

Psychological Distress, Self-Harming Behavior, and Suicidal Tendencies in Adults with Disorders of Sex Development

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Abstract Evaluation of psychological distress has received relatively little attention in research on persons with disorders of sex development (DSD). Results of previous studies varied considerably, but most studies did not find increased levels of psychological distress. We conducted a pilot study based on a sample of 37 persons with diverse forms of DSD recruited via various strategies. The Brief Symptom Inventory (BSI) was used to assess self-reported psychological distress. Psychological distress varied broadly across all diagnostic subgroups. Overall, the BSI Global Severity Index indicated higher distress in the sample of persons with DSD compared to a non-clinical norm population of women, with an effect size of $d = 0.67$. According to predefined BSI criteria, 59% of participants were classified as a clinical case. Self-harming behavior and suicidal tendencies were also assessed and compared to a community based sample of women, including subgroups of traumatized women with a history of physical or sexual abuse. The prevalence rates of self-harming behavior and suicidal tendencies in the DSD sample exceeded the rates of the non-traumatized comparison subgroup, with rates comparable to the traumatized comparison groups of women with physical or sexual abuse. As possible explanations for the higher distress found here compared to most previous studies, differences in measures and sample recruitment are discussed. Our results suggest that adults with DSD are markedly psychologically distressed with rates of suicidal tendencies and self-harming behavior on a level comparable

to non-DSD women with a history of physical or sexual abuse, but sample recruitment procedures do not permit a firm generalization.

Keywords Intersexuality · Disorders of sex development · Hermaphroditism · Psychological distress · Suicidal tendencies · Self-harming behavior

Introduction

Psychological well-being is an important aspect of health-related quality of life. In previous research on persons with disorders of sex development (DSD), there were two domains which, in some ways, evaluated psychological distress: studies on the quality of life which focused on psychological functioning and outcome studies of medical interventions. In both domains, however, psychological distress was only rarely assessed directly. Meyer-Bahlburg (1999) concluded from his literature review focusing on quality of life that “Intersex syndromes differ markedly in their impact on psychological functioning and the combinations of problems encountered. Within syndromes, there is marked variability in severity” (p. 114). Most psychological outcome studies have concentrated on psychosexual development, especially gender dysphoria and gender change (e.g., Cohen-Kettenis, 2005; Dessens, Slijper, & Drop, 2005; Mazur, 2005; Meyer-Bahlburg, 2005) and the impact of sexual functioning on development (e.g., Bosinski, 2005; Warne, 2003; Wisniewski et al., 2003).

Previous research on psychological distress in persons with different diagnoses of DSD is reviewed based on Medline and PsycInfo data base searches with the key words “intersexuality”/“intersex”/“hermaphroditism” and “outcome”/“psychological distress”/“psychological symptoms,”

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and on reference lists of previous research. The focus was on the emotional and psychological consequences of development by DSD conditions. Table 1 summarizes all available studies comprising a total of 483 persons with different diagnoses of DSD.

Only some of the studies assessed psychological distress directly (see Table 1, Studies 1, 4, 8, 9, 11; with limitations also 7 and 10); and only 6 out of 11 studies used standardized measures to assess psychological distress (Studies 1, 4, 7, 8, 9, 11). Some studies were rather casuistic (2, 5, 8) while other samples were large enough to derive general conclusions (1, 4, 7, 10, 11). In some studies, participants with certain diagnoses (e.g., late onset CAH or Kallmann syndrome) were included because they were classified as a DSD, while other studies excluded such persons.

The studies listed in Table 1 are hardly comparable because they involved different diagnostic groups and heterogeneous samples, and also varied markedly in overall quality, measures, age groups (children vs. adults), sample sizes, and recruitment strategies. Consequently, their results were inconsistent, and many findings cannot be generalized. Thus, systematic comparisons of the results could not be performed.

For children, the best quality study by Slijper, Drop, Molenaar, and de Muinck Keizer-Schrama (1998) reported mild psychological problems in 19% of their sample, and 39% met diagnostic criteria for a mental disorder according to *DSM-IV*. For heterogeneous adult samples, the study by Warne et al. (2005) fulfilled methodologically high standards. In their DSD sample, the rates of psychological distress were similar to samples of persons with chronic somatic diseases. The influential study by Money, Hampson, and Hampson (1956) fulfilled methodologically high standards at the time of its publication but would not be comparable in methodology to the majority of studies in the last decade. In their DSD sample, 15% were classified as moderately non-healthy and 1% as severely non-healthy according to predefined criteria.

Noticeable, consistent findings were reported for persons with congenital adrenal hyperplasia (CAH). All studies including this diagnostic subgroup (resulting in a total $N = 268$; 56% of all participants) described persons with CAH as psychologically well adjusted, with rates of psychological distress comparable to non-clinical reference groups.

Previous research on psychological distress in persons with DSD is clearly limited by either small sample sizes or lack of standardized measures. Additionally, almost all studies (except for Studies 6 and 10) were limited by a selection bias because the samples consisted only of patients who were treated in a certain medical institution with its specific treatment approach. The aims of our study were, therefore, to present data on psychological distress in persons with diverse diagnoses of DSD who were (1)

assessed with standardized measures and, thereby, comparable to norm data and (2) constitute a relatively large sample which was not limited to one clinic with its specific treatment approach. As an additional specific indicator of psychological distress, prevalence rates of self-harming behavior and suicidal tendencies are presented and compared to a community based sample of non-DSD women, including subgroups of traumatized women with a history of physical or sexual abuse. Most likely, any collection of new samples based on a different mix of DSD syndromes, treatment histories, and sampling sources will produce a different pattern of results. Thus, we consider our study a pilot study for hypothesis generation.

Method

Participants

The study was part of a research project on quality of life and subjective treatment experiences in persons with DSD and was a joint project of the Institute for Sex Research and Forensic Psychiatry at the University Hospital Hamburg-Eppendorf and the Department of Pediatrics, Division of Pediatric Endocrinology and Diabetes at the University Hospital of Schleswig-Holstein, Campus Lübeck.

The sample of persons with DSD was recruited via several different strategies: medical professionals (endocrinologists, gynecologists, general practitioners) were informed about the study and information brochures for potential study participants were provided; the German self-help groups, “XY-Frauen [XY-women]” and “AGS Eltern- und Patienteninitiative e.V. [CAH initiative for patients and parents],” were contacted and informed, and information brochures were also distributed at scientific and patients’ meetings and conferences and published on several internet pages. These rather uncommon recruitment strategies did not allow for calculation of participation rates since the number of all eligible patients was unknown.

Participation in the study was voluntary and, apart from expense allowance, no incentives were given, but psychological counseling was offered. The participants were informed that the study investigated treatment experiences of persons with DSD. All participants gave their written informed consent to participate in the study and their permission to use the data for research purposes and publication. They also gave written consent to contact their physicians.

A total of 37 persons with DSD participated in the study, 11 participants with the karyotype 46,XX (all of them living in the female gender role), 25 participants with the karyotype 46,XY (22 of them living in the female gender role), and 1 participant with the karyotype 45,XO/46,XY (living in the female gender role). All participants with underlying

Table 1 Studies on psychological distress in persons with different diagnostic subtypes of disorders of sex development (DSD)

No.	Study	Country	Subjects	N	Diagnostic subtypes of DSD ^a	Comparison groups	Psychological variables	Measures	Results
1	Money et al. (1956)	USA (Baltimore)	Children and adults with different subtypes of DSD	94	CAH (48); GD (16); Th (1); Other (29)		Psychological healthiness	Classifications according to predefined exact criteria for psychological tests, interviews with patients and relatives, behavioral observations	67% healthy; 17% mildly non-healthy; 15% moderately non-healthy; 1% severely non-healthy
2	Hurtig and Rosenthal (1987)	USA (Chicago)	Female adolescents and young adults, aged 13–21	9	CAH (9)	Adolescents with chronic diseases (N = 6)	Affect; Interpersonal relations; Reality testing; Sexual identity; Body concerns	Draw-a-Person test, Rorschach test and Thematic Apperception Test for personality traits	Increased body concerns in persons with DSD
3	Kuhnlé et al. (1995)	Germany (Munich)	Female adult patients with CAH: M = 27.0 y; SD = 6.6 y	45	CAH (17); CAH-SW (20); Lo CAH (8)	Healthy women selected from hospital staff, matched according to age, education level, professional background (N = 46)	Psychological well-being; psychosocial integration; personality traits	Profile of mood states, psychological general well-being scale, Freiburger coping with illness quest., Gießen personality test	No significant differences between patients and controls in psychological well-being. Patients scored lower in coping styles of: depressive coping, information seeking, religious. Patients scored lower in social competences
4	Slijper et al. (1998)	Netherlands (Rotterdam)	Children with different subtypes of DSD	59	CAH (18); CAIS (12); PAIS (8); Lch (2); Ec (4); Rgs (1); 17 β -HSD (2); Tpenis (1); GD (9); Th (2)		General psychopathology	Structured Clinical Interview for DSM-IV, separately with parents and patients	N = 25 (42%) showed no psychological problems; N = 11 (19%) mild psychological problems; N = 23 (39%) with DSM-IV-Diagnosis (excluding gender identity disorders)
5	Schober (1999)	USA (Erie)	Adults with DSD, aged 22–47	10			Quality of life	Semi-structured interviews	Unimpaired self-reported quality of life in all participants; many report family related stress centered on gender issues
6	Hines et al. (2003)	Great Britain (London)	Adult women with CAIS: M = 21.3 y; SD = 8.3 y/ M = 32.4 y; SD = 11.8 y	22	CAIS (22)	22 matched female controls	Self-esteem; psychological well-being; gender related psychological characteristics	Self-esteem scale, Psychological general well-being scale	No significant differences on any of the quantitative measures

Table 1 continued

No.	Study	Country	Subjects	N	Diagnostic subtypes of DSD ^a	Comparison groups	Psychological variables	Measures	Results
7	Berenbaum et al. (2004)	USA (Pennsylvania)	Children and adults with CAH, aged 3–31	114	Sample 1: Females with CAH (54); Males with CAH (33)	Sample 1: Non-DSD relatives: females: N = 31 (30 sisters; 1 cousin); males: N = 51 (48 brothers; 3 cousins)	Sample 1: Children's behavior; self image	Sample 1: Child Behavior Checklist, Self image quest. for young adolescents	Sample 1: Children with CAH do not differ significantly from relatives; psychological adjustment generally unrelated to indicators of disease or genital characteristics
8	Mazur et al. (2004)	USA (New York)	Adult 46,XY individuals reared female, aged 29–34	5	Sample 2: Females with CAH (18); Males with CAH (9)	Sample 2: 13 non-DSD sisters; 13 non-DSD male relatives (4 cousins)	Sample 2: Personality traits	Sample 2: Multidimensional personality quest.	Sample 2: Adolescent and adult males with CAH scored higher than male controls on measures of negative emotionality
9	Morgan et al. (2005)	Great Britain (London)	Adult women with CAH, aged 18–36	18	PAIS (3); Kallmann syndrome (1); Undetermined (1)	Emotional distress	Eating disorders; psychopathology; general health	Brief Symptom Inventory, SF-36 health survey, functional status	2 participants reported potentially clinically significant levels of emotional distress, 1 participant an increased level, 1 participant reported a low level of social functioning and mental health
10	Diamond & Watson (2004)	USA (Honolulu)	Adult persons with CAIS and PAIS	57	CAIS (39); PAIS (18).	Emotional distress; suicidal thoughts; suicide attempts	Structured Clinical Interview for DSM-IV, general health quest., social adjustment scale, self-esteem scale	Women with CAH are psychologically well adjusted, do not show increased rates of psychiatric disorders or deficits of social adjustment compared to norm data	Major distress related to CAIS or PAIS: Secrecy, shame, stigma, concerns about infertility, identity problems
									Suicidal thoughts: 62% of the persons with CAIS; 61% of the persons with PAIS
									Suicide attempts: 23% of persons with CAIS; 17% of the persons with PAIS
									Suicide attempts: 23% of the persons with CAIS; 17% of the persons with PAIS

Table 1 continued

No.	Study	Country	Subjects	N	Diagnostic subtypes of DSD ^a	Comparison groups	Psychological variables	Measures	Results
11	Wame et al. (2005).	Australia (Melbourne)	Adult individuals with DSD, aged 18–32	50	GD (5); CAH (16); CAIS (3); PAIS (4); Vag ag (5); Hypos (11); 17 β -HSD (2); 5 α -RD (1); other (3)	2 similar-aged clinical comparison groups: persons with Hirschsprung disease (HPD, N = 27); persons with insulin dependent diabetes mellitus (IDDM, N = 19)	Health; psychological adjustment; sexuality	Inventory of Interpersonal Problems, Rand-36 health status invent., Eysenck Personality Questionnaire, Coppersmith Self-Esteem Inventory, State-Trait-Anxiety Inventory, Impact of Event scale, Beck Depression Inventory	No group differences in mental health, depression, current anxiety, neuroticism, psychoticism or stressful life events. Group with DSD reported lower self-esteem, higher trait anxiety, higher extraversion, and more interpersonal problems than one of the comparison groups

^a Diagnostic subtypes of DSD:

CAH = congenital adrenal hyperplasia; CAH-SW = CAH with salt wasting syndrome; Lo CAH = late onset congenital adrenal hyperplasia; CAIS = complete androgen insensitivity syndrome; PAIS = partial androgen insensitivity syndrome; GD = gonadal dysgenesis; 17 β -HSD = 17 β -hydroxysteroid dehydrogenase deficiency; 5 α -RD = 5 α -reductase deficiency; Vag ag = vaginal agenesis; Hypos = Hypospadias; Th = true hermaphroditism; Tpenis = transversal penis; Rgs = rudimentary gonadal syndrome; Ec = extrophia cloacae; Lch = leydig cell hypoplasia

XY-karyotype were assigned female directly after birth. Two participants with CAH with salt wasting syndrome were assigned male at birth and reassigned female at 9 months and 2 years of age, respectively. Diagnoses and previous medical treatments are shown in Table 2. Overall, the frequency and intensity of previous and recent contact with medical services related to the DSD differed markedly among our participants.

The mean age was 30.5 years ($SD = 10.3$; range = 16–60). Regarding the level of education, 6 (16%) participants had 9 years of education (corresponding to the German *Hauptschulabschluss*), 10 (27%) had 10 years of education (corresponding to the German *Realschulabschluss*), and 19 (51%) had 13 years of education (corresponding to the German *Abitur* which qualifies for university; data for level of education were missing in 2 cases). Two (5%) participants had not yet undergone any kind of occupational training (in German: *Ausbildung*), 5 (14%) were in an occupational training, 8 (22%) had finished their occupational training, 2 (5%) graduated from a technical college, and 12 (32%) graduated from university (data were missing in 8 cases). Eight (21%) participants were unemployed, 6 (16%) were working part-time, and 15 (40%) full-time (data were missing in 8 cases). Sixteen participants knew about the study from their physicians, 12 were informed via self-help groups, and 9 via the internet.

A total of 16 (43%) participants were born with ambiguous external genitals. Twenty-two (59%) participants had a history of genital surgery, 9 (41%) before the age of 11. The mean age at the first genital surgery was 10.5 years ($SD = 6.3$; range = 2–21). Twenty-three (62%) participants underwent gonadectomy, 3 before the age of 11. The mean age at gonadectomy was 14.7 years ($SD = 4.1$; range = 5–23).

For comparison purposes, a community based sample of women ($N = 451$), predominantly university students with a mean age of 24.3 years from a study by Richter-Appelt and Tiefensee (1996a, b) on sexual and physical abuse and the impact of the parent–child-relationship, was used. Four different comparison groups were derived from this sample: A subsample of women without sexual or physical abuse ($N = 209$), women with sexual abuse only ($N = 71$), women with physical abuse only ($N = 98$), and women with both sexual and physical abuse ($N = 73$) (for further information, see also Tiefensee, 1997). The latter two subsamples were chosen as comparison groups since many persons with DSD report being touched and examined in the genital region for medical purposes against their will.

Measures

Diagnoses, Medical History, and Previous Treatments

Diagnostic, medical, and treatment data were based on medical record information obtained from specialized

Table 2 Sample characteristics: diagnoses, reported previous treatments, sexual orientation, and relationship status

Age	Diagnosis ^a	Karyotype	GRI ^b	Situation at birth	Situation at puberty	Surgical treatment	At age	Medical treatment ^c	At age	Sexual orient./relationship
60	17β-HSD	46,XY	F	Female genitalia (blind ending vagina, no uterus), inguinal testes, assigned female	Clitoris growth, increased body and facial hair, voice break, no female development, acne, hair loss, male habitus	Number of surgeries: 2 Herniotomy Gonadectomy	7 17	Female HRT	17	Bisexual/partner
43	17β-HSD	46,XY	F	Female genitalia (blind ending vagina, no uterus), inguinal testes, assigned female	Clitoris growth, voice break, no female development	Number of surgeries: 3 Gonadectomy Clitoris reduction and vaginoplasty Secondary corrections	7 21 30	Female HRT	14	Heterosexual
31	5α-RD	46,XY	F	Female genitalia (blind ending vagina, no uterus), inguinal testes, assigned female	Clitoris growth, increased body and facial hair growth, voice break, male habitus, no menstruation, acne	Number of surgeries: 2 Gonadectomy and treatment of open processus vaginalis peritonei, daily dilation of the vagina with hegar-pens	17	Female HRT	17	Homosexual/partner
32	5α-RD	46,XY	F	Enlarged clitoris, inguinal testes, assigned female	Clitoris growth, voice break, no female development (no menstruation and breast development)	Number of surgeries: 5 Orchidopexy Gonadectomy, vaginoplasty, clitoris reduction, correction of urethra	6 13	Female HRT	13	Bisexual/single
36	5α-RD	46,XY	F	Enlarged clitoris, inguinal testes, assigned female	Clitoris growth, increased body and facial hair growth, no female development	Number of surgeries: 3 Gonadectomy, clitoris reduction Vaginoplasty, daily dilation of vagina with hegar-pens	27 28	Female HRT	27	Bisexual
25	CAIS	46,XY	F	Female genitalia (blind ending vagina, no uterus), inguinal testes, assigned female	Normal breast development, no pubic hair, no menstruation	Number of surgeries: 2 Herniotomy Gonadectomy	3 12	Female HRT	12	Heterosexual/single
24	CAIS	46,XY	F	Female genitalia (blind ending vagina, no uterus), inguinal testes, assigned female	Normal breast development, no pubic hair, no menstruation	Number of surgeries: 2 Herniotomy Gonadectomy	3 12	Female HRT	12	Heterosexual/single
47	CAIS	46,XY	F	Female genitalia (blind ending vagina, no uterus), inguinal testes, assigned female	Normal breast development, no pubic hair, no menstruation	Number of surgeries: 1 Gonadectomy	23	Female HRT	23	Heterosexual/partner

Table 2 continued

Age	Diagnosis ^a	Karyotype	GR1 ^b	Situation at birth	Situation at puberty	Surgical treatment	At age	Medical treatment ^c	At age	Sexual orient./ relationship
42	CAIS	46,XY	F	female genitalia (blind ending vagina, no uterus), inguinal testes, assigned female	Normal breast development, no pubic hair, no menstruation	Number of surgeries: 1 Gonadectomy	15	Female HRT	15	Heterosexual/ partner
36	CAIS	46,XY	F	Female genitalia (blind ending vagina, no uterus), inguinal testes, assigned female	Normal breast development, no pubic hair, no menstruation	Number of surgeries: 1 Gonadectomy	18	Female HRT	18	Heterosexual
46	PAIS	46,XY	F	Female genitalia (blind ending vagina, no uterus), inguinal testes, assigned female	Clitoris growth, hardly any breast development and pubic hair growth	Number of surgeries: 1 Gonadectomy	14	Female HRT	14	Heterosexual/ partner
35	PAIS	46,XY	F	Female genitalia (blind ending vagina, no uterus), inguinal testes, assigned female	Clitoris growth, no female development, no pubic hair	Number of surgeries: 3 Herniotomy Gonadectomy and clitoris reduction	2 12	Female HRT	12	Homosexual/ single
17	PAIS	46,XY	F	Enlarged clitoris, labia contained testes, vaginal opening (2 cm), assigned female	Moderate breast development (with hormone substitution)	Number of surgeries: 4 Clitoris reduction, testicular fixation Gonadectomy Vaginoplasty	3 13 16	Female HRT	13	Heterosexual/ single
22	PAIS	46,XY	M	Hypospadia, undescended testicles, assigned female	Gynecomastia, small genitals, no voice break, no facial hair, problems with urethra	Number of surgeries: 5 Correction of urethra (3x) Orchidopexy Mastectomy	2–6 6 13	Male HT	14	Heterosexual/ partner
18	PAIS	46,XY	M	Hypospadia, undescended testicles, assigned female	Gynecomastia, small genitals	number of surgeries: 2 Planned mastectomy correction of urethra and orchidopexy	9	Planned male HT		Heterosexual/ partner
45	PAIS	46,XY	M	Hypospadia during childhood, assigned female	Gynecomastia, small genitals, no voice brake and body hair	Number of surgeries: 2 Correction of urethra Mastectomy	5 14	Male HT	13	Heterosexual/ partner
46	GD	46,XY	F	Enlarged clitoris, rudimentary uterus, blind ending vagina, dysgenetic testis structures, assigned female	No menstruation, heavy body stature, deep voice, breast development (after hormone treatment)	Number of surgeries: 2 Clitoris reduction, gonadectomy Opening of the sinus urogenitalis and dilation of vagina	5 20	Female HRT	11	Heterosexual/ single

Table 2 continued

Age	Diagnosis ^a	Karyotype	GRI ^b	Situation at birth	Situation at puberty	Surgical treatment	At age	Medical treatment ^c	At age	Sexual orient./ relationship
37	GD	46,XY	F	Female genitalia, inguinal testes, no uterus, assigned female	No menstruation and breast development, tall and thin body stature	Number of surgeries: 3 Gonadectomy and dilation of vagina during anaesthesia (2x)	21	Female HRT	17	Heterosexual/ partner
33	GD	45X0/ 46,XY	F	Female genitalia, assigned female	No menstruation, breast development and pubic hair, tall body stature	Number of surgeries: 1 Gonadectomy	18	Female HRT	18	Heterosexual/ partner
31	GD	46,XY	F	Female genitalia, streak gonads and fallopian tubes, assigned female	Enlarged clitoris, no menstruation, no breast development, increased body hair	Number of surgeries: 1 Gonadectomy	16	Female HRT	16	Homosexual/ partner
32	GD	46,XY	F	Female genitalia (blind ending vagina, no uterus), assigned female	No menstruation, no breast development	Number of surgeries: 2 Hermiotomy Gonadectomy	8 15	Female HRT	15	Bisexual/single
28	GD	46,XY	F	Female genitalia, streak gonads, rudimentary uterus, assigned female	No menstruation, breast development and pubic hair, male body stature	Number of surgeries: 1 Gonadectomy	17	Female HRT	17	Heterosexual/ single
27	GD	46,XY	F	Enlarged clitoris, blind ending vagina, no uterus, dysgenetic testis, assigned female	No menstruation, breast development after hormone therapy	Number of surgeries: 3 Clitoris reduction Gonadectomy Vaginoplasty	3 13 18	Female HRT	13	Heterosexual/ partner
28	GD Mixed	46,XY	F	Enlarged clitoris, dysgenetic testis (left) and fallopian tube (right), assigned female	Breast development and menstruation after hormone therapy	Number of surgeries: 3 Gonadectomy Clitoris reduction and vaginoplasty	13 14	Female HRT	13	Heterosexual
23	GD	46,XY	F	Female genitalia, rudimentary uterus, assigned female	No menstruation, no breast development and pubic hair,	Number of surgeries: 1 Gonadectomy	16	Female HRT	16	Heterosexual
18	GD	46,XY	F	Female genitalia, no uterus, inguinal testes, assigned female	No menstruation and pubic hair, mild breast development after hormone therapy	Number of surgeries: 1 Gonadectomy	10	Female HRT	14	Heterosexual
23	CAH-SV	46,XX	F	Enlarged clitoris (Prader IV), assigned female	Normal pubertal development (menstruation, breast development)	Number of surgeries: 2 Clitoris reduction and vaginoplasty	12	Hydrocortisone and fludrocortisone Contraceptive pill	1 12	Heterosexual/ partner
18	CAH-SV	46,XX	F	Female genitalia (Prader II), assigned female	Enlarged clitoris, normal pubertal development (menstruation, breast development)	None (lives with a moderate clitoris hypertrophy)		Hydrocortisone and fludrocortisone	1	Heterosexual/ single
37	CAH-SV	46,XX	F	Enlarged clitoris (Prader III), assigned female	Normal menstruation and breast development, gave birth to child via caesarean at age 34	Number of surgeries: 1		hydrocortisone and fludrocortisone	1	Heterosexual/ partner

Table 2 continued

Age	Diagnosis ^a	Karyotype	GRI ^b	Situation at birth	Situation at puberty	Surgical treatment	At age	Medical treatment ^c	At age	Sexual orient./relationship
33	CAH-SW	46,XX	F	Enlarged clitoris (Prader IV), assigned female	Menstruation	Clitoris reduction Number of surgeries: 3 Clitoris reduction Vaginoplasty Dilation of vagina	2	Hydrocortisone and fludrocortisone	1	Heterosexual/partner
20	CAH-SW	46,XX	F	Enlarged clitoris (Prader III), assigned female	Normal pubertal development (menstruation, breast development)	Number of surgeries: 2 Vaginoplasty Clitoris reduction	17	Hydrocortisone and fludrocortisone	1	Heterosexual/single
16	CAH-SW	46,XX	F	Enlarged clitoris, no vaginal opening (Prader IV), assigned female	Normal pubertal development (menstruation, breast development)	Number of surgeries: 2 Vaginoplasty Secondary corrections	12	Hydrocortisone Fludrocortisone	12	Heterosexual/single
21	CAH-SW	46,XX	F	Enlarged clitoris (Prader V), assigned male, reassigned female with 2 years	Normal pubertal development (menstruation, breast development)	Number of surgeries: 2 Clitoris reduction Vaginoplasty and daily dilation of vagina	2	Hydrocortisone and fludrocortisone	1	Heterosexual/single
21	CAH-SW	46,XX	F	Enlarged clitoris (Prader IV), assigned male, reassigned female with 9 months	Normal pubertal development (menstruation, breast development)	Number of surgeries: 2 Clitoris reduction Vaginoplasty	2	Hydrocortisone and fludrocortisone	1	Heterosexual/partner
33	CAH-SW	46,XX	F	Enlarged clitoris (Prader V), no vagina, assigned female	Normal pubertal development (menstruation, breast development)	Number of surgeries: 2 Clitoris reduction Vaginoplasty and daily dilation	3	Hydrocortisone and fludrocortisone	1	Homosexual/partner
24	CAH-SW	46,XX	F	Enlarged clitoris (Prader IV), assigned female	Normal pubertal development (menstruation, breast development)	Number of surgeries: 2 Clitoris reduction Vaginoplasty	3	Hydrocortisone and fludrocortisone	1	Bisexual/single
26	CAH-SW	46,XX	F	Enlarged clitoris (ventral urethra opening), assigned female	Normal pubertal development (menstruation, breast development), increased body hair	Number of surgeries: 3 Clitoris reduction, vaginoplasty and dilation of vagina	16	Hydrocortisone and fludrocortisone	1	Bisexual/single

^a 5 α -RD = 5 α -reductase deficiency; 17 β -HSD = 17 β -hydroxysteroid dehydrogenase deficiency; PAIS = partial androgen insensitivity syndrome; CAIS = complete androgen insensitivity syndrome; GID = gonadal dysgenesis; CAH-SV = congenital adrenal hyperplasia simple-virilizers; CAH-SW = CAH with salt wasting syndrome

^b GRI = gender role identity at assessment: F = Female, M = Male

^c HRT = hormone replacement therapy; HT = hormone therapy

physicians (in most cases endocrinologists and gynecologists). All participants gave their written consent to contact their current and former physicians. Information regarding diagnoses and previous treatments was obtained for all participants (i.e., no medical history data are based on self-report only). In addition, all diagnostic and treatment data were reviewed by a pediatric endocrinologist specialized in DSD.

Psychological Distress

The *Brief Symptom Inventory-German Version (BSI)* by Franke (2000) was used. This is a German standardized version of the original *BSI* by Derogatis and Melisaratos (1983), which is widely used in clinical and research settings. This self-report questionnaire assesses subjective distress caused by different psychological symptoms during the last 7 days. Response choices were in 4-point Likert scale format; 49 out of the 53 items are assigned to 9 subscales with varying internal consistencies given in parentheses: *Somatization* ($\alpha = 0.63$); *Obsessive-Compulsive* (0.72); *Interpersonal Sensitivity* (0.61); *Depression* (0.72); *Anxiety* (0.62); *Hostility* (0.54); *Phobic Anxiety* (0.39); *Paranoid Ideation* (0.60); and *Psychoticism* (0.42). In addition, three global indices are calculated: *Global Severity Index* (the total score of psychological distress, $\alpha = 0.92$); *Positive Symptom Distress Index* (indicating the intensity of the distress); *Positive Symptom Total* (indicating the total number of present symptoms). Psychometric data of the scale were derived from diverse samples with retest-reliabilities ranging from 0.73 to 0.93; evidence of validity is based on correlative data and factor analyses (Franke, 2000).

For evaluation and comparison purposes, absolute *BSI*-values were transformed into *T*-scores ($M = 50$; $SD = 10$) based on norm data of an unselected community based sample of 300 men and 300 women. According to Derogatis and Melisaratos (1983) and Franke (2000), *T*-scores ≥ 63 are used as the cut-off for evaluating *BSI*-scores (i.e., exceeding the sample mean of the norm population by $>1 SD$). Subscale scores of $T \geq 63$ indicate significant distress in the respective subscale while overall the criteria for being classified as a clinical case are either (1) a *Global Severity Index* of $T \geq 63$ or (2) two single subscale scores of $T \geq 63$. With use of this statistical cut-off point, about 10% of the non-clinical sample was classified as clinical cases. In a sample of 213 patients with chronic kidney insufficiency with planned kidney transplantation, 44.6% were classified as clinical cases, and of the 316 patients with chronic kidney insufficiency who had already undergone kidney transplantation, 35.4% were classified as clinical cases. In a

further sample of 98 HIV-infected persons, 63.3% were classified as clinical cases.

Self-Harming Behavior, Suicidal Thoughts, and Suicide Attempts

Introduced by the question “Have you ever had one or more of the following problems over a longer period of time?” separately for childhood, adolescence and adulthood, participants were asked to answer “yes” or “no” to “self-harming behavior”, “thoughts to end my life”, and “actual attempts to take my life”. Additionally, participants were asked to specify any kind of self-harming behavior. A total score of self-harming behavior and suicidal tendencies was computed (named lifetime prevalence rates) by summing the answers to all three life time periods.

Results

Psychological Distress

The *BSI*-scores of the participants are shown in Tables 3 and 4. Table 3 shows *T*-scores of the DSD sample derived from different norm samples (women, men, combined). All mean subscale scores (except for *Somatization*) exceeded the norm mean subscale scores. The magnitude of most effect sizes of the group differences between the DSD sample and the respective norm sample was medium or large (following Cohen, 1988). *Interpersonal Sensitivity* and *Depression* indicated the most distress since these subscale scores were almost 1 *SD* above the norm mean. All *BSI*-indices exceeded the norm means as well with a mean *Global Severity Index* of $T = 57$, a mean *Positive Symptom Total Index* of $T = 55$, and a markedly increased mean *Positive Symptom Distress Index* of $T = 60$ (based on the norm sample of women).

Table 3 also shows *BSI*-values of a comparison sample of HIV-infected persons provided by Franke (2000). For the DSD sample, the *T*-scores based on the norm sample of women were used to calculate effect sizes of the group differences between the DSD sample and this comparison sample of HIV-infected persons. On three subscales, the group differences reached the magnitude of small effect sizes ($d \geq 0.2$) with higher distress in the sample of HIV-infected persons: *Anxiety* (0.25), *Phobic Anxiety* (0.34), and *Somatization* (1.08). The mean *Global Severity Index* in the sample of HIV-infected persons was higher as in the DSD sample. The corresponding effect size of this difference in means was small (0.24).

Table 4 shows further comparison samples of persons with chronic kidney insufficiency (provided by Franke,

Table 3 BSI-scores (T -scores^a) and effect sizes (d) for group differences^b in the sample of persons with disorders of sex development (DSD; $N = 37$) and comparison samples

BSI-subscale or index scores	Persons with DSD ($N = 37$)											
	T-scores derived from non-clinical norm-samples ^a									HIV-infected persons ^c		
	Combined ($N = 600$)			Women ($N = 300$)			Men ($N = 300$)			$(N = 98)$		
	M_T	SD_T	d	M_T	SD_T	d	M_T	SD_T	d	M_T	SD_T	d
Somatization	51.2	9.6	0.12	50.1	9.9	0.01	52.6	9.5	0.26	62.8	10.7	1.08
Obsessive–compulsive	54.4	11.5	0.44	54.2	11.8	0.42	54.8	11.0	0.48	56.7	13.7	0.07
Interpersonal sensitivity	59.2	13.5	0.92	57.6	14.0	0.76	60.6	13.2	1.06	57.1	13.4	0.16
Depression	58.0	12.5	0.80	56.9	12.3	0.69	59.9	13.0	0.99	60.3	14.2	0.16
Anxiety	54.5	10.7	0.45	52.8	10.7	0.28	55.5	10.6	0.55	58.0	14.1	0.25
Hostility	56.6	9.7	0.66	55.6	10.4	0.56	58.0	9.0	0.80	56.8	12.2	0.02
Phobic anxiety	54.3	8.5	0.43	53.5	8.7	0.35	54.6	8.6	0.46	58.8	13.1	0.34
Paranoid ideation	57.8	11.0	0.78	57.6	11.3	0.76	57.8	10.6	0.78	56.8	12.8	0.08
Psychoticism	57.1	10.9	0.71	57.2	11.5	0.72	56.6	10.6	0.66	59.2	13.0	0.16
Global severity index	57.9	13.0	0.79	56.7	13.5	0.67	59.1	12.5	0.91	61.6	15.1	0.24
Positive symptom total	55.6	12.4	0.56	55.4	14.4	0.54	57.0	12.4	0.70	60.6	13.8	0.36
Positive symptom distress index	60.6	8.3	1.06	59.9	8.4	0.99	60.9	8.4	1.09	60.0	14.4	0.04

^a T -scores were derived using norm data provided by Franke (2000), $M = 50$, $SD = 10$

^b Effect sizes were computed as differences between the respective group means divided by the SD of the comparison group (Cohen, 1988)

^c Data from Franke (2000). For calculation of effect sizes, T -scores of the DSD sample derived from the female norm sample were used

2000) and psychiatric outpatients with anxiety disorders before the beginning of the treatment (provided by Geisheim et al., 2002). The mean BSI-values of the DSD sample were comparable or higher as in the sample of persons with chronic kidney insufficiency (with exception of the subscale *Somatization*). In contrast, the DSD sample showed lower levels of distress than the sample of patients with anxiety

disorders on most BSI-subcales while the values for *Interpersonal Sensitivity* were comparable.

Table 5 shows the number and percentage of participants classified as clinically distressed stratified by diagnostic subgroups. A total of 59% of all participants met the pre-defined criteria of clinical caseness. The comparison of the diagnostic subgroups of persons with CAH, CAIS, and the

Table 4 BSI-scores (absolute values) in the sample of persons with disorders of sex development (DSD; $N = 37$) and comparison samples

BSI-subscale or index scores	Persons with DSD ($N = 37$)		Persons with chronic kidney insufficiency ^a ($N = 529$)		Outpatient psychotherapy patients with anxiety disorders ^b			
	M	SD	M	SD	Women ($N = 764$)		Men ($N = 453$)	
					M	SD	M	SD
Somatization	0.30	0.37	0.70	0.63	1.06	0.77	0.94	0.78
Obsessive–compulsive	0.75	0.58	0.63	0.59	1.18	0.87	1.16	0.87
Interpersonal sensitivity	1.01	0.91	0.53	0.65	1.31	0.99	1.20	0.96
Depression	0.72	0.69	0.43	0.64	1.33	1.01	1.19	0.95
Anxiety	0.50	0.43	0.56	0.60	1.63	0.89	1.44	0.85
Hostility	0.58	0.45	0.49	0.55	0.86	0.71	0.74	0.68
Phobic anxiety	0.24	0.26	0.28	0.44	1.68	1.19	1.27	0.99
Paranoid ideation	0.77	0.91	0.49	0.57	0.88	0.84	0.82	0.77
Psychoticism	0.44	0.46	0.31	0.44	0.84	0.78	0.77	0.75
Global severity index	0.56	0.37	0.51	0.45	1.2	0.68	1.06	0.65
Positive symptom total	18.51	9.95	17.51	11.35	30.36	11.57	28.99	12.41
Positive symptom distress index	1.52	0.38	1.45	0.49	1.94	0.56	1.81	0.53

^a Data from Franke (2000)

^b Data from Geisheim et al. (2002)

remainder of the sample revealed no significant differences in the percentage of cases classified as clinical (CAH: 54.5%, CAIS: 80.0%, other: 57.1%; $\chi^2(2) = 1.03$, ns). Comparing the CAH-subgroups of persons with salt wasting syndrome vs. simple-virilizers, there appeared to be a trend of more distress in the group of persons with salt wasting syndrome.

Table 6 shows significant associations between psychological distress and demographic data as well as medical history data in the DSD sample. Only the *BSI*-subscale *Somatization* was significantly associated with the patients' age, while the *BSI*-scores were independent of other demographic data, the presence of ambiguous external genitals at birth, age at first genital surgery, and age at gonadectomy. Comparing participants with and without gonadectomy, some significant differences became apparent with the presence of gonadectomy being linked to increased distress (see Table 6). The subgroup of participants without gonadectomy comprised 3 persons with PAIS (all of them living in the male gender role) and 10 persons with CAH (6 of them with salt wasting syndrome).

The CAH-subgroup of 11 participants was less distressed than the remainder of the sample with significant differences in *Interpersonal Sensitivity* (CAH: 50.4 (13.0) vs. other: 63.0 (12.1): $t = 2.84$; $df = 35$; $p < .01$), *Depression* (CAH: 51.9 (12.4) vs. other: 60.6 (11.9); $t = 2.02$; $df = 35$; $p = .05$), and the *Global Severity Index* (CAH: 50.9 (14.1) vs. other: 60.9 (11.5); $t = 2.26$; $df = 35$; $p = .03$). The same group differences between the CAH-subgroup and the remainder of the sample were apparent when the persons with CAIS were excluded from

the analyses. Due to small (sub)sample sizes, the relative contribution of the impact of subdiagnoses and experienced gonadectomy to psychological distress could not be statistically analyzed.

Self-Harming Behavior and Suicidal Tendencies

The comparison groups used for self-harming behavior and suicidal tendencies differed from the DSD sample in demographic data (the comparison sample mainly consisted of university students and was therefore younger and had higher educational levels than the DSD sample; see Table 7). However, in the total sample of 488 participants, including both persons with DSD and the four comparison samples, no meaningful associations between self-harming behavior/suicidal tendencies and demographic data could be shown. Age did not have a significant impact on the presence of self-harming behavior ($t = -1.55$, $df = 445$, $p = .12$). Participants who reported suicidal tendencies were slightly older than participants who did not report suicidal tendencies (26.2 (5.6) years vs. 24.3 (3.8) years, $t = -4.26$, $df = 452$, $p < .001$), but the effect size of $d = 0.41$ was rather small. The variability of the other demographic variables (education, work status) was too restricted in the comparison samples for finding associations between demographic variables and self-harming/suicidal tendencies. Thus, confounding of the comparisons between the DSD and the comparison samples by demographic variables cannot be ruled out.

Table 5 Significant distress^a in *BSI* subscales^b and *clinical cases*^c in the sample of persons with disorders of sex development (DSD)

Diagnosis ^d	<i>N</i>	SOM	OC	INTSENS	DEP	ANX	HOST	PHOANX	PARID	PSYCHOT	GSI	Clinical cases
17 β -HSD	2	1	1	2	2	1	0	0	1	1	2	2 (100%)
5 α -RD	3	0	1	2	2	1	2	1	1	2	2	2 (67%)
CAIS	5	0	1	4	2	2	2	1	2	3	4	4 (80%)
PAIS f	3	0	1	1	1	0	2	0	1	1	1	2 (67%)
PAIS m	3	0	0	1	1	1	2	1	2	0	1	2 (67%)
GD	10	2	3	5	4	4	3	2	2	4	4	4 (40%)
CAH-SV	3	0	1	0	0	0	1	0	0	0	0	1 (33%)
CAH-SW	8	2	1	2	2	1	0	1	3	3	2	5 (64%)
Sum	37	5 (14%)	9 (24%)	17 (46%)	14 (38%)	10 (27%)	12 (32%)	6 (16%)	12 (32%)	14 (38%)	16 (43%)	22 (59%)

^a Using a cut-off of $T \geq 63$ according to Derogatis and Melisaratos (1983) and Franke (2000)

^b *BSI*-subscales: SOM = somatization; OC = obsessive compulsive; INTSENS = interpersonal sensitivity; DEP = depression; ANX = anxiety; HOST = hostility; PHOANX = phobic anxiety; PARID = paranoid ideation; PSYCHOT = psychoticism; GSI = global severity index

^c Clinical case: $T_{GSI} \geq 63$ or two subscales scores of $T \geq 63$ according to Derogatis and Melisaratos (1983) and Franke (2000)

^d 5 α -RD = 5 α -reductase deficiency; 17 β -HSD = 17 β -hydroxysteroid dehydrogenase deficiency; PAIS = partial androgen insensitivity syndrome, m = living in masculine sex role, f = living in feminine sex role; CAIS = complete androgen insensitivity syndrome; GD = gonadal dysgenesis; CAH-SV = congenital adrenal hyperplasia simple-virilizers, CAH-SW = CAH with salt wasting syndrome

Table 6 Correlates and covariates of psychological distress in the sample of persons with disorders of sex development (DSD; $N = 37$)

Correlates/Covariates	Significantly associated with	Statistics	<i>p</i>	
Demographic data				
Age	BSI-subscale somatization	$r = .35$.03	
Level of education	No associations			
Level of vocational education	No associations			
Vocational status	No associations			
Medical history				
Ambiguous genitals at birth	No associations			
Age at first genital surgery	No associations			
Presence of gonadectomy	Linked to higher BSI- scores of:	Psychoticism	60.4 (10.0) vs. 50.9 (10.3); $t = 2.73$; $df = 34$.01
		Depression	61.1 (12.5) vs. 54.0 (11.3); $t = 1.66$; $df = 34$.10
		Global severity index	61.5 (11.8) vs. 52.4 (13.5); $t = 2.10$; $df = 34$.04
Age at gonadectomy	No associations			

Table 7 Demographic data in persons with disorders of sex development (DSD), non-traumatized, and traumatized comparison groups

Demographic data	Persons with DSD ($N = 37$)	Comparison groups of women with ^a			
		No trauma ($N = 209$)	Sexual abuse ($N = 71$)	Physical abuse ($N = 96$)	Sexual and physical abuse ($N = 72$)
Age in years M (SD)	30.5 (10.3)	23.7 (3.2)	24.5 (3.2)	25.11 (3.4)	25.6 (3.5)
Level of education ^b					
9 years of education (Hauptschulabschluss)	6 (16%)	1 (0.5%)	1 (1%)	1 (1%)	1 (1%)
10 years of education (Realschulabschluss)	10 (27%)	11 (5%)	4 (5%)	7 (7%)	8 (11%)
13 years of education (Abitur)	19 (51%)	196 (94%)	66 (94%)	88 (92%)	62 (87%)
Level of vocational education					
None or trainee/student	7 (19%)	118 (57%)	38 (54%)	44 (46%)	32 (45%)
Finished occupational training	8 (22%)	47 (23%)	14 (20%)	33 (34%)	22 (31%)
Graduated from technical college	2 (5%)	20 (10%)	6 (9%)	9 (10%)	8 (11%)
Graduated from university	12 (32%)	19 (9%)	9 (13%)	10 (11%)	6 (9%)
Vocational status					
Unemployed	8 (21%)	121 (59%)	31 (44%)	43 (45%)	27 (38%)
Working part-time	6 (16%)	68 (33%)	34 (50%)	44 (46%)	31 (43%)
Working full-time	15 (40%)	17 (8%)	4 (6%)	9 (9%)	14 (19%)

^a Data from Tiefensee (1997)

^b The corresponding German terms are given in parentheses

Self-Harming Behavior

Five (13.5%) participants, all 46,XY, reported self-harming behavior: three of them diagnosed with gonadal dysgenesis (all raised female), two with PAIS (with 1 person living in the male and 1 living in the female gender role). Two were born with ambiguous external genitals. Three had a history of genital surgery (1 of them before the age of 10). Four had a history of gonadectomy (in all cases

after the age of 11). The rate of self-harming behavior in the DSD sample was significantly higher than in the non-traumatized comparison group and did not significantly differ from the rates in the other comparison groups. The rate in the DSD sample was somewhat higher than in women with sexual abuse or physical abuse, while in the group of both sexually and physically abused women, the rate of self-harming behavior was higher than in the DSD sample (see Table 8).

Table 8 Prevalence rates of self-harming behavior in the samples of persons with disorders of sex development (DSD), non-traumatized, and traumatized comparison groups

Sample	Self-harming behavior ^b		Persons with DSD vs. comparison groups		
	<i>N</i>	%	χ^2	<i>df</i>	<i>p</i>
Persons with DSD (<i>N</i> = 37)	5	13.5	–	–	–
Non-traumatized women (<i>N</i> = 198) ^a	7	3.5	6.40	1	.01
Women with sexual abuse (<i>N</i> = 62) ^a	7	11.3	0.11	1	ns
Women with physical abuse (<i>N</i> = 87) ^a	6	6.9	1.41	1	ns
Women with both sexual and physical abuse (<i>N</i> = 64) ^a	18	28.1	2.85	1	.09

^a Data from Richter-Appelt and Tiefensee (1996a, b)

^b Lifetime prevalence rates

Suicidal Thoughts

Seventeen (46%) participants reported lifetime suicidal thoughts; 5 (29%) of them were born with ambiguous external genitals. However, the impact of presence of ambiguous external genitals at birth was not significant ($\chi^2 = 2.95$; $df = 1$; $p = .09$). The presence of suicidal thoughts was independent of age, age at first genital surgery, and age at gonadectomy, but significantly linked to the presence of gonadectomy ($\chi^2 = 4.76$; $df = 1$; $p = .03$) with 23% (*N* = 3) of persons without gonadectomy and 61% (*N* = 14) of persons with gonadectomy reporting suicidal thoughts. Overall, this prevalence rate of suicidal thoughts

in persons with DSD was comparable to prevalence rates of the sexually and/or physically traumatized comparison groups (see Table 9). In the subgroup of persons with CAH, the prevalence rate of suicidal thoughts was rather low (18%), being comparable to the non-traumatized comparison group. Grouping the DSD sample into the diagnostic subgroups CAH (karyotype 46,XX), karyotype 46,XY excluding CAIS (17 β -HSD, 5 α -RDD, PAIS, GD), and CAIS, revealed significant differences in the frequencies of suicidal thoughts: The rate was lowest in the CAH subgroup with 18% vs. 48% in the subgroup of 46,XY excluding CAIS vs. 100% in the CAIS subgroup, $\chi^2 = 9.32$; $df = 2$; $p < .05$.

Table 9 Prevalence rates of suicidal thoughts in the samples of persons with disorders of sex development (DSD), non-traumatized and traumatized comparison groups

Sample	Suicidal thoughts ^b		Persons with DSD vs. comparison groups		
	<i>N</i>	%	χ^2	<i>df</i>	<i>p</i>
Persons with DSD (<i>N</i> = 37)	17	46			
Non-traumatized women (<i>N</i> = 196) ^a	40	20	10.98	1	.01
Women with sexual abuse (<i>N</i> = 65) ^a	29	45	0.02	1	ns
Women with physical abuse (<i>N</i> = 88) ^a	39	44	0.03	1	ns
Women with both sexual and physical abuse (<i>N</i> = 69) ^a	49	71	6.44	1	.01
Sample with DSD stratified by diagnoses ^c					
17 β -HSD (<i>N</i> = 2)	2	100			
5 α -RD (<i>N</i> = 3)	2	67			
CAIS (<i>N</i> = 5)	5	100			
PAIS f (<i>N</i> = 3)	2	67			
PAIS m (<i>N</i> = 3)	1	33			
GD (<i>N</i> = 10)	3	30			
CAH-SV (<i>N</i> = 3)	0	0			
CAH-SW (<i>N</i> = 8)	2	25			

^a Data from Richter-Appelt and Tiefensee (1996a, b)

^b Lifetime prevalence rates

^c 5 α -RD = 5 α -reductase deficiency; 17 β -HSD = 17 β -hydroxysteroid dehydrogenase deficiency; PAIS = Partial Androgen Insensitivity Syndrome, m = living in masculine sex role, f = living in feminine sex role; CAIS = Complete Androgen Insensitivity Syndrome; GD = Gonadal Dysgenesis; CAH-SV = Congenital Adrenal Hyperplasia simple-virilizers, CAH-SW = CAH with salt wasting syndrome

Suicide Attempts

Two (5.4%) participants reported suicide attempts: 1 person with 17 β -HSD (aged 44, living in the female gender role) and 1 person with CAIS (aged 36, living in the female gender role). This prevalence rate of suicide attempts in the sample of persons with DSD was slightly higher than the prevalence rate in the non-traumatized comparison group and lower than the rates in the traumatized comparison groups (women with a history of sexual abuse: 9.4%; women with physical abuse: 6.8%; women with both sexual and physical abuse: 18.2%), but these differences did not reach statistical significance ($\chi^2 = 3.23$; $df = 1$; $p = .07$).

Discussion

In this sample of persons with different diagnoses of DSD, which was rather large compared to other studies and which consisted of persons who were recruited via diverse strategies, psychological distress was assessed using standardized self-report measures. The distress varied broadly across all diagnostic subgroups. However, regarding the total sample of persons with DSD compared to non-clinical norm data, the persons with DSD were markedly more distressed. As indicated by mean standardized *BSI*-scores, the psychological distress in persons with DSD was increased across all subscales with most effect sizes being medium or large. In particular, the participants demonstrated marked distress caused by negative experiences in social situations and by depressive symptoms. Significant distress (predefined by clinical cut-offs) was most prevalent, ranging from 32 to 46%, in these symptom subscales. Overall, 59% of the sample was classified as a clinical case. The level of distress in the DSD sample was comparable to samples of chronic somatically ill persons but markedly lower as in a clinical sample of psychiatric patients with anxiety disorders (presumably 100% of clinical cases). The prevalence rates of self-harming behavior and suicidal tendencies in the sample of persons with DSD were twice as high as in a community based comparison group of non-traumatized women, with rates comparable to traumatized women with a history of physical or sexual abuse.

In our sample, the distress was independent of the presence of ambiguous external genitals at birth and of age at genital surgery. Even though significantly distressed persons were present in all diagnostic subgroups, as a whole, the subgroup of persons with CAH was significantly less distressed than the rest of the sample. Prevalence rates of self-harming behavior and suicidal tendencies were lower in the CAH-subgroup as well compared to the rest of the sample. Within the total sample, the subgroup of persons

with DSD with gonadectomy was significantly more distressed, with depression being particularly increased.

Only a few previous studies are comparable to our study in terms of the use of standardized measures of psychological distress. Three of those studies reported results similar to ours. Only the study by Mazur et al. (2004) also used the *BSI*. They reported that two out of their five participants were potentially clinically distressed and one had increased levels of psychological distress. However, these findings were clearly limited by the very small sample size and sample characteristics. In the study by Warne et al. (2005), the persons with DSD were similarly as distressed as a comparison group of chronic somatically ill persons. Even though the rates of psychological distress are not directly comparable to our measures, the results similarly indicate markedly increased distress in persons with DSD. (For comparison, German prevalence rates of significant psychological distress in chronically somatic ill persons range from 43% to 50%, see Harter, 2000). Slijper et al. (1998) reported a comparable prevalence rate of 58% of clinical cases in their DSD sample which, however, consisted of children.

Our results were in contrast to the majority of previous studies. Money et al. (1956) reported no increased rates of psychological distress in their DSD sample but this study would not be comparable in methodology to the majority of studies in the last decade. Especially our finding that four out of five persons with CAIS were classified as clinical cases is not in line with most previous research (e.g., Hines, Ahmed, & Hughes, 2003) and contradicts clinical intuition (Cohen-Kettenis & Pfäfflin, 2003).

In contrast to previous research, which described persons with CAH as well adjusted, and with rates of psychological distress being comparable to non-clinical reference groups (Berenbaum et al., 2004; Kuhnle et al., 1995; Morgan et al., 2005), 55% of our subgroup of persons with CAH were classified as clinical cases, even though the mean *BSI* values in the CAH group were significantly lower than in the remainder of the DSD sample. However, due to small diagnostic subgroup sizes, the non-significant differences in percentages of clinical cases in persons with CAH vs. CAIS vs. the remainder of the sample should be interpreted with caution. Only for a subgroup of persons with CAH (adolescents of both sexes and male adults), Berenbaum et al. (2004) reported significantly increased levels of negative emotionality. Our data suggest that the subgroup of persons with CAH with salt wasting syndrome might be more distressed than simple-virilizers, which might be related to the fact that they have a more complex disorder to treat.

A possible explanation for the divergent findings of our study might be the use of different measures. The *BSI* is a clinical screening instrument for the assessment of psychological symptoms which aims at detecting clinical cases.

In contrast, other studies (except for Mazur et al., 2004; Money et al., 1956; Slijper et al., 1998) used scales which do not explicitly assess psychological symptoms but such variables as mood states, personality traits, or well-being. A further possible explanation for the divergent findings of our study might be linked to different recruitment strategies. Except for Hines et al. (2003), all studies were based on treatment populations of the respective medical institutions where the studies were done whereas in our sample only 43% of all participants were recruited from physicians. Based on our clinical impression, we assume that some persons with DSD and high levels of psychological distress attribute their distress to their histories of medical interventions; thus, medical institutions would have negative connotations for those persons with DSD. As a consequence, certain persons with DSD might be more willing to participate in studies which are not related to medical institutions. As a result, it appears plausible that different recruitment strategies reach different subgroups of persons with DSD.

Only one previous study (Diamond & Watson, 2004) investigated suicidal tendencies in persons with DSD and reported even higher rates of suicidal thoughts (>60%) in their sample of persons with CAIS or PAIS and markedly higher prevalence rates of suicide attempts (about 20%) than in our sample. Diamond and Watson (2004) used an assessment of suicidal tendencies comparable to ours, and both our study and theirs employed support groups in their recruitment procedures. However, Diamond and Watson (2004) recruited all of their participants via support groups, while in our study, other recruitment strategies were used in addition. A further difference between the two studies is that the syndrome categorization by Diamond and Watson (2004) was based on self-report, while in our study diagnoses were obtained from medical records and reviewed by a pediatric endocrinologist specialized in DSD.

The specific determinants of psychological distress in persons with DSD could not be evaluated in this study. In general, persons with DSD experience special physical and psychological challenges which are more or less directly related to DSD (e.g., Bosinski, 2005; Cohen-Kettenis & Pfäfflin, 2003; Hiort et al., 2003; Reinecke, Hampel, Richter-Appelt, Hiort, & Thyen, 2004; Slijper, Frets, Boehmer, Drop, & Niermeijer, 2000). Some studies analyzed further specific factors (e.g., parent-child-relationships and the family context) (Cohen-Kettenis & Pfäfflin, 2003; Richter-Appelt, Brinkmann, & Schützmann, 2006; Slijper et al., 2000). Only two of the summarized studies in Table 1 systematically investigated the impact of covariates on psychological distress. Money et al. (1956) reported less psychological distress in younger patients with DSD and those with unambiguous external body morphology (regardless of gonads and chromosomes). Kuhnle et al. (1995) reported correlations between psychological distress

and marital status, number of surgeries, clinical complications, psychosexual identification, level of psychosocial integration, coping strategies, and social support.

The generalizability of our results was limited by several methodological weaknesses of the study. Our sample was recruited via different strategies. On the one hand, this source heterogeneity makes it difficult to specify to which subgroup of persons with DSD our results can be generalized to. However, on the other hand, our aim was to include not only patients treated in one specific medical institution but patients with diverse treatment histories. One of our aims was to evaluate the impact of the sample recruitment strategy on the psychological distress in persons with DSD. Our offer of psychological counseling may have constituted a possible selection bias by attracting persons with DSD who were less satisfied with their treatment experiences and/or were more psychologically distressed than most samples of previous research. For instance, a subgroup of persons in German DSD self-help groups rather criticizes and refuses conventional treatment standards for DSD (see also Zucker, 2002, for the representativeness of support groups). Thus, it may be assumed that our recruitment strategies reached persons that are less represented in clinical samples. However, there may have been additional self-selection biases at work in our sample which remain unknown.

Our sample of persons with DSD differed from the comparison samples used for self-harming behavior and suicidal tendencies in terms of the demographic factors. Because the variability of the demographic data was too restricted in the comparison samples for finding associations between demographic variables and self-harming/suicidal tendencies, confounding of the comparisons between the DSD and the comparison samples by demographic variables cannot be ruled out. Thus, the results should be interpreted with caution.

While the *BSI* is a well-established measure with known psychometric qualities, we used no standardized measures for the assessment of self-harming behavior and suicidal tendencies. Our questionnaire section has face validity only, and no analyses of the psychometric properties were performed. Therefore, our results should only be interpreted as preliminary data which clearly necessitate further research.

The *BSI* yields a differentiated assessment of self-reported psychological distress. However, in clinical practice and research, it is used as a screening instrument and does not provide psychiatric diagnoses. The *BSI* criteria by Derogatis and Melisaratos (1983) and Franke (2000) for the classification of clinical cases may be questioned since a categorical cut-off is used, possibly resulting in different classifications of quite similar cases. Based on our clinical impression and on the absolute *BSI* scores, we assume that the rate of clinical distress might rather be higher in our sample than indicated by the categorical *BSI* criteria.

The *BSI* is a broadly used instrument which has not specifically been developed for certain clinical groups, i.e., particularities of certain groups could not be taken into account. Therefore, it may be misleading that some of our participants scored extremely high on the *Paranoid Ideation* and *Psychoticism* subscales. First, it should be mentioned that the internal consistency of the *Psychoticism* subscale is quite low and does not allow for adequate interpretation. Second, the subscale scores indicating increased paranoid ideation and psychoticism in our sample should, in our opinion, not be interpreted as truly paranoid or psychotic ideations but as indicative of distress resulting from marked social insecurities which also affect the perception of self and others. These insecurities (also indicated by the markedly increased *BSI*-scores for *Interpersonal Sensitivity*) may lead to markedly different perceptions which are also observable in psychotic persons. Therefore, these increased subscale scores should not be interpreted as the experience of psychotic symptoms but indicate the marked distress associated with social insecurities of some persons with DSD.

A general limitation of our study is the small sample size. Even though our sample was still rather large compared to other studies on persons with DSD, the absolute sample size and particularly the subgroup sizes are too small to allow for multivariate analyses of correlates and covariates of psychological distress.

The results of our study complement findings from previous studies which were mainly based on samples recruited via single medical institutions and which often reported lower levels of psychological distress in persons with DSD than in our study. Our results suggest that adults with DSD are markedly psychologically distressed but sample recruitment procedures do not permit a firm generalization. As expected, any collection of new samples based on a different mix of DSD syndromes, treatment histories, sampling sources, and self-selection biases will produce a different pattern of results. Thus, we consider our study a pilot study for hypothesis generation. Although tentative, our findings nevertheless suggest the possibility that psychological distress, especially interpersonal insecurities, suicidal tendencies, and self-harming behavior, are more frequent in DSD than generally assumed which should generate both more research (to investigate the specific causes and determinants of psychological distress in DSD) and more attention to mental-health issues in the planning of care for these patients (see also Houk, Hughes, Ahmed, and Writing Committee for the International Intersex Consensus Conference Participants, 2006).

Methodologically, future research using standardized measures of psychological distress is needed to investigate to what extent the different results of studies on psychological distress in DSD can be explained by different sample

recruitment strategies. Particularly, larger sample sizes are required which may enhance the representativeness and which would allow for multivariate analyses and the consideration of possible determinants of psychological distress in persons with DSD.

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References

- Berenbaum, S. A., Bryk, K. K., Duck, S. C., & Resnick, I. M. (2004). Psychological adjustment in children and adults with congenital adrenal hyperplasia. *Journal of Pediatrics*, *144*, 741–746.
- Bosinski, H. A. G. (2005). Psychosexuelle Probleme bei Intersex-Syndromen [Psychosexual problems in intersex syndromes]. *Sexuologie*, *12*, 31–59.
- Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2nd ed.). Hillsdale, NJ: Lawrence Erlbaum Associates.
- Cohen-Kettenis, P. T. (2005). Gender change in 46,XY persons with 5 α -reductase-2 deficiency and 17 β -hydroxysteroid dehydrogenase-3 deficiency. *Archives of Sexual Behavior*, *34*, 399–410.
- Cohen-Kettenis, P. T., & Pfäfflin, F. (2003). *Transgenderism and intersexuality in childhood and adolescence: Making choices*. Thousand Oaks, CA: Sage.
- Derogatis, L. R., & Melisaratos, N. (1983). The Brief Symptom Inventory: An introductory report. *Psychological Medicine*, *13*, 595–605.
- Dessens, A. B., Slijper, F. M. E., & Drop, S. L. S. (2005). Gender dysphoria and gender change in chromosomal females with congenital adrenal hyperplasia. *Archives of Sexual Behavior*, *34*, 389–397.
- Diamond, M., & Watson, L. A. (2004). Androgen insensitivity syndrome and Klinefelter's syndrome: Sex and gender considerations. *Child and Adolescent Psychiatric Clinics of North America*, *13*, 623–640.
- Franke, G. H. (2000). *Brief Symptom Inventory von L. R. Derogatis (Kurzform der SCL-90-R)-Deutsche Version-BSI: Manual* [Brief Symptom Inventory from L. R. Derogatis (Short-form of the SCL-90-R)—German Version—BSI: Manual]. Göttingen: Belz Test.
- Geisheim, C., Hahlweg, K., Fiegenbaum, W., Frank, M., Schröder, B., & Witzleben, I. (2002). Das Brief Symptom Inventory (BSI) als Instrument zur Qualitätssicherung in der Psychotherapie [The German version of the Brief Symptom Inventory (BSI): Reliability and validity in a sample of outpatient psychotherapy patients]. *Diagnostica*, *48*, 28–36.
- Harter, M. C. (2000). Psychische Störungen bei körperlichen Erkrankungen [Mental illness and physical disorders]. *Psychotherapie Psychosomatik Medizinische Psychologie*, *50*, 274–286.
- Hines, M., Ahmed, S. F., & Hughes, I. A. (2003). Psychological outcomes and gender-related development in complete androgen insensitivity syndrome. *Archives of Sexual Behavior*, *32*, 93–101.
- Hiort, O., Reinecke, S., Thyen, U., Jürgensen, M., Holterhus, P. M., Schön, D., et al. (2003). Puberty in disorders of somatosexual differentiation. *Journal of Pediatric Endocrinology & Metabolism*, *16*, 297–306.
- Houk, C. P., Hughes, I. A., Ahmed, S. F., Lee, P. A., & Writing Committee for the International Intersex Consensus Conference Participants (2006). Summary of consensus statement on intersex disorders and their management. International Intersex Consensus Conference. *Pediatrics*, *118*, 753–757.

- Hurtig, A. L., & Rosenthal, I. M. (1987). Psychological findings in early treated cases of female pseudohermaphroditism caused by virilizing congenital adrenal hyperplasia. *Archives of Sexual Behavior*, *16*, 209–223.
- Kuhnle, U., Bullinger, M., & Schwarz, H. P. (1995). The quality of life in adult female patients with congenital adrenal hyperplasia: A comprehensive study of the impact of genital malformations and chronic disease on female patients life. *European Journal of Pediatrics*, *154*, 708–716.
- Mazur, T. (2005). Gender dysphoria and gender change in androgen insensitivity or micropenis. *Archives of Sexual Behavior*, *34*, 411–421.
- Mazur, T., Sandberg, D. E., Perrin, M. A., Gallagher, J. A., & MacGillivray, M. H. (2004). Male pseudohermaphroditism: Long-term quality of life outcome in five 46,XY individuals reared female. *Journal of Pediatric Endocrinology & Metabolism*, *17*, 809–823.
- Meyer-Bahlburg, H. F. L. (1999). Health-related quality of life in intersexuality. *Acta Paediatrica Supplement*, *88*, 114–115.
- Meyer-Bahlburg, H. F. L. (2005). Gender identity outcome in female-raised 46,XY persons with penile agenesis, cloacal extrophy of the bladder, or penile ablation. *Archives of Sexual Behavior*, *34*, 423–438.
- Money, J., Hampson, J. G., & Hampson, J. L. (1956). Sexual incongruities and psychopathology: The evidence of human hermaphroditism. *Bulletin of the Johns Hopkins Hospital*, *98*, 43–57.
- Morgan, J. F., Murphy, H., Lacey, J. H., & Conway, G. (2005). Long term psychological outcome for women with congenital adrenal hyperplasia: Cross sectional survey. *British Medical Journal*, *330*, 340–341.
- Reinecke, S., Hampel, E., Richter-Appelt, H., Hiort, O., & Thyen, U. (2004). Erfahrungen mit Intersexualität: Ergebnisse einer Interviewstudie mit Eltern und Betroffenen [Experiences with intersexuality: Results of an interview-based study with parents and persons with intersexuality]. *Psychotherapie und Sozialwissenschaft*, *6*, 263–295.
- Richter-Appelt, H., Brinkmann, L., & Schützmann, K. (2006). Elterliche Bindung in der Kindheit und psychische Symptombelastung in einer Stichprobe von Erwachsenen mit Intersexualität [Parental bonding in childhood and psychological symptoms in a sample of adults with intersexuality]. *Psychotherapie Psychosomatik Medizinische Psychologie*, *56*, 325–335.
- Richter-Appelt, H., & Tiefensee, J. (1996a). Sozial und familiäre Gegebenheiten bei körperlichen Misshandlungen und sexuellen Missbrauchserfahrungen in der Kindheit aus der Sicht junger Erwachsener. Ausgewählte Ergebnisse der Hamburger Studie (Teil 1) [Social and familial aspects in physical abuse and sexual abuse experiences in childhood from the viewpoint of young adults. Selected results of the Hamburg study (1)]. *Psychotherapie Psychosomatik Medizinische Psychologie*, *46*, 367–378.
- Richter-Appelt, H., & Tiefensee, J. (1996b). Die Partnerbeziehung der Eltern und die Eltern-Kind-Beziehung bei körperlichen Misshandlungen und sexuellen Missbrauchserfahrungen in der Kindheit aus der Sicht junger Erwachsener. Weitere Ergebnisse der Hamburger Studie (Teil II) [Partnership relations of parents and parent-child relations of physical abuse and sexual abuse experiences in childhood from the viewpoint of young adults. Further results of the Hamburg study (2)]. *Psychotherapie Psychosomatik Medizinische Psychologie*, *46*, 405–418.
- Schober, J. M. (1999). Quality-of-life studies in patients with ambiguous external genitalia. *World Journal of Urology*, *17*, 249–252.
- Slijper, F. M., Drop, S. L., Molenaar, J. C., & de Muinck Keizer-Schrama, S. M. (1998). Long-term psychological evaluation of intersex children. *Archives of Sexual Behavior*, *27*, 125–144.
- Slijper, F. M. E., Frets, P. G., Boehmer, A. L. M., Drop, S. L. S., & Niermeijer, M. F. (2000). Androgen insensitivity syndrome (AIS): Emotional reactions of parents and adult patients to the clinical diagnosis of AIS and its confirmation by androgen receptor gene mutation analysis. *Hormone Research*, *53*, 9–15.
- Tiefensee, J. (1997). *Der Einfluss der Eltern-Kind-Beziehung auf die Entwicklung von Störungen nach sexuellem Missbrauch* [The impact of the parent-child-relationship on the development of disorders after sexual abuse]. Aachen: Shaker.
- Warne, G. (2003). Congenital adrenal hyperplasia: Long-term outcome studies. *Endocrinologist*, *13*, 179–181.
- Warne, G., Grover, S., Hutson, J., Sinclair, A., Metcalfe, S., Northam, E., et al. (2005). A long-term outcome study of intersex conditions. *Journal of Pediatric Endocrinology and Metabolism*, *18*, 555–567.
- Wisniewski, A. B., Migeon, C. J., Meyer-Bahlburg, H. F. L., Berkovitz, G. D., Gearhart, J. P., Rock, J. A., et al. (2003). Long-term outcome of patients with complete androgen insensitivity syndrome or congenital micropenis. *Endocrinologist*, *13*, 187–189.
- Zucker, K. J. (2002). Re: Sexual behaviors, sexual orientation and gender identity in adult intersexuals: A pilot study [Letter to the editor]. *Journal of Urology*, *168*, 1507.