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Psychosocial well-being in Dutch adults with disorders of sex development

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ABSTRACT

Objective: Atypical sex development is associated with psychosocial vulnerability. We investigated psychosocial well-being in individuals with disorders of sex development (DSD) and hypothesized that psychosocial well-being was related to degree of genital atypicality at birth.
Methods: 120 male ($n = 16$) and female ($n = 104$) persons with DSD, aged 14–60 years, participated in a follow-up audit on psychosocial well-being. They were stratified in: women with 1) 46,XY and female genitalia, 2) 46,XY or 46,XX and atypical genitalia, and 3) men with 46,XY and atypical genitalia. We used the Illness Cognition Questionnaire (ICQ), Checklist Individual Strength (CIS8R), TNO-AZL Quality of Life questionnaire (TAAQOL), Adult Self-Report (ASR), and the Rosenberg Self-Esteem Scale (RSES).
Results: Data were compared to reference groups. Participants generally were coping well with DSD (ICQ). Women with DSD reported elevated levels of fatigue (CIS8R) and slightly more attention and memory problems (TAAQOL, ASR). Women with atypical genitalia reported more emotional and behavioral problems. On the ASR Rule-breaking Behavior and Antisocial Personality scales, these women had similar scores as reference men. Women with DSD reported a higher self-esteem (RSES). No differences in psychosocial well-being were found between men with DSD and reference men.
Conclusion: Individuals with DSD across all diagnostic groups generally reported a good psychosocial well-being. The results further suggest involvement of prenatal androgens in the development of personality traits related to assertiveness and egocentricity. We recommend that individuals with a DSD and their families are involved in decision-making processes and have access to multidisciplinary care.

1. Introduction

In individuals with disorders of sex development (DSD) the development of chromosomal, gonadal, and/or anatomic sex is atypical [1]. It is assumed that this incongruence puts them in a vulnerable position in society [2]. Current clinical management strategies therefore will include advice for early gender assignment, genital corrections, and hormonal treatments [1]. Lately, these early interventions have raised debate: it has been argued that they reflect society's intolerance to variance in sex and gender and major decisions are made without consent of children themselves [3–6]. It has been suggested that postponement of gender assignment and genital surgery until the child is old enough to decide him/herself will benefit the child's well-being [7]. Randomized controlled comparison of the current treatment policy and the policy of delayed interventions is highly valued [8] but is difficult to conduct. The majority of parents living in Western countries choose gender assignment and genital surgery in early childhood [9–11].

Outcome studies on psychosocial well-being have been conducted. Due to differences in applied methodology and measures, findings are difficult to compare and show inconsistencies. These studies have mainly been carried out in females and focused on gender identity [12–18], sexual quality of life [19–23], and (psycho)sexual functioning [24–32], while studies on quality of life [33], social participation, self-esteem, and emotional problems are scarce. Studies addressing health related quality of life (HRQoL), emotional distress, and psychopathology in women with 46,XX congenital adrenal hyperplasia (CAH) revealed inconclusive outcomes, from reduced to a better HRQoL [20,34–36], and from no substantial emotional distress to increases in emotional problems [28, 37–40]. Women with complete androgen insensitivity syndrome (CAIS)

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reported to function psychologically well or even better than reference groups [20,41]. In individuals with partial androgen insensitivity syndrome (PAIS), disorders in the biosynthesis of androgens, or gonadal dysgenesis, mental health problems have been reported [42], but findings had not been replicated in another study [16].

A few studies have been conducted in men and focused on sexual functioning [29]. Men with 46,XY CAH suffer from adrenal problems and testicular adrenal rest tumors and its consequences [43,44]. These men reported more negative emotions [45], anxiety and depression [40], and psychiatric morbidity [46,47]. Impairments in subjective health status have been reported [40,48], but also a favorable health status compared to the general population [36].

In DSD there is a great variety in genital development between and within different diagnostic groups. In the current study we evaluated psychosocial well-being in relation to gender of rearing and degree of genital atypicality in Dutch individuals with DSD. In their prenatal development, persons with DSD have been exposed to atypical levels of androgens. We hypothesized that persons with DSD who underwent an atypical prenatal development leading to physical atypicality are more vulnerable to experiences that negatively affect their psychosocial well-being compared to persons with typical female or male genitalia [2].

2. Methods

2.1. Study design

The present study was embedded in a national follow-up audit on sexual well-being, gender identity development, and psychosocial well-being in persons with DSD [24,25,29,30]. The study protocol was in line with the World Medical Association declaration of Helsinki and was approved by the boards of the ethical committees of the three medical centers that joined the study [49]. Data collection was carried out between 2007 and 2012. The Dutch patient support groups were involved in the study; the study was presented and discussed with them, findings were presented at gatherings and published in the organizations' newsletters and the scientific publications were provided to them.

2.2. Participants

All participants consulted the DSD Teams from Erasmus Medical Center Rotterdam ($n = 67$), Radboud University Nijmegen Medical Center ($n = 38$), or VU Medical Center Amsterdam ($n = 15$). Persons with a clinically or molecularly proven DSD diagnosis were included. Excluded were patients with 1) intellectual disabilities, 2) a genital anomaly in combination with features suggestive of malformation syndromes [50], 3) anatomical mal-development of the genitalia and abdomen with normally developed and well-functioning gonads (e.g. cloacal/bladder malformations), 4) Klinefelter 47,XXY and Turner 45,X non-mosaic types as these patients suffer from somatic and psychological characteristics typical for these syndromes [51,52], and 5) Mayer–Rokitansky–Küster–Hauser syndromes as these women have normal ovarian development and function. Participants were between 14 and 60 years old, of which four persons were aged under 17 and three approached their 18th birthday.

All participants received written additional study information and gave their informed consent.

2.3. Procedure

To examine the influence of atypical prenatal action of testosterone and its related genital atypicality on psychosocial well-being, participants were initially divided into four subgroups according to karyotype, gender of rearing, and degree of genital masculinization [25]: 1) the 46,XY FG women group, $n = 35$. This group comprised women with 46,XY karyotype with normal appearing female external genitalia; women with a normally sized clitoris, normally developed labia minora and majora, vaginal dysplasia and gonads in the abdomen or groins. 2) The 46,XY AG women group, $n = 27$. This group comprised women with 46,XY karyotype with various degrees of virilization of the external genitalia; women with an enlarged clitoris, partially or completely fused labia, vaginal dysplasia and gonads in the abdomen or groins. 3) The 46,XX AG women group, $n = 42$. This group comprised women with 46,XX karyotype and CAH women with various degrees of virilization of the external genitalia; ambiguous genitalia such as an enlarged clitoris, partially or completely fused labia, small introitus, or confluence of the vagina and urethra. 4) The 46,XY AG men group, $n = 15$. This group comprised men with 46,XY karyotype with various degrees of undervirilization of the external genitalia; i.e. proximal hypospadias and unilateral/bilateral cryptorchidism. In this group we also included one person with 46,XX CAH, who had been assigned and raised in the male gender from birth onwards (CAH was identified at age 19).

We initially tested the justification of our grouping method for intergroup comparisons by examining between-group differences on all outcome measures. Results revealed significant differences in scoring between 46,XY FG women and 46,XY and 46,XX AG men on the one hand, and 46,XY AG women and 46,XX AG women on the other hand. Subsequently we tested for differences between 46,XY AG women and 46,XX AG women, but no significant differences were found. As no contraindications were found for combining the 46,XY AG women and 46,XX AG women groups, we combined these groups for further analyses. Table 1 summarizes participants' characteristics and their diagnoses.

2.4. Instruments

2.4.1. ICQ

The Dutch 18-item Illness Cognition Questionnaire (ICQ) measures cognitions in chronic diseases [53]. It contains three subscales that measure helplessness (e.g. 'My illness limits me in everything that is important to me'), acceptance (e.g. 'I have learned to live with my illness'), and perceived benefits (e.g. 'Dealing with my illness has

Table 1
Diagnostic information of participant subgroups.

Raised as	*Females*		*Males*
	46,XY Female genitalia ($n = 35$)	46,XY or 46,XX Atypical genitalia ($n = 69$)	46,XY or 46,XX Atypical genitalia ($n = 16$)
Diagnosis	**46,XY** 22 CAIS 14 Complete GD	**46,XY** 2 Partial GD 8 17β3 HSD 5 PAIS 2 Hypomasculinisation e.c.i. 3 Leydig cell hypoplasia 1 17,20 LD 1 NR5A-1 **45,X/46,XY** 4 Mixed GD **46,XX/46,XY** 1 Mixed GD **46,XX/46,XY/46,XXY** 1 Mixed GD **46,XX** 39 CAH, CYP21A 2 CAH, 11B1	**46,XY** 2 PAIS 6 Severe hypospadias e.c.i 1 Hypomasculinisation e.c.i. **45,X/46,XY** 3 Mixed GD **46,XX/46,XY** 1 Ovotesticular DSD **46,XX** 1 CAH 2 Ovotesticular DSD

Note. Abbreviations: CAIS = Complete androgen insensitivity syndrome, GD = Gonadal dysgenesis, 17β HSD = 17β hydroxysteroid dehydrogenase deficiency type 3, PAIS = Partial androgen insensitivity syndrome, e.c.i = unknown cause, 17,20 LD = 17,20 Lyase deficiency, NR5A-1 = NR5A-1 gene mutation, CAH = Congenital adrenal hyperplasia, CYP21A = 21-hydroxylase deficiency, CYP11B1 = 11β-hydroxylase deficiency.