphoric individuals and members of their natal sex have been found. However, these differences were not found for all measures and the direction of the differences is not always consistent or not yet sufficient to form a basis for a broad theory on gender identity development. The current evidence makes clear that there is no simple relationship between psychological - and social factors and gender identity development, and brain development and the development of gender identity. In addition to this, although several researchers have acknowledged that nature and nurture interact, they have not tried to integrate both aspects in their studies thus

As for the future development of gender dysphoric children, our overview of the literature indicated that gender identity in childhood seems more malleable than later in adolescence or in adulthood. Furthermore, we described that adolescence is a crucial period for the consolidation of gender identity and persistence of gender dysphoria. We discussed that the onset of physical puberty in this period may steer this process, but that there are also indications that cognitive aspects of gender identity (e.g. confusion and ambivalence with ones gender identity) has its own influence. For those without a history of childhood gender dysphoria, adolescence may initiate gender dysphoria. Regardless of the various developmental trajectories of a non-normative gender identity development, adolescence can be denoted as a crucial developmental period for gender identity.

In **chapter 3** we reported on a study where we validated a 12-item dimensional scale that aims to measure gender dysphoria, in a sample of 1119 adolescents and adults (M age 24.6, range 12-75). The male (UGDS-M) and female (UGDS-F) versions of the Utrecht Gender Dysphoria Scale (UGDS) were assessed in a group of participants diagnosed with a GID (N=545), a group who was subthreshold for GID (N=103), participants with a DSD (N=60), and non-transgender heterosexual (N=219), gay/lesbian (N=150), and bisexual (N=42) controls. Both versions of the UGDs appeared to be reliable scales with a strong ability to discriminate between clinically referred gender dysphoric individuals and non-clinically referred controls and DSD participants. Sensitivity was 88.3% (UGDS-M) and 98.5% (UGDS-F), specificity was 99.5% (UGDS-M) and 97.9% (UGDS-F). Comparison of the mean total scores showed that there was significantly more gender dysphoria in participants diagnosed with a GID, compared to participants who were subthreshold for GID, for both versions. The two transgender groups showed significantly more gender dysphoria than the DSD and control participants. We concluded from our findings that these qualities make the instrument useful for clinical and research purposes.

Chapter 4 reported on a 24 years longitudinal study where we examined whether childhood gender variance was associated with the report of a bior homosexual sexual orientation and gender discomfort in adulthood in the general population. In a sample of 406 boys and 473 girls we measured gender variance in childhood (M age 7.5, range 4-11) and sexual orientation and gender dysphoria in adulthood (M age 30.9, range 27-36). Our findings showed that the intensity and presence of childhood gender variance was higher in girls than in boys, and that gender variance was reported more frequently in younger children than in older children. Furthermore, we found that the presence of childhood gender variance was associated with the presence of a homosexual orientation in adulthood, but not with bisexuality. The chance of a homosexual orientation in sexual attraction, sexual fantasy, sexual behavior, and sexual identity were 8 to 15 times higher for both male and female participants with a history of gender variance as reported by the parents (10.2% to 12.2%), compared to participants without a history of gender variance (1.2% to 1.7%). The presence of childhood gender variance was not significantly associated with gender discomfort / gender dysphoria in adulthood. We concluded in this study that childhood gender variance, at least as measured by the Child Behavior Checklist (CBCL), is not predictive for a gender dysphoric outcome in adulthood in the general population. Furthermore, the presence of childhood gender variance and a homosexual sexual orientation in adulthood are associated in the general population, but this association is much weaker than in clinically referred gender dysphoric children.

Chapter 5 described the findings from a qualitative study where we tried to obtain a better understanding of the developmental trajectories of persistence and desistence of childhood gender dysphoria and the psychosexual outcome of gender dysphoric children. We interviewed 25 adolescents (*M* age 15.9, range 14–18), who were diagnosed with a Gender Identity Disorder (DSM-IV or DSM-IV-TR) in childhood (*M* age 9.4, range 6-12). Our findings on possible predictors in childhood for the different trajectories showed

that the 14 persisters and 11 desisters reported quite similar childhood experiences, but subtle differences in their experience of gender and the labeling of their feelings were observed.

As for underlying mechanisms and experiences that may have steered the persistence and desistence of gender dysphoria, we identified the period between the ages of 10 and 13 to be crucial. In the perceptions of the adolescents, three factors were related in this period to the intensification of gender dysphoria in persisters or remittance of gender dysphoric feelings in the desisters; (1) the changing social environment, where the social distance between boys and girls gradually increases, (2) the anticipation of, and actual body changes during puberty, and (3) the experience of falling in love, sexual attraction and sexual experiences. Interestingly, even in this relatively small sample of adolescents, we observed that the feelings of gender dysphoria did not completely remit in all desisters. Furthermore, our observation of high reports of sexual orientations and sexual attractions directed towards individuals of the same natal sex seemed to be in concordance with the earlier findings from the prospective quantitative literature on gender dysphoric children. Finally, the stories of the persisters and desisters on the effect of social role transitioning (in appearance and/or a name change or pronoun change) revealed that transitioning was experienced as a relief in persisters, but could result in a troublesome process of changing back to their original gender for desisters.

Chapter 6 reported on a quantitative follow-up study that examined the factors associated with the persistence and desistence of childhood gender dysphoria, and adolescent feelings of gender dysphoria and sexual orientation. In a sample of 127 adolescents (79 boys, 48 girls), who were referred for gender dysphoria in childhood (age range 6-12) and followed up in adolescence (age range 15-19), we observed a persistence rate of 37% (47 persisters out of the 127 adolescents). We examined childhood differences among persisters (N=47) and desisters (N=80) in demographics, developmental background, childhood psychological functioning, the quality of peer relations and childhood gender dysphoria, and adolescent reports of gender dysphoria, body image and sexual orientation. Our findings showed that persisters reported higher intensities of gender dysphoria, more body dissatisfaction and higher reports of a same natal-sex sexual orientation, compared to the desisters, and were in line with earlier findings from prospective follow-up studies in clinical populations.

As for the factors associated with the persistence of gender dysphoria, we found that a higher intensity of childhood gender dysphoria (through self and parental report, and through cognitive and/or affective gender identity responses), an older age at referral, and transitioning (at least partially) to the preferred gender role were predictive of childhood gender dysphoria persistence. In addition to this, we found that the chance of persisting was higher in natal gender dysphoric girls than in boys, but that factors such as psychological functioning, the quality of peer relations, demographic (e.g. family structure, parents' social economic class), and developmental background (e.g. birth weight, pregnancy duration) were not associated with the persistence of childhood gender dysphoria. Finally, our findings showed that the factors associated with the persistence of gender dysphoria were different for the two natal sexes. For natal boys, the age at referral, the gender role presentation, the self report of a cross-gender identification ("I am a boy" or "I am a girl"), and the parental report of the intensity of gender role behavior showed to be the major predictive factors for the persistence of gender dysphoria, whereas for girls, the self reported cross-gender identification and the intensity of gender dysphoria turned out to have a higher predictive value than the other evaluated factors.

Chapter 7 presented a communication where we addressed the topic of social transitioning in gender dysphoric children in early childhood. We reported on our observation of increasing numbers in our clinical population of children who completely (change in clothing and hair style, first name, and use of pronouns) or partially (change in clothing and hair style, but did not have a name and pronoun change) transitioned between the period of the year 2000 and 2009.

Before the year 2000, 2 prepubertal boys, out of 112 referred children to our clinic, were living completely in the female gender role. Between 2000 and 2004, 3.3% (4 out of 121 children) had completely transitioned, and 19% (23 out of 121 children) were partially transitioned when they were referred. In the period between 2005 and 2009 we observed that 8.9% (16 out of 180 children) completely transitioned and 33.3% (60 out of 180 children) partially transitioned at the time of referral.

In discussing the increasing rates of socially transitioned gender dysphoric children we noted that follow-up studies show that the persistence rate of childhood gender dysphoria is about 15.8%, and wondered what would happen to children who transitioned in childhood, but turned out to be desisters. We referred to two cases of natal girls, who transitioned early in childhood and for whom the gender dysphoria desisted. Their process of changing back to their original gender was reported to be a troublesome process (Chapter 5 and Steensma et al. 2011). We concluded that it is advisable to be very careful when taking steps regarding social transitioning during the early childhood years, as they might be difficult to reverse.

In **chapter 8** we described a cross-national investigation that examined the psychological functioning and the quality of peer relations between

gender dysphoric youth from Toronto, Canada and Amsterdam, the Netherlands. In a sample of 544 children and 174 adolescents, referred to the specialized gender identity clinics in both countries, we assessed the Teacher's Report Form to measure emotional and behavioral problems, the quality of peer relations and gender dysphoria. Our findings in both countries showed that the children were, on average, better functioning than the adolescents, and that the gender dysphoric boys showed to have poorer peer relations and more internalizing than externalizing problems compared to the gender dysphoric girls. As for the degree of behavioral problems in both countries, the quality of peer relations showed to be the strongest predictor. In discussing our findings we concluded that gender dysphoric children and adolescents showed the same pattern of emotional and behavioral problems in both countries, although there were significant differences in the prevalence of problems.

Between the two countries, we found clear differences: Both the children and the adolescents from Canada had more emotional and behavioral problems and a poorer quality of peer relations than the children and adolescents from the Netherlands. In line with previous comparisons of gender dysphoric children from the two countries, we found that children and adolescents from the Netherlands presented with significantly more cross-gender behavior than those from Canada. The differences between the two countries seemed to be an effect of a poorer quality of peer relations in Canada, compared to the Netherlands. We hypothesized that this may be the result of a difference in social tolerance towards gender variant expressions, as cross-cultural studies indicate that the Netherlands is much more tolerant towards homosexuality, and most likely also towards gender variance, than most countries in the world (Veenhoven 2005).

General discussion

This thesis described a number of prospective studies on the psychosexual development of gender atypical children and adolescents, the validation of a gender dysphoria scale, and a cross-sectional comparison between gender dysphoric children and adolescents from Canada and the Netherlands with regard to their psychological functioning.

Earlier prospective studies of gender dysphoric children, for whom the majority would meet the DSM-IV-TR diagnostic criteria for GID, indicated that, for a substantial minority of the children (2-27% across studies), the gender dysphoric feelings persisted into adolescence or adulthood. The same studies showed that the presence of childhood gender dysphoria was associated with an increased prevalence of a homosexual or bisexual outcome (Bakwin 1968; Davenport 1986; Drummond et al. 2008; Green 1987; Kosky 1987; Lebovitz 1972; Money and Ruso 1979; Wallien and Cohen-Kettenis 2008; Zucker and Bradley 1995; Zuger 1984). Retrospective studies in the general population confirmed these findings by showing that individuals with a homosexual sexual orientation recalled more cross-gender behaviors from their childhood years, compared to heterosexual individuals (see for an overview, Bailey and Zucker 1995; Zucker et al. 2006).

The findings from our prospective follow-up studies of gender variant children in the general population and clinically referred gender dysphoric children seem to be in line with these earlier findings. For both groups we showed that childhood gender non-conformity was associated with a greater chance of a sexual orientation that is directed towards the same natal sex. We also found that the gender dysphoria remitted for the majority of gender dysphoric children. However, with regard to the psychosexual outcome at the time of follow-up, the outcome for sexual orientation as well as the intensity of gender dysphoria showed variability. The gender variant and gender dysphoric children did not all report a homosexual orientation or complete remittance of the gender dysphoric feelings at the time of followup. For the gender variant children the chance of a homosexual orientation was 8 to 15 times higher than for children without a history of gender variance, but approximately 85% of the gender variant children still turned out to be identifying as heterosexual. In addition, in our study of clinically referred gender dysphoric children, not all the persisters reported homosexuality across the different domains of sexual orientation, and within the group of desisters the variability in sexual orientation outcome was even greater. As for the outcome of gender dysphoria, we observed that the intensity of gender dysphoria decreased to a non-clinically relevant level for the majority of desisters, but we also found one desister in our quantitative follow-up study, and one in our qualitative follow-up study for whom the gender dysphoric feelings did not completely remit to a non-clinical level.

Interestingly, in the UGDS validation study we found that in adolescents and adults the severity of gender dysphoria was also highly variable in all groups. In both the non-referred natal males and females, gay and lesbian participants reported more gender dysphoria than heterosexuals, although the majority of these participants had a UGDs score below our cut-off point of clinical relevance. However, in some, the reported levels of gender dysphoria were comparable to the scores of individuals who applied for gender reassignment to our clinic. By contrast, in the group of referred participants, the majority showed clinical levels of gender dysphoria, but there were still a proportion of participants, especially in natal males, who applied to our clinic but did not show levels of gender dysphoria that seemed of clinical relevance.

Diversity in gender dysphoria and the need for clinical attention of some, but not of all gender dysphoric people, has been a topic of discussion in the realization of the DSM-5 (see for an overview Cohen-Kettenis and Pfäfflin 2010). The acknowledgement of the heterogeneity of gender dysphoria has resulted in proposed polythetic criteria (www.dsm5.org) that capture a wider range of manifestations of gender dysphoria than in the previous DSM versions.

Persistence of gender dysphoria and associated factors

One of the central findings from a prospective (Wallien and Cohen-Kettenis 2008) and a retrospective study (Drummond et al. 2008), was that the childhood reports of cross-gender behaviors, interests and preferences, and gender dysphoria were more extreme in the persisters (those for whom the gender dysphoric feelings persisted into adolescence or adulthood) than in the desisters (those for whom the gender dysphoric feelings remitted after puberty). In addition to this, Drummond et al. (2008) showed that gender dysphoric girls who were classified as bisexual or homosexual at the time of follow-up reported higher degrees of childhood cross-gender identification than their heterosexual counterparts, whereupon they hypothesized a "dosage" effect: The association of a higher degree of childhood cross-gender identification with a greater likelihood of a later minority sexual orientation.

Our findings support such a "dosage" effect, with regard to both the sexual orientation directed towards the same natal sex, and the persistence of gender dysphoria. Across our two prospective studies on gender variant and gender dysphoric children, we found that for the gender variant children, childhood measures of gender variance were associated with later

homosexuality (but not with later gender dysphoria). In gender dysphoric children, where the intensity of childhood gender dysphoria was likely to be greater than in gender variant children, a homosexual and gender dysphoric outcome was much higher. Indeed, in the prospective study of gender dysphoric children, the intensity of gender dysphoria was significantly correlated with the persistence of gender dysphoria into adolescence. A very recent study by Singh (2012), which reported on the persistence and desistence of gender dysphoria in 139 gender dysphoric boys, also showed that the intensity of childhood gender dysphoria was a significant predictor for the persistence of gender dysphoria and a higher rate of a bisexual or homosexual outcome.

With regard to other factors associated with the persistence and desistence of childhood gender dysphoria, some findings from our qualitative and quantitative follow-up studies supported earlier findings (e.g. gender referred girls have a higher chance to persist than boys), but our studies also provided new information. Non-significant in the former studies (Drummond et al. 2008; Wallien and Cohen-Kettenis 2008), but discussed as a potential predictor for the persistence of gender dysphoria, we found that an older age at childhood assessment was associated with persisting gender dysphoria. In addition, we showed that unstudied developmental factors (e.g. birth weight, pregnancy duration) were not predictive for the persistence of gender dysphoria, but cognitive gender labeling ("I am a boy" in natal girls or "I am a girl" in natal boys) and social transitioning were predictive factors.

Of particular interest is that, at least in boys, social transitioning predicts the persistence of gender dysphoria. This finding raises two questions. First: Does social transitioning in itself lead to the persistence of gender dysphoria? For instance, a transitioned boy may 'forget' how it was to live in the male gender role and therefore will no longer be able to feel the desire to change back. Transitioning may also result in a child losing the ability to function in the original gender role over time and/or losing his or her cognitive gender representation as someone belonging to the natal sex (if they even had such a representation). Interesting in this respect was our finding that children (both boys and girls) who expressed cross-gender identification, when asked what their sex was, had a greater chance of persistence. The findings from our qualitative study also indicated subtle differences between persisters and desisters in the experience and labeling of their gender feelings, although they did not report on the effect of a social transition in relation to the cognitive gender identification. Another possibility is that transitioned children may repress doubts about the transition out of fear that they have to go through the process of making his or her desire to

socially transition public for a second time. Our qualitative findings are in support of the idea that children may struggle with changing back to their original gender role, because they dread being teased or excluded by their peers if they would revert to their original gender role. We found that for one natal girl this struggle to go back to the female gender role took a period of nearly two years. As we also found that transitioned boys showed more gender dysphoria and cross-gender behaviors, this could indicate that transitioning is an indicator of the intensity of gender dysphoria and there is no reason to be concerned that early socially transitioned children will create 'false positives'. Although we cannot answer the question with the data in our study, this highly clinically relevant aspect of children's development is something that certainly needs more study. The second question that arises is: Why is transitioning predictive in boys but not in girls? The most likely explanation comes from our findings where we showed that the majority of girls (irrespective of a later persistence or desistence) were already partially transitioned at the time of referral, whereas boys were not. Possible reasons for this difference between gender referred boys and girls may be threefold: First, the dividing line between transitioning and nontransitioning may be clearer for boys than for girls. For instance, boys who have long hair and who wear a dress or a pink T-shirt are likely to be perceived as a girl, whereas it is less clear how girls who dress in pants and have a short hair style will be perceived. As a result, many gender dysphoric girls may already be able to function to their satisfaction among boys so that they may not need the more explicit social gender role change. Second, several studies of children in the general population indicate that gender nonconforming behaviors are often evaluated negatively by other children (e.g. Carter and McCloskey 1984; Levy et al. 1995; Ruble et al. 2007; Signorella et al. 1993; Smetana 1986; Stoddart and Turiel 1985). Furthermore, there is evidence that peer relations are poorer for clinically-referred gender dysphoric children than for non-referred children (e.g. Cohen-Kettenis et al. 2003; Fridell 2001; Zucker et al. 1997, but see Wallien et al. 2010), which likely is due to the social ostracism that results from their marked gender nonconforming behavior (e.g. Fridell 2011). In line with earlier findings (Cohen-Kettenis et al. 2003; Wallien et al. 2010; Zucker et al. 1997) we also found that gender dysphoric boys had poorer peer relations than girls. As a consequence, gender dysphoric boys may repress their desire to transition to avoid the situation where social ostracism increases and peer relations get worse. As a third possibility, the difference between gender referred boys and girls may be due to a difference in the intensity of gender dysphoria. Several previous studies (e.g. Cohen-Kettenis et al. 2003; Cohen-Kettenis et al. 2006; Johnson et al. 2004; Wallien et al. 2009) and our own findings in gender dysphoric children showed that gender referred girls are more gender dysphoric than boys. The difference with regard to the social transitioning could therefore be a reflection of the difference in intensity of gender dysphoria between boys and girls; irrespective of social transitioning the gender dysphoria in referred girls is so severe that the chance for persistence is higher.

Although the purpose of our studies was not to estimate the rate of persistence, we did find a higher proportion of referrals where the gender dysphoria persisted into adolescence (37%) compared to prior studies (15.8 % on average) (Bakwin 1968; Davenport 1986; Drummond et al. 2008; Green 1987; Kosky 1987; Lebovitz 1972; Money and Ruso 1979; Wallien and Cohen-Kettenis 2008; Zucker and Bradley 1995; Zuger 1984). Although our higher percentage likely reflects that our sample did not consist of all consecutive child referrals within in a specific time period (some were still too young to be included), there are reasons to assume that the average of 15.8% is an underestimation of the true persistence rate of childhood gender dysphoria. Over the last decades the reported sex ratios for gender referred boys and girls have gradually changed. In Canada the ratio between boys and girls was 5.75:1 in the period between 1975 and 2000, in the Netherlands this ratio was 2.93:1 in the period between 1988 and 2000 (Cohen-Kettenis et al. 2003). Wood et al. (2012) reported that in the period after 2000, the sex ratios decreased in Canada and that between 2000-2011 the sex ratios ranged from 2.77:1 (2000-2003) to 3.41:1 (2008-2011) for boys and girls. Based on our own calculations we observe the same pattern of lower sex ratios after the year 2000, we found that between the period 2000-2011 the sex ratios for boys and girls ranged from 1.68:1 (2008-2011) to 1.83:1 (2000-2003). For both countries this change in ratios is caused by fewer referrals of boys. The percentage of boys in the total number of referrals before 2000 in Canada well exceeded the 75%, and this percentage decreased and hovered around the 75% in the period between 2000-2011 (Wood et al. 2012). In the Netherlands we observe the same decrease, where 74% of the referrals before 2000 were boys, and the percentage of referred boys between 2000-2011 showed to be 64%. Although evidence is currently not available, it is conceivable that the decrease in referred boys has resulted from fewer referrals of mildly gender variant boys, for whom the probability of a persisting gender dysphoria has been shown to be smaller. This trend will presumably result in higher persistence rates in the future in referred children. The decrease of referrals in boys may further indicate a greater tolerance towards gender non-conforming behaviors in Canada as well as in the Netherlands.

The relatively large percentage of desistence in general is likely to be caused by the inclusion of mildly gender non-conforming children. This

may have resulted from the broadness of the current DSM-IV-TR criteria for a childhood GID diagnosis. Currently, children who show gender variant behaviors only, but do not express a desire to be another gender or do not show signs of anatomic dysphoria can fulfill the DSM criteria for GID. These children may have been included in the diagnostic groups of the follow-up studies so far. Given the now repeatedly reported finding that the intensity of childhood gender dysphoria is a strong predictor for the persistence of gender dysphoria, it is unlikely that the gender dysphoria in these children will persist in the future. The currently proposed criteria for a diagnosis in the DSM-5 of the American Psychiatric Association are stricter to prevent false positives (www.dsm5.org). For instance, the first criterion (A1) "a strong desire to be of the other gender or an insistence that he or she is the other gender (or some alternative gender)" is now required as one of 6 out of 8 criteria. Furthermore, two criteria now reflect anatomic dysphoria.

Clinical implications

A central question in the counseling of gender dysphoric children and their families is what their psychosexual outcome will be. Will my child grow up and identify as a gay man or a lesbian woman or will my child need medical treatment in the future because of a persisting cross-gender identification and anatomical dysphoria? Predicting with certainty whether a child will persist or what his or her sexual orientation will be is, however, currently impossible. Nevertheless, our findings on the trajectories of persisters and desisters and the identified predictors for the persistence of gender dysphoria can provide some guidance for clinicians during the diagnostic phase and in the further counseling process.

In principle, during the diagnostic procedure information on the intensity of the gender dysphoria, emotional and cognitive, as well as social-, school and family functioning, should be addressed and taken into account during the assessment (de Vries and Cohen-Kettenis 2012). Inquiring information through self-report as well as through the parents and the teachers can provide valuable information on cross-informant agreement over the different environments and setting-specific behaviors (e.g. Achenbach et al. 1987a; Renk 2005). When we compared the earlier findings on the psychological functioning of gender dysphoric children (Cohen-Kettenis et al. 2003), assessed through parents by the Child Behavior Checklist (CBCL) (Achenbach and Edelbrock 1983) with our findings on the psychological functioning, assessed through teachers by the Teachers' Report Form (TRF) (Achenbach and Edelbrock 1986), parents and teachers appeared to be in agreement and seem to be reliable informants. We also found that the parent and teacher reports on the intensity of gender dysphoria, as well as the self-report by the child (through the Gender Identity Interview for Children (GIIC; Zucker et al. 1993a) were predictive for the persistence of gender dysphoria. Children with higher intensities of gender dysphoria, measured through self-report and reports of others have a higher chance to be persisters. As for the use of the GIIC in children, it might be that some clinicians are reluctant to use this interview because it explicitly asks from gender dysphoric children with which sex they identify. This might be perceived as offensive and/or as distressful for the child. One should, however, realize that the cognitive responses in the interview ("I am a boy" or "I am a girl") were the strongest shared predictor for the persistence of childhood gender dysphoria for both boys and girls. This all means that the scales and interviews are useful clinical instruments.

In line with the findings by Wallien and Cohen-Kettenis (2008), our findings showed that girls have a higher chance to persist. This might be the result of girls showing more indications of gender dysphoria than boys at the time of referral, as indicated by previous studies (e.g. Cohen-Kettenis et al. 2003; Cohen-Kettenis et al. 2006; Johnson et al. 2004; Wallien et al. 2009) and our own findings. However, besides the intensity of gender dysphoria, two other factors, are also of clinical relevance. The first is the age at assessment: Older children have a higher chance that the gender dysphoria will persist. This was specifically found in our study for gender referred boys, but it is likely that the absence of age as a predictor for persistence in girls was an artifact of our population. The referred girls were generally older in age at the time of referral than boys. The second is the social role transition: Children who are partially or completely transitioned at the time of referral have a higher chance that the gender dysphoria will persist. This was also specifically found for gender dysphoric boys, however, since we observed that the majority of girls were partially transitioned at the time of referral, one should be extra alert when, for instance, feminine looking girls present at a younger age for assessment with a desire for gender reassignment.

Besides quantitative information on the persistence of gender dysphoria, information from our qualitative study showed that addressing the experiences of older gender dysphoric children (above the age of 10), regarding certain developmental topics may be useful. Valuable information can be obtained by discussing how they experience the changes in their social environment, when the social distance between boys and girls gradually starts to increase. Another topic to address is how they anticipate the imminent feminization or masculinization of their bodies, and how they experience the actual body changes if puberty had already started. The third topic is the experience of falling in love. In discussing this, the actual sexual attraction that they report (e.g. towards males or females) seems to be of

less importance than how they experience their sexual attraction in relation to their gender identity. For instance, for a gender dysphoric boy who is attracted to natal boys, the awareness of his sexual attraction may function as a confirmation of his cross-gender identification, strengthening his identity of a heterosexual female. For another gender dysphoric natal boy who discovers his sexual attraction to natal boys, this may result in questioning his cross-gender identification and remittance of gender dysphoric feelings, resulting in identification as a gay male.

The qualitative findings in general seem to address the importance of psychological maturation before it can be concluded whether a child is a persister or a desister. This is relevant in the current discussion on whether the age criterion of 12 years, often used as an eligibility criterion for puberty suppression in gender dysphoric youth, should be adjusted. Since a number of children, mainly natal girls, are already beyond Tanner stage 3 at the age of 12, some clinics do not use an age limit of 12 (e.g. Spack et al. 2012). This approach, in which the start of medical interventions is primarily guided by the physical maturation of the body, raises the question when children are psychologically mature enough to be identified as a persister or a desister. In our own clinical experience, the ability of children, before the age of 12, to reflect on and talk about their body image, their desire for certain physical changes or for having certain body parts, their social position in relation to their gender role, and their awareness of their sexual attraction, is highly variable. Some are certainly capable of doing so. By contrast, for a number of adolescents for whom the puberty already started before age 12, but had to wait for puberty suppression until they were 12 years old, it seems in retrospect that they were psychologically mature enough to be eligible for an earlier start. From this psychological perspective, it seems that medical interventions before the age of 12 can be considered for some, but not for all children. The safest approach in this respect seems to be that, if gender dysphoric children are pursuing gender reassignment before the age of 12 and are physically beyond Tanner stage 3, it is advisable to balance their psychological distress as a consequence of the physical development and their psychological maturation before intervening.

As for the counseling of the young gender dysphoric children, for whom medical interventions are not yet to be considered, clinicians may be helpful in counseling parents and the child regarding the uncertainty of the child's psychosexual outcome. For instance, some parents who find it hard to bear the uncertainty are helped by practical advice or by discussing potential reasons for their inability to cope with uncertainty.

It is also advisable to encourage parents to use an approach, in which all future possibilities remain open for the child and to provide enough space to explore for the child as possible. In our view, this implies that behaviors or desires of the child should not be blocked, but specific behaviors and desires that can be harmful for the child should be restricted to a safe environment. For instance, for families who live in a neighborhood where gender non-conforming expressions are negatively evaluated and where a high risk of extreme social ostracism or physical aggression runs, a boy's desire to cross-dress may be restricted to a safe place, such as at home. It is important that the child receives a good explanation why such decisions are made, because he may infer that everyone disapproves his cross-gender behaviors and - feelings and may as a consequence start to feel rejected or isolated. Behaviors may also be labeled more carefully: "You are a boy who feels like a girl" instead of fully going along with the experienced cross-gender identification of the child. Even if he will appear to be a persister, he should be aware that he still has a male body that will need many medical interventions to align his body with his gender identity. Furthermore, we recommend that one should be careful not to take steps that are hard to reverse, such as a complete social role transition. As discussed in the previous section, social role transitioning may well be an indicator of the intensity of gender dysphoria. However, it may also have an effect in itself we know little about yet.

Regardless of what decisions parents will make, the role of the clinician should be to help the parents by providing psycho-education on what is currently known about the development of gender dysphoric children and what the pro's and con's may be of certain decisions. Parents can thereby be supported to weigh this information against the desires of the child, the safety of the child, and the psychological distress the child experiences, in order to make balanced decisions. Naturally, they should be encouraged to involve the child in this process, by informing and explaining him or her why decisions were made.

Directions for future research and limitations

The results from the studies described in this thesis support existing knowledge on the development of gender non-conforming children and adolescents, but also provide new insights on the developmental trajectories and factors associated with the persistence of childhood gender dysphoria. However, a number of limitations should be addressed, some of which result in a need for further research.

Firstly, the follow-up periods: With the exception of our prospective follow-up study on gender variant children in the general population, the used follow-up periods in our studies on gender dysphoric children were rather short. Although the majority of adolescents indicated that their feelings of gender dysphoria completely remitted, we found that some of them still experienced some gender dysphoria but did not present at our adolescent clinic. It is conceivable that if our follow-up period had been longer (e.g. when they were adults), that such individuals would have been incorporated in our sample as persisters. Although our findings on the reports of sexual orientation were largely in line with the earlier findings, and the literature shows that the average age of the first feelings of same-sex attraction is generally during puberty and before the age of 18 (e.g. Barber 2000; Herek et al. 1998), there is also evidence that the moment at which men and women identify and come out as gay, lesbian, or bisexual generally may lie above the age of 18 (e.g. Barber 2000; Herek et al. 1998; Rust 1996).

Secondly, the samples used in our prospective follow-up studies primarily consisted of gender variant and gender dysphoric children below the age of 12. As a consequence of this selection, our results are only applicable to individuals with an early onset of gender variance and gender dysphoria. Since gender dysphoria can have its onset in adolescence (e.g. Lawrence 2010; Nieder et al. 2011; Zucker 2012), and there is very limited knowledge about the development of gender non-conforming adolescents in general, future research should focus on the development of these adolescents. To study the developmental trajectories, preferably population based samples should be used in which different groups are sufficiently represented to cover the wide spectrum of gender diversity.

Thirdly, the lack of a bio-psychosocial perspective: The aim of our studies was to enhance our understanding of the development of gender non-conforming children and adolescents from a psychological perspective. However, as we described in our overview on gender identity development in adolescence there is a need for an integration of biological and psychosocial factors in future research. With regard to our own studies on the factors that are associated to the persistence of gender dysphoria, we had no opportunity to take the pubertal development of the children into account. Future research on the development of gender dysphoric children should also include Tanner stage and/or hormonal measures with psychosocial measures.

Fourthly, the role of sexuality in the development of gender dysphoric children and adolescents: The information from our qualitative follow-up study, where the awareness of sexual orientation and/or certain sexual experiences seemed to be indicative for a persistence or desistence of gender dysphoria, is currently the only information we have. Further exploration of this aspect of life in relation to gender development is needed. In addition, there is a clear need to know more about the sexual development and the sexual health of adolescents who (re)apply to our clinic for gender reassignment. The medical interventions, by means of suppressing puberty, and providing cross-sex homones and genital surgery, are likely to have an effect on the sexual experiences and sexual functioning of these adolescents, which should be addressed in future research.

Finally, the possible side effects of social transitioning: In our discussion we have addressed a possible cause of social transitioning (the intensity of gender dysphoria), but also stated our concerns about potential effects of a social transition on the cognitive and social development of gender dysphoric children. It is of great importance to gain more insight in such effects in order to know what clinically responsible care is.