Chapter 2

Gender Identity Development in Adolescence

Thomas D. Steensma, M.Sc. 1,2
Baudewijntje P.C. Keukels, Ph.D. 1,2
Annelou L.C. de Vries, MD., Ph.D. 3,3
Peggy T. Cohen-Kettenis, Ph.D. 1,2

1 Center of Expertise on Gender Dysphoria, vU University Medical Center, Amsterdam, the Netherlands
2 Department of Medical Psychology and Medical Social Work, vU University Medical Center, Amsterdam, the Netherlands
3 Department of Child and Adolescent Psychiatry, vU University Medical Center, Amsterdam, the Netherlands

Hormones and Behavior, accepted for publication
Abstract

This article aims to provide an outline of what is currently known on trajectories, and contributing factors to gender identity development in adolescence. We give a historical overview of the concept of gender identity, and describe general identity development in adolescence, gender identity development in the general population and in gender variant youth. Possible psychosocial (such as child and parental characteristics) and biological factors (such as the effects of prenatal exposure to gonadal hormones and the role of genetics) contributing to a gender variant identity are discussed.

Studies focusing on a number of psychosocial and biological factors separately, indicate that each of these factors influence gender identity formation, but little is known about the complex interplay between the factors, nor about the way individuals themselves contribute to the process. Research into normative and gender variant identity development of adolescents is clearly lagging behind. However, studies on persons with gender dysphoria and disorders of sex development, show that the period of adolescence, with its changing social environment and the onset of physical puberty, seems to be crucial for the development of a non-normative gender identity.

Introduction

In recent years, adolescents who experience gender incongruence with their birth-assigned gender received much clinical and media attention. A sharp increase in the number of referrals to gender identity clinics and a decline in age at which medical interventions, aiming at gender reassignment, are requested, is observed in Europe (de Vries and Cohen-Kettenis 2012), as well as in Northern America (Wood et al. 2013). One of the reasons might be the availability of puberty suppression as an aid to provide adolescents with gender incongruence with time and without the accompanying distress caused by the physical changes of puberty before a more definite decision regarding gender reassignment is made (e.g. Olsen et al. 2011). This increase in attention raises the question what knowledge we have on gender identity development in adolescence and what factors are of theoretical and clinical relevance during this critical developmental phase. This article provides a historical overview of the terminology and describes what we know about developmental pathways and contributing factors.
The concept of gender identity

The term identity comes from the Latin noun “identitas,” which means the same. The term, referring to a person’s mental image of him or herself thus implies some sameness with others in a particular way. Each individual may have a number of identities, such as an ethnic identity, a religious identity, or a national identity (Kroger 2007). A very fundamental identity, however, is one’s gender identity. Gender identity refers to the extent to which a person experiences oneself to be like others of one gender. One’s sense of being male or female largely determines how people view themselves and provides an important basis for their interactions with others.

Over the years the terms gender identity and also gender role (behaviors, attitudes, and personality traits which, within a given society and historical period, are typically attributed to, expected from, or preferred by persons of one gender) have been used in different ways. In the 1950s, the terms were introduced in the clinical literature when psychologists working with individuals with disorders of sex development (DSM; previously called intersex conditions), and with gender dysphoria started to study gender identity development.

In most cases, gender identity will develop in accordance with physical gender characteristics. A baby with XY sex chromosomes and male genitalia will generally be assigned to the male gender, will show male typical behaviors, and have a male gender identity. Discordance between these gender aspects does occur, however, in some conditions. DSM are congenital conditions in which the development of chromosomal, gonadal, or anatomical sex is atypical (Hughes et al. 2006). For instance, in DSM, external male appearing genitalia may not correspond with the gonads, and/or sex chromosomes. Gender identity may be in line with the chromosomes and gonads, but not with the external genitalia. Gender dysphoria refers to the distress resulting from incongruence between experienced/expressed gender and assigned gender. In gender dysphoric individuals, a gender identity may develop that does not match with sex chromosomes, gonads and genitalia, although the physical sex characteristics all correspond with each other.

Albert Ellis was one of the first to report on gender identity and sexual orientation variations in adults with DSM (Ellis 1945). A decade later, this line of research was continued and elaborated by John Money, a modern sexologist who worked with children with DSM (Money 1994). He proposed to make a clear distinction between the terms sex and gender, because, particularly in the field of DSM, sex is a confusing concept. For instance, does a 46,XY person with a complete androgen insensitivity syndrome (CAIS), characterized by high testosterone levels, undescended testes, and a vulva
belong to the male or female sex? Money also introduced the dual concept of gender identity/role (gi/r). He considered gender identity to be the private manifestation of gender role, and gender role the public manifestation of gender identity. However, in gender dysphoric persons, the gender role, which, according to Money is the public expression of one's gender identity, is at least for some period, seriously blocked. Their gender identity, but not their gender role, may thus be different from their assigned gender. For this reason, and because in research the concepts are often dealt independently, gender identity and gender role are currently used separately.

Some decades ago, Stoller (1968) introduced the concept of core gender identity. He considered it the “…essentially unalterable core of gender identity (e.g. I am male) to be distinguished from the related but different belief, I am manly (or masculine)….(p 40) and speaks of an “inner conviction that the sex of assignment was right.” (Stoller 1985, p.11).

Gender identity has not only been investigated in clinical research. Cognitive developmental psychologists also made use of the concept. For a few decades, they mainly focused on cognitive components of gender identity (Fagot and Leinbach 1985; Kohlberg 1966; Ruble and Martin 1998). For instance, Kohlberg (1966, p. 88) defined gender identity as the “cognitive self-categorization as boy or girl” and Fagot and Leinbach (1985, p. 685) considered gender identity to be “the concept of the self as male or female.” More recently, researchers in this field gave more attention to affective components of gender identity, such as feelings of contentment with one’s gender (Egan and Perry 2001), and they started studying its relationship with mental health. They also considered felt pressure for gender conformity and felt compatibility aspects of gender identity. Tobin et al. (2010) proposed a five dimensional model, subdivided into membership knowledge of a gender category, gender centrality (the importance of gender to other identities), gender contentedness, felt gender conformity, and felt gender typicality, to conceptualize gender identity. In their conceptualization of gender identity, the recent cognitive developmental researchers are much closer to clinical theorists than their predecessors.

In clinical psychology and psychiatry, individuals who do not identify with their assigned gender, became known as transsexuals (World Health Organisation, WHO 1992) or individuals with a gender identity disorder (GID; APA 2000). Clinically they were, and still are, categorized according to criteria as formulated by the APA and WHO. If they fulfill the criteria for the diagnosis and are able to live in the preferred gender for a period of time, supported by prescribed cross-sex hormones, and are capable to handle the complex issues surrounding treatment, they are referred for gender reassignment surgery. In DSM-IV-TR’s accompanying text, terms such as “the
other sex” are frequently used, and within the DSM-5 criteria, the term “cross-gender identification” also suggests that there are only two gender identity categories, male and female. For long, gender identity, gender role, and gender problems were conceptualized dichotomously rather than dimensionally.

During the last decade, the dimensionality and diversity of gender identity and gender problems has received increasing attention and criticism in the literature (e.g. Fausto-Sterling 2000). It is argued that individuals who experience gender problems not necessarily experience a complete cross-gender identity and not always need clinical attention (e.g. Diamond and Butterworth 2008; Lee 2001). Bockting (2008) showed that the gender identification of individuals covers a wide spectrum of gender identity labels, such as; “shemale,” “third gender,” “pan-/poly-/or omnigendered,” “gender fluid;,” instead of male and female or even transsexual. These individuals may or may not experience distress and they may or may not want to live as “the other gender” (see Cohen-Kettenis and Pfäfflin 2010, for an overview).

Regarding treatment, some only want parts of the classical gender reassignment, consisting of hormone treatment and gender reassignment surgeries. For example, in a specific condition, men desire to obtain chemical or surgical castration (in some with additional penectomy) without the desire to transition to the female gender, because they do not identify as females but as eunuchs. They are referred to as Male-to-Eunuch individuals (e.g. Johnson and Wassersug 2010; Wassersug et al. 2004).

As an umbrella term for aspects of gender that are gender non-conforming or non-normative the term gender variant is often used. With regard to gender identity development, a normative (or conforming) gender identity development and a variant (or non-normative) gender identity development can be distinguished.

Adolescent identity development
Developmental psychologists like Erikson (1968) and Marcia (1966; Marcia et al. 1993), have demonstrated that adolescence serves as an important period for the formation of a personal identity. A personal identity includes values, principles and roles an individual has adopted as his or her own. Identity formation is an individual process in which adolescents explore and commit to identity-defining roles and values in a variety of life domains (politics, occupation, religion, intimate relationships, friendships, and gender roles). The variation in styles through which this process evolves will lead to differences in identity development and identity outcome. For example; in early adolescence commitment to a domain may be made without any prior explorations (this is called foreclosure), often based on parental
values, or commitment may not be formed at all because of disinterest in finding personally expressive adult roles and values (called diffusion). Later in adolescence, commitment may (still) not yet been formed but the adolescent searches for meaningful adult roles and values (called moratorium), eventually followed by a style where commitment is based on thoughtful exploration (called identity-achieved) (Kroger 2008; Marcia et al. 1993).

More recently, the focus on identity development has been expanded and directed at the role of context (e.g. Adams and Marshall 1996; Yoder 2000). Here, identity development is presented as an individual as well as a social process at which identity shapes and is shaped by the surrounding milieu (Adams and Marshall 1996). Also, the role of gender and possible gender differences regarding identity structure, the importance of identity domains and the process of identity formation have been examined (Kroger 1997). Kroger (1997) reviewed the literature up to 1995 reporting on these topics and concluded that there was little evidence for gender differences. However, instead of gender differences, empirical evidence suggests a potential role of gender-role orientation (masculine, feminine, androgynous) on the identity-formation during adolescence (e.g. Bartle-Haring and Strimple 1996; Sochting et al. 1994). Whether gender-role orientation may affect gender identity-formation, lead to actual gender identity fluctuations, gender identity changes, or results in gender role experimenting alone, without an influence on gender identity is, however, currently unclear.

**Gender identity development**

Cognitive developmental researchers studying gender identity development have almost exclusively focused on the role of cognitive factors in young children (Ruble et al. 2006). They found that gender learning starts early, is a gradual process taking many years, and passes through various stages (Kohlberg 1966). Most children develop the ability to label their own and others' gender between 18 and 24 months. This ability is related to increased gender typed preferences such as the preference for stereotyped toys (e.g. boys preferring trucks and girls preferring dolls) (e.g. Serbin et al. 2001; Zosuls et al. 2009), the preference for certain play behaviors (rough-and-tumble play in boys, cooperative play in girls) (e.g. Ruble and Martin 1998), and the gradual increase in the preference for same-sex playmates (e.g. Lobel et al. 2000). There are indications for gender differences at the end of childhood with boys having a stronger gender identity than girls, reporting to be more content with their gender, viewing themselves as more gender typical than other boys, and placing more pressure on themselves to conform to the expected gender role, than girls (Egan and Perry 2001). For
most children, gender identity is largely congruent with their gender role behaviors.

Hill and Lynch (1983) proposed that in adolescence, gender intensification occurs. This means that an increased pressure to conform to culturally sanctioned gender roles results in a further differentiation in gender-role identification in boys and girls. Studies testing this idea showed mixed results. For example, Galambos et al. (1990) indicated that sex differences in masculine personality qualities (instrumental qualities such as independence and leadership) increased in early adolescence, but sex differences in feminine personality qualities (expressive qualities such as sensitivity and kindness) did not. A longitudinal study by Priess et al. (2009) showed that adolescents did not become more stereotypical in their gender-role identity across adolescence, and the authors contributed the lack of support for the gender intensification hypothesis to changed patterns of socialization in present-day adolescents. In present day society boys are free to be more expressive and girls are promoted to be more independent than they were in the past.

From another perspective, McHale and colleagues (2009), focused on the influence of the time youth spend in gendered social contexts on the development of their gendered personality qualities and interests. They also studied whether this was moderated by the increased levels of testosterone in early adolescence. By the age of 13, they found higher reports of feminine personality qualities and interests in girls and higher reports of masculine personality qualities and interests in boys. Through adolescence, the time in gendered social contexts generally showed to be associated with the development of more gender stereotyped qualities. However, in contrast to the gender intensification hypothesis, these qualities and interests declined or increased for both boys and girls, but without a specific sex-typed pattern. For some aspects measured, the pace of testosterone increase in early adolescence showed to have a moderating effect instead of the levels of testosterone.

Although there are indications that gendered personality qualities and interests tend to change during adolescence, for the majority of adolescents gender identity is in concordance with assigned gender and seems to be fairly fixed from early childhood (Diamond and Butterworth 2008). This is probably why relatively little research has been conducted on gender identity development in this age group.

Gender variant identity development
Little is known about the cognitive gender development of persons with a gender variant identity from very early on. One study by Zucker et al. (1999),
in clinically referred gender dysphoric children, showed that gender dysphoric children had a developmental lag with respect to gender learning, compared to control children (without gender variant behaviors, interests or gender dysphoria). Although the gender-referred children showed the same sequence of cognitive gender development as the control children, their development appeared to be slower. From clinical experience, it appears that most gender dysphoric children are perfectly able to label their natal sex. Identifying with their natal sex, affective aspects included, is however another matter. Children as young as two years may indicate that they want to be the other gender, dislike the gender associated with their natal sex, and behave accordingly. They may even express anatomic dysphoria (“I do not want to have a penis” or “I do not want to have breasts”), and state that they want to be the other gender as soon as they can talk (Cohen-Kettenis 2005a).

Prospective follow-up studies show that childhood GID does not invariably result in gender dysphoria or GID in adolescence and adulthood. If the results from all outcome studies are combined, about 15% (range 2%-27%) of the children, who mostly had a diagnosis of childhood GID, appear to remain gender dysphoric in adolescence or even fulfill criteria for GID (Steenisma et al. 2011). One explanation of the relatively large percentages of desistence is that many mildly gender non-conforming children might have been included in the follow-up studies because the DSM-IV-TR criteria for a GID diagnosis were too broad, whereas the persistence of GID into adolescence is more likely if the gender dysphoria had been extreme in childhood (Wallien and Cohen-Kettenis 2008). A recent study by Steensma et al. (2011), points to the importance of adolescence in early onset gender variant children. In their qualitative follow-up study, adolescents with a childhood diagnosis of GID, for whom the gender dysphoria had persisted or remitted into adolescence, retrospectively indicated the period between 10 and 13 years to be crucial. They identified three possible contributing factors to an increase or decrease of their gender discomfort and gender identification: 1) physical puberty; 2) the changing environment and being more explicitly treated as one’s natal sex (first years in high school); and 3) the discovery of sexuality. The reported changes and consolidation in gender identity shortly before or in the early stages of puberty in this study correspond with the impression of some clinicians that, before puberty, gender identity is more malleable than later in adolescence or in adulthood (e.g. Byne et al. 2012). It may be that pubertal hormones only steer the process. However, as the adolescents themselves indicate that the perception of others and their sexual feelings (and perhaps even related factors, such as body image) also play a role, it is more likely that in the process of consolidation of their experi-
enced gender all these elements had to be experienced, explored, and weighed, particularly when gender identity was not yet firmly established in childhood.

Adult gender dysphoria is not a homogeneous condition and there are various ways of classifying gender dysphoric individuals (see Lawrence 2010, for an overview). In a significant number of natal males with gender identity problems (little is known about females), gender dysphoria only develops during or after puberty. In the early stages of puberty, these adolescents discover that they find wearing female clothing sexually exciting (Zucker et al. 2012). According to themselves and their parents, they often have not been particularly feminine in childhood. During adolescence, or much later, the role of sexual arousal diminishes or vanishes, and the desire to live permanently in the female role becomes so strong that they apply for gender reassignment. This late onset gender dysphoria thus seems to be erotically motivated (at least initially) and is denoted in the literature as autogynephilia, because Blanchard (1985) stated that the sexual arousal in these men is accompanied with the thought or image of oneself as a female. Therefore this form of gender dysphoria could be conceptualized as a paraphilia. Because they are usually sexually attracted to women, gender dysphoric individuals should, according to Blanchard, be classified on the basis of their sexual orientation: homosexual - in relation to their natal sex- or non-homosexual. Blanchard’s conceptualization has created much debate (e.g. Nuttbrock et al. 2011) and onset age has been proposed as a valid classification criterion as well (e.g. Nieder et al. 2011). Although sexuality certainly plays a role in late onset gender dysphoria, autogynephilic fantasies may not be the only reason why adolescents start cross-dressing. For instance, clinically some report that they started cross-dressing as some form of comfort-seeking.

Irrespective of the underlying mechanism, in both the late and early onset routes, adolescence seems to serves as a crucial period, either because it consolidates an already existing development or because it initiates a development that eventually leads to a full blown gender dysphoria.

Factors related to gender variant identity development
Because gender identity generally develops in accordance with one’s natal sex it is virtually impossible to assess the separate contribution of biological and psychosocial factors in normative developing individuals. Studies focusing on the development of gender identity in individuals with DSD and individuals with gender dysphoria or GID offer more possibilities to determine the relative contribution of these factors to the development of gender identity.
Psychosocial factors
In the older literature on gender variant identity development certain parental characteristics such as a maternal wish for a daughter, paternal absence, parental reinforcement patterns, or a symbiotic relationship between mother and son have been considered to be the primary or even the single factor for the development of gender dysphoria (e.g. Green 1974; Stoller 1968). Some of these hypotheses have been tested, but either no support for the hypotheses was found, or the interpretation of the outcome was problematic.

More recently, theories have been formulated that included multiple cumulative parent- and child-related risk factors responsible for the development of gender dysphoria (Coates 1990; Zucker and Bradley 1995). In these theories, gender dysphoria was hypothesized to develop if both general child and parental factors (e.g. anxiety of the child, psychopathology of the parents) and specific factors (e.g. lack of limit setting of parents, fear of male aggression in mothers, and a feminine/beautiful appearance in boys or a tough appearance in girls) converged during a critical period early in the child’s life. Some support has been found for the role of a few of the general factors, such as elevated levels of psychopathology in parents (e.g. Marantz and Coates 1991; Wolfe 1990, but see Wallien 2008), and the role of elevated anxiety of the child (e.g. Cohen-Kettenis et al. 2003; Zucker et al. 1996, but see Wallien et al. 2007). Evidence for the role of more specific child and parental factors for a gender dysphoric outcome is however scarcer. Some evidence supports the assumption that the appearance in gender dysphoric boys was more feminine and beautiful (e.g. Zucker et al. 1993b) and mothers showed a lack of limit setting, particularly with respect to cross-gender behaviors (e.g. Zucker and Bradley 1995).

Biological factors

Effects of gonadal hormones on sexual differentiation of the brain
A hypothesis for the etiology of gender dysphoria is that it is a central-nervous-system limited form of DSD: the brain may not have been sexually differentiated in line with the chromosomes, gonads and genitals. For example, gender dysphoria may be the result of a more or less feminized brain in an XY individual with testes and male genitals.

From animal studies we have learned that prenatal sex hormones not only direct the sex-typical development of the genitals, but also direct and organize the sexual differentiation of the brain (McCarthy et al. 2012), so called organizational effects. In animals, behaviors that show sex differences seem to be susceptible to influences of sex hormones (Hines 2009): sex hormones are known to affect sex-typed behavior, but its effects on gender
Gender Identity Development in Adolescence

Identity are for obvious reasons impossible to study in animals. Because the largest of all psychological sex differences in humans is gender identity (Hines 2009), sex hormones likely contribute to its development.

**DSD studies**

In humans, studies in individuals with atypical prenatal hormonal levels, such as individuals with DSD could help to determine whether prenatal sex hormones affect gender identity development. Gender identity development in DSD has been most extensively studied in 46,XX individuals with congenital adrenal hyperplasia (CAH). CAH is caused by a deficiency in one or more of the enzymes required for synthesis of cortisol, aldosterone, and sex steroids in the adrenal gland. As a consequence, the brains are exposed prenatally to elevated levels of androgens (Merke and Bornstein 2005). Female raised 46,XX individuals with CAH show more masculine and less feminine interests, behaviors, and preferences than control girls and women without CAH (Cohen-Bendahan et al. 2005). However, despite the increased male-typical behaviors and interests in these women, the effect of the prenatal androgen exposure on their gender identity seems to be less strong (Berenbaum and Bailey 2003). The vast majority of women with CAH develop a female gender identity, although they may have a less strong female identification, and gender dysphoria occurs more often in this group than in women without CAH (Dessens et al. 2005; de Vries et al. 2007). A relationship between prenatal androgenization and the degree of masculinization on one hand and the prevalence of gender identity problems on the other hand was not found (Dessens et al. 2005).

In a critical review Jordan-Young (2012) suggests that other factors like postnatal biological variables, medical interventions, and social context may be more important for differences between females with CAH and control women than the conventional explanation that early androgens have "masculinized" their brains (Jordan-Young 2012). For example, a slightly more masculine appearance, caused by physiological effects of CAH, might contribute to the somewhat higher prevalence of a masculine gender identity in girls and women with CAH. In spite of the elevated androgen levels, gender dysphoria does not seem to occur more frequently in female raised patients compared to those raised male (Dessens et al. 2005) and gender identity development in these individuals thus seems remarkably adaptive.

Individuals with complete androgen insensitivity syndrome (CAIS) have 46,XY chromosomes, and produce androgens, but their external genitals develop in the female direction because of a receptor defect. At birth, the diagnosis is often missed, and they are assigned to the female sex. For long, it has been assumed that these girls develop a female gender identity
throughout their lives (Mazur 2005). In addition to their physical appearance as a woman, the total absence of androgen effects on the brains of these XY-women with CAIS might lead to the development of the usually encountered female gender identity. However, they are generally reared unambiguously as females and perceived and treated as females. Therefore, socialization may contribute to their female gender identity as well (Hines 2009). Despite the fact that all possible factors seem to support a female typical development, CAIS individuals scoring lower on a female gender identity scale than controls (Richter-Appelt et al. 2005) have been reported, as well as a case with such severe gender dysphoria that it lead to a female-to-male gender transition (T’Sjoen et al. 2011). It may, of course, be that these unexpected masculine features stem from a thus far undetected type of androgen receptors that are intact, but in this light the description by Cadet (2011), a woman with androgen insensitivity, about her gender identity is of interest. She describes it as “a malleable conviction, vulnerable to changes in perception of facts.” In her idea, information about the condition, social responses and other factors that can be perceived and evaluated, may result in gender identity changes. It may well be that some women with CAIS only need minor deviances from the norm to conclude that they do not want to live in their assigned gender, whereas others will not be dissatisfied about much larger discrepancies between their sex or gender characteristics.

In contrast to individuals with CAIS, gender transitions are considerably more prevalent among persons born with partial androgen insensitivity syndrome (PAIS) (Mazur 2005). Gender dysphoria seems to develop at similar rates in individuals with PAIS (nearly 25%), whether they are reared as boys or girls (Warne 2008). Although the discrepancies between various elements of their sex and gender development differs (e.g. male raised individuals may not have adequate male genitalia, female raised individuals may be masculine appearing and do not have internal female reproductive organs) the related distress seems to be equally severe. Yet again, most individuals with PAIS, male and female raised, do not seem to be dissatisfied with their assigned gender.

With regard to gender identity development, two other conditions are of particular interest. Five α-reductase-2 deficiency (5α-RD-2) and 17β-hydroxysteroid dehydrogenase-3 deficiency (17β-HSD-3) are both conditions resulting from errors of androgen biosynthesis. Forty six, XY children with 5α-RD-2 and 17β-HSD-3, are usually born with female appearing or ambiguous genitalia. They are often raised as girls. Female raised individuals with 5α-RD-2 whose gonads are removed before puberty, generally maintain a female gender identity (Hines 2009), but a considerable percentage of the others with 5α-RD-2, as well as 17β-HSD-3, experience gender dysphoria to
the extent that they decided to live as boys/men after puberty (e.g. Cohen-Kettenis 2005b), particularly if the condition is not diagnosed before puberty and male secondary sex characteristics have developed. The occurrence of gender dysphoria after puberty might result from the hormonal changes of puberty with direct effects on brain and gender identity development. Like in PAIS, these persons may be somewhat masculine in appearance, preferences and interests. Masculine-looking and -behaving girls may develop a different sense of self and evoke different responses from family members and peers than feminine-looking and -behaving girls. Many known cases live in societies that favor the male social role. Especially when there was already some gender discomfort present, it is likely that a masculinizing puberty increases distress to clinically significant levels into a full-blown gender dysphoria. Gender role changes occur at different rates in different societies (Hughes et al. 2006). We should therefore not overlook the impact of culture.

In conclusion, studies in individuals with DS show that prenatal testosterone exposure influences the development of male-typical gender role behaviors. It is likely that it also increases the chance of a male gender identity development. However, even in circumstances in which the person had been prenatally exposed to high levels of testosterone and has been reared as a girl from birth on, a female adult gender identity is the rule rather than the exception (e.g. Dessens et al. 2005), whereas, in the absence of prenatal testosterone exposure, a male gender identity may develop (e.g. T’Sjoen et al. 2011). In contrast to what was long assumed, it is therefore unlikely that androgens influence gender identity in a very simple and direct way.

The timing of most of the self-initiated (patient instead of physician) gender transitions is after puberty. This does not mean that gender dysphoria is absent in prepubertal children with DS. Unfortunately, most studies report very little on the gender identity development of these children. The gender changes that were reported in childhood seemed to be more often physician imposed, after the diagnosis became apparent, than patient initiated (e.g. Dessens et al. 2005; Mazur 2005; Meyer-Bahlburg 2005). Gender transitions were generally not welcomed by many parents, and patients’ requests to change gender might only have been taken more seriously as the child grew older. Another reason for the relatively late patient initiated gender changes may be that the natural pubertal changes or hormone treatment in puberty make youth with DS more aware of their bodies and their DS. Although they may not have been troubled by their DS in childhood, their physical changes and the responses of the environment to their increasing male- or femaleness may become a new source of distress. Once adolescents with
dysunderstanding more about their condition, they may start to feel uncomfortable and fear that there will be no suitable (sexual) partner for them (Warne 2008), which may influence their self esteem and make them question their position in society.

**GID studies**
The conceptualization of GID as a form of DSD limited to the central nervous system (Swaab and Garcia-Falgueras 2009) is referred to as the sexual differentiation hypothesis. To test this hypothesis, post mortem studies were conducted. They showed that male-to-female (MtF) transsexuals had a bed nucleus of the stria terminalis (central portion, BSTc) and interstitial nucleus of the anterior hypothalamus 3 (INAH3) of female volume and neuron number, that was smaller than those of men (Swaab and Garcia-Falgueras 2009). Recent work shows that the volume and neuron number of another hypothalamic nucleus, the intermediate nucleus, of MtF transsexuals has intermediate values compared to those of men and women (Garcia-Falgueras et al. 2011). These post-mortem studies suggest a sex reversal in certain nuclei in the brains of transsexuals and were significant for the formulation of the sexual differentiation hypothesis. A methodological problem, however, is that possible influences of the cross-sex hormone treatment on the findings of these studies can never be completely ruled out. Studies into the effects of sex hormones on the sexual differentiation of the brain should be done before, rather than after the start of cross-sex hormone treatment.

Support for the sexual differentiation hypothesis came also from two neuropsychological studies in transsexuals before administration of cross-sex hormones. It was found that untreated transsexuals performed in the direction of their desired gender on sex-specific tasks (Cohen-Kettenis et al. 1998; van Goozen et al. 2002). In contrast, a Norwegian study failed to replicate these findings (Haraldsen et al. 2003).

The first structural and functional imaging studies into anatomic variations of the corpus callosum, by Emory and colleagues (1991), revealed no differences between the sexes nor between transsexuals and controls. However, the majority of the participants in this study were already on hormonal treatment. More recent studies, using participants before the start of treatment, did find similarities between transsexuals and controls with the same gender identity in white matter microstructure (FtM transsexuals, Rametti et al. 2011a), hypothalamic activation while smelling odourous steroids (MtF’s, Berglund et al. 2008), brain activation patterns while viewing erotic videos (MtF’s, Gizewski et al. 2009), and sources in EEG frequencies (MtF’s, Flor-Henry 2010). In addition, untreated transsexuals differed from
controls of their natal sex in regional cerebral blood flow in the left anterior cingulate cortex and right insula (FtM’s, Nawata et al. 2010) and brain activation during mental rotation (Schöning et al. 2010).

Other imaging studies give reason to believe that there are less straightforward gender-atypical patterns of brain structure in individuals with GID. For instance, before hormonal intervention, androphilic (sexual attracted to natal males) MtFs appeared to have a white matter microstructure pattern that differs from male as well as from female controls (Rametti et al. 2011b), and similar volumes of gray matter compared to control men, except for the putamen, in which MtFs showed greater similarity with the female volume (Luders et al. 2009). In contrast, Savic and Arver (2011) found the putamen volume to be smaller in non-androphilic MtFs compared to men and women. In addition, they found smaller volumes in the thalamus and higher volumes in gray matter in the temporoparietal junction and the insular and inferofrontal cortex in MtFs compared to controls. The authors state that their findings argue against a sex-atypical dimorphism in MtFs, but that the differences between MtFs and male and female controls may be associated with gender dysphoria (Savic and Arver 2011). Recently, Zubiaurre-Elorza et al. (2012) found evidence for subcortical masculinization in FtMs and cortical thickness feminization in MtFs.

As mentioned before, transsexuals (especially MtFs), form a heterogeneous group with regard to the age of onset and sexual orientation. Although the brains of the various subtypes may differ from control men, only those of androphilic/homosexual MtFs are thought to have developed in the direction of the female sex, according to Blanchard (see Cantor 2011). Not all imaging studies provide information on onset age and sexual orientation, but some do (see for a summary Table 1). In MtFs two studies in particular were noted for their support of Blanchard’s typology (Cantor 2011): Savic and Arver (2011) only studied non-androphilic/non-homosexual MtFs and did not find any evidence for feminization in their brains, whereas Rametti et al. (2011b) only studied androphilic/homosexual (and early onset) MtF transsexuals and found white matter microstructure patterns to be in between those of male and female controls, which could be explained as demasculinization or incomplete masculinization. However, some of the other studies in non-androphilic/non-homosexual MtFs also observed similarities with female controls (see Table 1). FtMs constitute a rather homogeneous group with regard to sexual orientation and onset age and both studies in FtMs show differences compared to control women, which may be explained as a result of masculinization of their brains.
### Table 1 (part 1)  Imaging studies before the start of hormonal treatment in transsexuals (adapted from Kreukels 2011)

<table>
<thead>
<tr>
<th>Study</th>
<th>Technique</th>
<th>Measure</th>
<th>Subjects (N, Sexual orientation and onset age)</th>
<th>FtM</th>
<th>MtF</th>
<th>Control men</th>
<th>Control women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rametti et al. 2011a</td>
<td>DTI</td>
<td>FA, white matter microstructure</td>
<td>18 Homosexual Early onset</td>
<td>-</td>
<td>24</td>
<td>Heterosexual</td>
<td>19 Heterosexual</td>
</tr>
<tr>
<td>Nawata et al. 2010</td>
<td>SPECT</td>
<td>rCBF</td>
<td>11 Homosexual Early onset</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>9 Heterosexual</td>
</tr>
<tr>
<td>Berglund et al. 2008</td>
<td>PET</td>
<td>Activation in hypothalamus while smelling odourous steroids</td>
<td>12 Non-homosexual OA before/at puberty</td>
<td>12</td>
<td>12</td>
<td>Heterosexual</td>
<td>Heterosexual</td>
</tr>
<tr>
<td>Gizewski et al. 2009</td>
<td>fMRI</td>
<td>BOLD response while viewing erotic material</td>
<td>12 Non-homosexual 2 Homosexual OA unknown</td>
<td>12</td>
<td>12</td>
<td>Heterosexual</td>
<td>Heterosexual</td>
</tr>
<tr>
<td>Schöning et al. 2010</td>
<td>fMRI</td>
<td>BOLD response during mental rotation</td>
<td>11 SO unknown OA unknown</td>
<td>11</td>
<td>-</td>
<td>Heterosexual</td>
<td>-</td>
</tr>
<tr>
<td>Flor-Henry 2010</td>
<td>EEG</td>
<td>Power and sources of frequency bands</td>
<td>14 SO unknown OA unknown</td>
<td>29</td>
<td>20</td>
<td>SO unknown</td>
<td>SO unknown</td>
</tr>
</tbody>
</table>
### Table 1 (part 2)  
*Imaging studies before the start of hormonal treatment in transsexuals (adapted from Kreukels 2011)*

<table>
<thead>
<tr>
<th>Study</th>
<th>Technique</th>
<th>Measure</th>
<th>Subjects (N, Sexual orientation and onset age)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>FtM</td>
</tr>
<tr>
<td><strong>In between men and women</strong></td>
<td>MRI</td>
<td>Gray matter volumes</td>
<td>24</td>
</tr>
<tr>
<td>Luders et al. 2009</td>
<td>DTI</td>
<td>FA, white matter microstructure</td>
<td>-</td>
</tr>
<tr>
<td>Rametti et al. 2011b</td>
<td>MRI</td>
<td>Cortical thickness, volumetric subcortical measurement</td>
<td>24</td>
</tr>
<tr>
<td>Zubiaurre-Elorza et al. 2012</td>
<td>MR</td>
<td>Voxel based morphometry and structural volumetry</td>
<td>24</td>
</tr>
</tbody>
</table>

* this group also tested an MtF group on hormone treatment

**Abbreviations**: DTI = diffusion tensor imaging, FA = fractional anisotropy, SPECT = single photon emission tomography, rCBF = regional cerebral blood flow, PET = positron emission tomography, (f)MRI = (functional) magnetic resonance imaging, EEG = electroencephalogram, MR = magnetic resonance, FtM = female-to-male transsexuals, MtF = male-to-female transsexuals, SO = Sexual orientation in relation to natal sex, OA = onset age, onset of cross-gender identification.
Adolescent gender identity development and the brain

Although adolescence seems to be a crucial period in gender variant identity development, none of the aforementioned brain studies included gender dysphoric adolescent participants. Sex differences in the brain are present before adolescence, for example, sex differences were observed at the age of 7 in total brain volume, gray and white matter volume (Giedd et al. 2012). However, puberty is the period in which male and female brains increasingly diverge (Lenroot and Giedd 2010), and some brain sex differences may only be present after puberty. For example, Chung and colleagues (2002) showed that the sex difference in the BSTc, the nucleus that was found to differ between transsexuals and non-transsexuals (Swaab and Garcia-Falgueras 2009) became significant only in adulthood. Trajectories of brain development show sex differences as well: gray matter volumes seem to follow inverted U shaped trajectories with a peak size occurring earlier in females, whereas white matter volumes become increasingly divergent as men and women reach adulthood (Giedd et al. 2012).

Pubertal sex hormones are associated with development of the brain: changes in cortical thickness are related to testosterone levels (Nguyen et al. 2012), increased levels of estradiol with gray matter development in girls (Peper et al. 2009), and functional polymorphism of the androgen receptor moderates the effect of testosterone on relative white and gray matter volumes in boys (Paus et al. 2010). Recently, it has been postulated that puberty is an organizing period in itself, either as a separate period of sensitivity (Sisk and Zehr 2005), or as a continuum of declining sensitivity from gestation until adulthood (Schulz et al. 2009), but separate from the prenatal sexual differentiation of the brain by organizing effects of gonadal hormones. One way to test this hypothesis suggested by Berenbaum and Beltz (2011) is to compare sex typed characteristics of adolescents with g1d and having no hormonal interventions with those of adolescents with g1d whose puberty was suppressed in a randomized clinical trial. The assumption would be that adolescents under gonadal suppression would be less sex-typed than those who have a typical puberty, if sex hormones (testosterone and estradiol) organize the brain during puberty. They mention that this design is limited by the fact that it remains unclear to what extent the effects of pubertal hormones are influenced by the effects that have started during the prenatal period. There are also other problems related to such a study. It would not only be unethical to deny adolescents with g1d puberty suppression, but one could expect the willingness to participate in such a study to be nil. Puberty suppression by use of GnRH analogues is part of a careful clinical approach to gender dysphoria in adolescents that also comprises an extensive diagnostic procedure and psychological interventions, if neces-
Gender Identity Development in Adolescence

This fully reversible medical intervention provides adolescents with GID with time and rest before making definite decisions on gender reassignment without the distress of developing secondary sex characteristics. Denying an adolescent puberty suppression might lead to depression, anxiety and arrests in social and cognitive development, and consequently hinder reliable measurement of gendered cognitive abilities and personality traits, as was suggested (Berenbaum and Beltz 2011).

**Genetic studies**

Historically, studies into the biological roots of sex differences in brain and behavior focused on the role of prenatal exposure to gonadal hormones, but the interest in genetic factors in the development of sex differences is increasing (Ngun et al. 2011). This is also the case with regard to gender identity development. In a few studies in transsexuals associations were found between polymorphisms in genes related to sex steroid receptors or sex steroid metabolism and transsexualism, but results are very inconsistent (Ngun et al. 2011). Findings from twin studies show a more consistent picture: substantial heritability of gender dysphoria was estimated in children and adolescents (Coolidge et al. 2002), and a recent review of case reports on gender identity disorder in twins, showed that nearly 40% of the monozygotic twins were concordant for GID, whereas none of the dizygotic same-sex twins were (Heylens et al. 2012). These studies suggest genetic factors certainly play a role in the development of gender dysphoria, but altogether, their role in gender identity development is far from clear and warrants further study.

**Conclusion**

Despite the current interest among professionals and lay people in gender non-conforming adolescents and the growing use of puberty suppression as an aid in the clinical management, there is a surprising lack of knowledge on adolescent gender identity development. While earlier studies mainly focused on the role of psychosocial factors on gender identity development in gender variant or gender dysphoric children, recent research has merely concentrated on its biological roots.

Studies on individuals with DSD show that prenatal exposure to gonadal hormones affects gender role behavior, but its effects on gender identity are less straightforward. Although it is likely that prenatal hormone effects also affect gender identity development, the majority of individuals with DSD
who are prenatally exposed to elevated levels of androgens and are raised female, do not experience any gender identity problems. In brain imaging studies on individuals with gender dysphoria, evidence for a priori differences between individuals with GD and members of their natal sex prevails, although such differences have not been found on all measures, and the direction of the differences is not always consistent with the sexual differentiation hypothesis. On several, but not all, investigated brain measures, individuals with GD resemble members of their experienced gender or score in-between males and females. Data from post-mortem, neuropsychological and imaging studies support the idea that biological factors are of importance in the development of gender dysphoria and may be seen as a DS that is limited to the brain, but are as yet not sufficient to form a basis for a broad theory of GD (Meyer-Bahlburg 2011).

Despite the fact that the sexual differentiation hypothesis has been supported by quite a few studies, a number of points remain to be elucidated. One is the question of whether the brain differences between transsexuals and controls are a result of prenatal exposure to atypical levels of sex hormones only, need pubertal hormones to become manifest, are caused by other factors or need other factors to become manifest (Wallen 1996). Another issue is to what extent the differences that have been found are directly related to gender identity or more indirectly related to aspects of functioning that influence, but not determine, gender identity. Furthermore, brain structure and functioning may alter as a result of certain behaviors, which complicates interpretation of the findings. The current evidence makes clear that there is no simple relationship between brain development and function on the one hand, and gender identity development on the other. Despite the acknowledgement that nature and nurture interact, researchers have so far not tried to integrate both aspects. Psychological and environmental factors have been studied separately, but to a lesser extent than biological ones. Although 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 of atypical gender identity development, the evidence from these studies is, like in the brain studies, not unequivocal. Furthermore, it is unclear whether factors such as child anxiety and parental limit setting, are the cause of gender variant identity development or are a consequence of the gender variance.

Of great relevance for the clinical management of gender non-conforming adolescents, is the question of whether gender identity is already consolidated before adolescence or only becomes fixed in early or late adolescence or even in adulthood. Follow-up studies on gender variant children and gender dysphoric adults designate adolescence as a crucial period for
the consolidation of gender identity and persistence of gender dysphoria in early onset individuals and for the initiation of gender dysphoria in late onset individuals. More specifically, high rates of desistance of gender dysphoria in adolescence, its emergence in late onset gender dysphoric persons, with and without autogynephilia, and the high persistence of gender dysphoria once it is established after puberty, all denote that adolescence may be vital for various developmental trajectories of gender variant identity. Although parents and medical professionals may not be very open to the requests of children with DSD for a gender change in childhood, the fact that most gender changes happen after puberty are also in line with a post-pubertal consolidation of gender identity. There is, however, a wide variation in clinical presentations of youth with gender dysphoria. It is conceivable that in some, due to DSD or other factors, a (gender conforming, cross- or other) gender identity was not firmly established in childhood. For them, gender identity consolidation may be dependent on the hormonal and other, maybe psychosocial, changes that are associated with puberty. The study by McHale et al. (2009), designated the role of social context on gender development and gender interests during adolescence, and indicated a moderating role for testosterone for some of the aspects measured.

Also from other studies so far, not one causal factor can be determined and it is most likely that gender identity development is the result of a complex interplay between biological, environmental and psychological factors. Factors like hormones and genes cause differences in morphology and physiology that in turn may lead to different interactions with the environment (McCarthy et al. 2012). In addition to this, the evidence is growing that the environment and experiences, for example stress (Hunter 2012), can have permanent effects on the brain. It is also conceivable that sex-related experiences as experienced during adolescence shape the human brain. If biological, environmental and psychological factors are all in concordance with each other, gender identity seems to be fixed early in development and hardly susceptible to change over time. In case of discordance between or ambiguity of any of the factors, as in DSD and gender dysphoric individuals, the outcome may be more variable and the period in which gender identity becomes crystallized is less clear. As was indicated by Cadet (2011), gender identity has a cognitive component, also later in life. This implies that those who have been dissatisfied or confused about their gender identity (individuals with DSD and the children with less extreme gender dysphoria, or males who discover the association between dressing in female clothing and intensely pleasant sexual sensations in early adolescence), may change gender identity more easily than those with a strongly established gender identity and associated interests.
As for the clinical management of gender dysphoric adolescents, the introduction of puberty suppression has proven to relieve their acute suffering. However, despite its success one should realize that little is known as yet on what exactly happens around puberty concerning gender identity development, and that the role of gonadal hormones is largely unexplained. Clinical decisions therefore remain to be made with great caution, and the advantages of puberty suppression and early medical interventions should be weighed against possible disadvantages and the lack of knowledge on not only the causal factors, but also on its long-term effects.