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Gender role behavior in children with XY karyotype and disorders of sex development

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Abstract

Children exhibit gender-typical preferences in play, toys, activities and interests, and playmates. Several studies suggest that high concentrations of pre- and postnatal androgens contribute to male-typical behavior development, whereas female-typical behavior develops in the absence of high androgens levels. This study aims to explore the consequences of hypoandrogenization on gender-typical behavior in children who have an XY karyotype and disorder of sex development (DSD). Participants included 33 children (ages 2–12 years) with an XY karyotype and DSD; 21 reared as girls and 12 reared as boys. Children's preferred activities and interests and playmate preferences were assessed with parent report questionnaires, a structured free-play task, and choice of a toy to keep as a gift. Participant's responses were compared to those of children recruited in a pre-school and elementary school survey ($N=166$). In this study, the degree of hypoandrogenization as indicated by genital stage and diagnosis showed a significant relationship to nearly all of the gender-related behaviors assessed, supporting the hypothesis that masculinization of gender role behavior is a function of prenatal androgen exposure. Despite the fact that children with partial androgen effects reared as girls showed increased "boyish" behaviors, they did not show increased signs of gender identity confusion or instability on a group level. We conclude that androgen exposure plays a decisive role in the development of gender-typical behavior in children with XY karyotype and DSD conditions.

Keywords: Intersexuality; Disorder of sex development; Gender role; Psychosexual development; Sex differences; Play; Androgens

Introduction

Gender-typical behavior in humans is influenced by biological, psychological, social, and cultural factors. These factors are associated with differences between boys and girls in certain behaviors (e.g., aggressive and pro-social behaviors), as well as gender-typical preferences in toys and activities, playing habits, and friends (Bosinski, 2000; Hines, 2004; Ruble et al., 2006). Given the complexity of influences on psychosexual development, it is difficult to estimate the effect size of each factor (e.g., biological, social, cultural, individual) on gender-related behavior and preferences (Houk et al., 2004; Iervolino et al., 2005).

In humans, gonadal hormones are thought to play an important role in the development of gender-related behaviors. Androgen effects on the developing brain and consequent behaviors have been documented in a range of mammals (Arnold, 2002; Dohler et al., 1984; Hines and Collaer, 1993; Lephart et al., 2001; Sato et al., 2004). High concentrations of prenatal androgens contribute to male-typical behavior development, whereas female-typical behavior develops in the absence of high levels of androgens (Breedlove et al., 1999; Collaer and Hines, 1995; Hines, 2002; Hines et al., 2002; Hrabovszky and Hutson, 2002).

Disorders of sex development (DSD) provide a unique opportunity to study the effects of prenatal androgen exposure and gender-specific socialization on the development of gender-related behavior. Several studies of girls with congenital adrenal hyperplasia (CAH), an enzymatic defect in adrenal steroid synthesis resulting in high levels of prenatal androgens that lead to genital masculinization in affected female children, show that they differ markedly in gender-related behavior from unaffected girls (Berenbaum, 1999; Cohen-Bendahan et al., 2005). Girls

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with CAH, as a group, show an increased preference for typical "boys' toys" (Berenbaum and Hines, 1992; Berenbaum and Snyder, 1995; Dittmann et al., 1990; Slijper, 1984) and male playmates (Berenbaum and Snyder, 1995), show more aggressive behavior (Berenbaum and Resnick, 1997), and are less interested in maternal rehearsal play, feminine make-up and accessories (Dittmann et al., 1990; Ehrhardt and Meyer-Bahlburg, 1981; Leveroni and Berenbaum, 1998).

Children with an XY karyotype may also be affected by DSD leading to physical hypoandrogenization. In androgen insensitivity syndrome (AIS), the testes produce normal to high levels of androgens, however, functioning of the androgen receptor is completely (cAIS) or partially (pAIS) impaired, affecting physiological masculinization of the urogenital tract and the external genitalia. Defects in androgen biosynthesis [e.g., 17β-hydroxysteroid-dehydrogenase-3 deficiency (17βHSD3)], 5α-reductase-2 deficiency (5αRD), and gonadal dysgenesis cause insufficient androgen production to induce normal male-typical anatomical development (Bahceci et al., 2005; Hiort et al., 2002; Hiort and Holterhus, 2003). These conditions lead to a lack of androgen action, and the phenotype of affected individuals may range from predominantly male to typically female (Ahmed et al., 2000; Boehmer et al., 1999; Galli-Tsinopoulou et al., 2003; Hiort et al., 1996; Holterhus et al., 2000; Melo et al., 2003; Simpson and Rajkovic, 1999; Sinnecker et al., 1996, 1997; Thiele et al., 2005).

Compared with the number of studies of girls with excessive androgen exposure in prenatal life, studies assessing the effects of androgen insensitivity or lack of androgens on gender-typical behavior in children with 46,XY karyotype are scarce (al-Attia, 1996; Cohen-Kettenis, 2005; Cohen-Kettenis and Pfäfflin, 2003; Hines et al., 1998, 2003; Mendonca et al., 2000; Wilson, 2001; Zucker, 1999).

The aim of this study was to evaluate gender-related activities, play preferences, and interests of prepubertal children with 46,XY karyotype and DSD with varying prenatal androgen exposure and to compare them with same-age children without such conditions. Following a dose–response hypothesis we assume that masculinization of gender-related behavior is a function of prenatal androgen effects. If prenatal androgen exposure contributes to the development of gender role behavior, then individuals with an XY karyotype with complete hypoandrogenization (i.e., complete androgen insensitivity syndrome; cAIS) would exhibit the least masculine behavior followed by those with partial hypoandrogenization. In addition to the biological influences of androgens on gender role development, sex of rearing may support gender-typical behavior; i.e., more female-typical and/or less male-typical behavior in those with partial androgen exposure reared as girls compared to those reared as boys.

Methods

Recruitment of the DSD group

75 children ages 3 to 12 with a 46,XY karyotype and a condition causing either insufficient androgen production (e.g., 17β-hydroxysteroid-dehydrogenase-3 deficiency, 5α-reductase 2 deficiency, XY gonadal dysgenesis), incomplete responsiveness to androgens (cAIS, pAIS), or those diagnosed with an XY-intersex-condition with ambiguous genitalia of unknown etiology were identified from the molecular genetic laboratory database in Lübeck (O. H.). Nine patients were contacted directly by the authors as they received services in the center in Lübeck. Because of data protection law, the other 66 participants had to be contacted via their local pediatric endocrinologist to whom we sent information about the study. The local pediatric endocrinologist, in turn, sent information about the study to eligible families. Mailings included an information sheet that described the study, an invitation to participate, and a reply card so that families could contact the study center for either further information or to decline participation.

Written informed consent was obtained from all participating parents and verbal assent from the children. The study was approved by the Ethics Committee on Human Studies of the Medical Faculty of the University of Lübeck. The study took place either in the study center in Lübeck or at the families' homes. Diagnostic information came from our molecular genetic laboratory and clinical information from the child's pediatric endocrinologist.

Eight of nine patients (88.9%) who received clinical care in Lübeck agreed to participate. For 7 of the other 66 families, the referring physician could not be located, and an additional seven families were lost to follow up by their endocrinologist. One child had died and parents were not contacted. Of the remaining 51 families, 23 participated (45.1%), 6 families (11.8%) rejected participation via the reply card, and 22 families (43.1%) did not contact the study center and it is uncertain whether or not information about the study was mailed. In addition to recruitment from the laboratory database, two participants were recruited via patient support groups. Medical data for these patients came from medical records parents obtained from their physicians in charge.

Recruitment of the control group

For comparative purposes, a school and pre-school based survey was conducted, including five pre-schools and five elementary schools in northern Germany. The schools were selected using socio-demographic small-area characteristics to include families from all social strata. Flyers with information about the study and a reply card were distributed in the classrooms and children asked to take them home. Consent from the school board was attained prior to data collection.

Parents were informed that the purpose of the study was to collect general information on children's psychosexual development. The study was explained at parent–teacher meetings in schools and parents were given the opportunity to ask a staff member for further information. Altogether, 1800 flyers were distributed in the schools. 266 families contacted the study center and received the questionnaires and a pre-paid envelope. 166 (62.4%) families returned completed questionnaires to the study center.

Measures

Demographics

Demographic characteristics of both groups included age and sex of rearing of the child, number, age and sex of siblings, parental education, marital status, and nationality of mothers and fathers. We used these variables to assess the comparability of the study and control group.

Sex-typed activities and interests

To assess sex-typed activities and interests we used multiple instruments: (1) the parent report questionnaire of children's preferred activities and interests ("Fragebogen zu Aktivitäten and Interessen", FAI), (2) observation of sex-typed toy play (structured free-play task), and (3) child's selection of a toy to keep. The control group children received only the FAI.

(1) Activities and Interests Questionnaire ("Fragebogen zu Aktivitäten & Interessen"; FAI). To assess children's preferred activities and interests, preferences in gender-typical games, and dressing-up in role play, we constructed a parent report questionnaire. We adopted the methodology from existing questionnaires, i.e., the CGPQ—Child Game Participation Questionnaire