
Psychosocial Competence of Unselected Young Adults With Sex Chromosome Abnormalities

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Very little is known about the adult adaptation of individuals with sex chromosome abnormalities (SCA) except for a few reports based upon biased samples of clinically identified patients. This first report from the Denver SCA study on the adult psychosocial adaptation of 36 unselected probands, identified at birth, shows a continuation of mild psychological and social problems. Psychiatric interviews and self-reported information revealed that adaptation is quite variable, with many of the nonmosaic probands not faring as well as their siblings, but in a few instances exceeding the success of brothers and sisters. Within this group of SCA subjects a subset demonstrated more marked pathology and a tendency to overrate their social adaptation relative to the psychiatric interviewer, suggesting that the exclusive use of self-report questionnaires may not provide accurate assessment of psychological characteristics in this and other special populations. The full adult SCA behavioral phenotype has not yet been established but is emerging through additional reports from this and other studies of unselected SCA adults. *Am. J. Med. Genet (Neuropsychiatr. Genet.)* 88:200–206, 1999.

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KEY WORDS: psychological adaptation; adults; sex chromosome abnormalities; Turner syndrome; Klinefelter syndrome; 47,XXX

INTRODUCTION

Sex chromosome abnormality (SCA) is even more common than Down syndrome or fragile X syndrome, occurring in 1 out of 400 live newborns. The most frequently occurring SCA karyotypes include 47,XXY, 47,XYY, 47,XXX, and 45,X or partial X monosomy, as well as mosaicism for each of these chromosome constitutions. With a probable normal life expectancy, it is estimated that close to three quarters of a million individuals with SCA live in the United States alone. Many if not most of these cases go undiagnosed, not because SCA has no effect on development, but because its effects are variable, sometimes subtle, and often difficult to distinguish from other developmental disorders. Study of unselected cohorts has revealed that SCA is a risk factor for speech and language problems, learning disabilities, and neuromotor deficits in childhood [Bender et al., 1984; 1987; 1990; 1991; 1993; Graham et al., 1988; Linden et al., 1988; 1990; 1996; Ratcliffe et al., 1982, 1986, 1990; Robinson et al., 1979, 1982, 1986, 1990; Rovet, 1990; Rovet and Netley, 1982; Rovet et al., 1996; Salbenblatt et al., 1981, 1985] which may lead to decreased psychosocial adaptation, particularly in adolescence [Bender et al., 1995; Ratcliffe et al., 1982, 1986].

This report addresses the transition to adulthood of unselected SCA adolescents followed since birth. Reports from the seven prospective studies of SCA adolescents worldwide revealed inconsistent opinions about ongoing psychosocial problems and the prospect for successful assumption of the responsibilities of adulthood. Some of the research groups identified patterns of improving adaptation [Leonard, 1990; Nielsen, 1990], while others saw increased difficulty [Stewart et al., 1990; Walzer et al., 1990]. The remaining studies, including the Denver study, described a range of psychological integration in SCA adolescents with no clear indication as to whether adulthood would see increased or decreased psychopathology [Evans et al., 1990; Ratcliffe et al., 1990; Robinson et al., 1990]. SCA adolescents from the Denver study had lower IQs, more learning difficulties, and decreased psychosocial adap-

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Received 19 May 1998; Accepted 26 August 1998

tation in comparison to sibling controls, yet some *propositi* demonstrated relative competence and steady progress toward young adulthood [Bender et al., 1995]. Although this variability was seen in all karyotype groups, adolescents with a 47,XXX karyotype demonstrated the most significant impediment of educational achievement or psychological development [Harmon et al., 1998]. The present report documents for the first time the psychosocial competence of a group of unselected young adults from the Denver SCA study, and it compares subjects' perceptions of their adaptation with those of the interviewing psychiatrist.

MATERIALS AND METHODS

Beginning in 1964 and continuing for 10 years, 40,000 consecutive newborns at two Denver hospitals were screened for aneuploidy of the sex chromosomes by examining amniotic membranes of the placentas for Barr bodies, with subsequent positive identification confirmed by chromosome analysis of peripheral blood cells. Sixty-one of the 68 infants thus identified survived. Of the 47 with 47,XXY, 47,XXX, or 45,X or mosaic karyotypes, 36 have been followed longitudinally from birth into early adulthood and were between 22 and 28 years of age during the current evaluation. Twenty-one siblings of the various *propositi* served as controls (Table I). The early adulthood protocol focused upon assessment of intellectual competence and psychological adaptation, from the perspectives of both the team psychiatrist and the *propositus*.

Psychological Testing

The Wechsler Adult Intelligence Scale [Wechsler, 1981] was administered by the team psychologist to all participants. The full-scale intelligence quotient (FSIQ) was employed as an overall index of intellectual capability.

Psychiatric Interview

Structured interviews were conducted by the team psychiatrist, who was uninformed about each subject's chromosome constitution, and were comprised of questions addressing history of psychiatric symptoms and areas of adaptation including family, social relationships, personal strengths and weaknesses, sexual behavior, and responses to life stressors. A single numerical rating was assigned following the Global Assessment of Functioning (GAF) criteria from the *Diagnostic*

and Statistical Manual of the American Psychiatric Association [American Psychiatric Association, 1994]. This scale is employed as a psychological, social, and occupational functioning index on a continuum of mental health rated from 1-100 (best).

The interviewing psychiatrist additionally assigned ratings for each area of adaptation from the Social Adjustment Scale-Interview, including social/leisure, work, extended family, and overall social adjustment [Weissman and Bothwell, 1976]. A self-reported version of the Social Adjustment Scale was also administered and is described below, and has been shown to produce self-adjustment assessments similar to a clinical rater as well as other informants [Weissman and Bothwell, 1976].

Self-Report Questionnaires

Each subject and control completed two questionnaires.

Social Adjustment Scale-Self Report [Weissman and Bothwell, 1976]. This 54-item questionnaire was employed to evaluate three "role areas" (social/leisure, work, extended family), and an overall index of social adaptation that were also rated by the interviewing psychiatrist. The parental and marital scales were not applicable to the majority of subjects and thus are not included in the analyses. A five-point rating scale was utilized, with higher scores indicating greater difficulty.

Symptom Checklist-90-R [Derogatis, 1992]. The SCL-90-R is a multidimensional self-report inventory composed of 90 items describing psychiatric symptoms most often identified by psychiatric and medical patients. Nine symptom dimensions (somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, psychoticism) and a Global Severity Index are generated. On each scale, elevated scores indicate increasing difficulty, with a score of 60 placing the individual at the 84th percentile, and a score of 70 at the 98th percentile relative to the nonpsychiatrically disturbed normative population.

RESULTS

Mixed effects models were used to determine whether means for the psychological variables differed across the six study groups (45,X, 47,XXX, 47,XXY, mosaic, male controls, female controls). The mixed models included a fixed effect for group and, since measures made on siblings are likely correlated, a random effect for families. For models of psychological variables, the additional covariate of FSIQ was included to ensure that differences between groups were not simply due to differences in intelligence. In most cases the fixed effects for FSIQ or the random family effect were non-significant and were dropped from the model, reducing the analysis to one-way analysis of variance or an analysis of covariance model. Mixed effects models were also used to examine group difference in the magnitude of self- versus psychiatrist-reported differences in social adjustment scales. These latter models were

TABLE I. Subjects

45 X & variants	9
45, x	(6)
46,X,Xq-	(2)
45,X/46,X,r(X)	(1)
47,XXX	11
47, xxY	11
Mosaics	5
45,X/46,XX	(3)
45,X/47,XXX	(1)
46,XX/47,XXX	(1)
Female siblings	11
Male siblings	10

also adjusted for GAF and FSIQ. All tests were two-tailed and conducted at the 0.05 significance level.

Descriptive statistics for the primary outcome measures, FSIQ and GAF, are seen in Table II. Mean GAF scores were significantly lower than those of controls for the 45,X and 47,XXX groups. Mean FSIQs were significantly lower than those of respective controls in the 45,X, 47,XXX, and 47,XXY groups.

SCL-90-R scores (Table III) also included significant propositi/control group differences. Greater symptom severity was reported by the 45,X group on the phobic anxiety scale (e.g., indicating feelings of anxiety in crowds and public places). In the 47,XXX group increased symptoms were reported on the phobic anxiety and interpersonal sensitivity scales (e.g., indicating feeling shy and anxious about criticism or rejection). The 47,XXY group, in contrast, reported less symptom severity in contrast to male controls for the depression scales (e.g., indicating concerns about low energy, loss of interest, worthlessness, and sadness) and paranoid ideation scales (e.g., indicating concerns about being watched or talked about and feelings that other people cannot be trusted) and for the Positive Symptom Total Score. For the most part, differences on this measure were small and did not clearly indicate karyotype-specific psychopathology. Five of 31 nonmosaic propositi produced Global Severity Index scores two standard deviations above the normative mean in contrast to 3 of 21 controls and no mosaics. Thus, the overall picture emerging from the SCL-90 scores is of slightly elevated self-reported dysfunction.

Mean Social Adjustment Scale (SAS) scores were produced from ratings by both the subject and by the interviewing psychiatrist (Table IV). In contrast to controls, 45,X women self-reported more difficulty with social/leisure pursuits (e.g., indicating absence of social activity and contact with friends), 47,XXX women indicated more difficulty on the social/leisure, extended family (e.g., indicating conflict or lack of contact with relatives), and overall social adjustment scales. The psychiatrist ratings indicated, on average, more difficulty with social adjustment, particularly among propositi, than emerged on the self-ratings. Mean psychiatrist ratings of increased difficulty with work were higher for the 45,X and 47,XXX groups compared with same-sex control groups. For the 47,XXX groups, psychiatrist ratings also indicated increased problems with social/leisure and overall adaptation. For the 47,XXY group, no differences from male controls were found either in the self-ratings or the psychiatrist ratings. For the mosaic group, self-ratings indicated more difficulty on the work subscale (indicating dissatisfac-

tion with work and contact with co-workers) while the psychiatrist ratings did not. Once again, mean differences were generally small and not indicative of markedly aberrant adaptation.

Because of the apparent discrepancy between self- and psychiatrist assessments on the SAS, direct comparisons were made of mean self- and psychiatrist-produced scores within each group, and then these differences were compared across groups. As a general pattern the psychiatrist/self-rating differences were higher in the nonmosaic SCA groups (45,X, 47,XXX, 47,XXY) than in the male or female sibling control groups. Within individual karyotype groups the self-ratings were significantly better (lower) than psychiatrist-ratings for all four SAS scales for the 47,XXX women and in the 47,XXY men for the overall, work, and extended family scales. In the 45,X women self-ratings were better (lower) than the psychiatrist ratings, but these differences were not statistically significant. Self-ratings were worse (higher) than psychiatrist ratings in the mosaic group but did not reach statistical significance. When the magnitude of these self/psychiatrist rating differences were compared across groups, the 47,XXX discrepancy differed from the female controls only for the work subscale. After further modeling of these psychiatrist/self differences was performed, adjusting for both GAP and FSIQ, no differences between group mean discrepancies were found. However, in these models, GAP but not FSIQ was significantly associated with degree of discrepancy between psychiatrist and self-ratings on the overall, extended family, and social scales.

DISCUSSION

Overall, young adults in this group with nonmosaic sex chromosome abnormalities have lower IQs, less satisfying social relationships, and a greater degree of maladaptation than their chromosomally normal siblings. For the most part, however, their intellectual and psychosocial decrements are mild to moderate and highly variable among individuals. The statistical model accounted for differences in IQ; thus, lower intelligence in the nonmosaic SCA group did not explain their decreased psychosocial adaptation. Differences arise between the various karyotypes, with 47,XXX women having the greatest degree of difficulty and the mosaic women showing no differences from controls.

47,XXX. 47,XXX women in this study have a full-scale IQ more than 20 points lower than the female control group. In previous reports we have noted that 9 of 11 (82%) 47,XXX girls in this study required

TABLE II. Full-Scale IQ and Global Assessment of Functioning Scores

		45,x (n = 9)	47,xXx (n = 11)	47,xxY (n = 11)	Mosaics (n = 6)	Female siblings (n = 11)	Male siblings (n = 10)
Global Assessment of Functioning	Mean	60.89**	54.82*	60.45	72.50	74.00	69.50
	Std error	4.59	3.89	3.67	2.00	3.11	4.27
Full-scale IQ	Mean	84.50*	81.22*	90.91*	98.00	104.40	109.20
	Std error	3.47	5.75	4.28	3.94	3.68	5.26

*p ≤ .01.

**Significantly different from same-sex controls (p ≤ .05).

TABLE III. Symptom Checklist-90 (SCL-90-R)

		45,x (n = 9)	47,xXx (n = 11)	47,xxY (n = 11)	Mosaics (n = 6)	Female siblings (n = 11)	Male siblings (n = 10)
Somatization	Mean	49.75	55.60	56.64	54.40	50.18	54.13
	Std error	4.50	3.69	4.15	4.71	2.35	4.90
Obsessive compulsive	Mean	53.88	55.70	55.27	59.60	54.36	57.38
	Std error	4.06	3.67	5.25	3.41	1.87	4.31
Interpersonal sensitivity	Mean	57.75	61.70*	55.27	55.80	49.45	59.00
	Std error	4.55	4.37	3.61	4.00	3.06	4.21
Depression	Mean	55.25	53.60	53.18*	59.60	50.00	58.88
	Std error	4.64	4.96	4.68	2.46	3.56	5.56
Anxiety	Mean	52.38	53.70	55.55	54.80	49.64	54.50
	Std error	5.17	3.67	4.57	2.18	1.85	4.27
Hostility	Mean	50.25	54.70	60.27	49.60	48.64	55.75
	Std error	4.31	4.24	3.68	2.91	3.33	4.84
Phobic anxiety	Mean	56.38*	56.80*	54.64	49.80	46.27	59.25
	Std error	3.82	2.75	3.17	3.83	2.72	3.65
Paranoid ideation	Mean	55.75	60.70	55.09*	53.00	49.82	59.50
	Std error	3.34	4.08	4.22	3.75	2.08	5.02
Psychoticism	Mean	56.88	58.70	53.64	60.00	48.82	58.13
	Std error	4.69	4.04	4.32	2.21	2.81	5.11
Global severity index	Mean	53.88	56.40	56.55	57.40	51.27	58.25
	Std error	4.78	5.22	5.14	3.08	2.74	6.01
Positive symptom distress index	Mean	56.38	54.20	55.00	51.40	48.27	50.88
	Std error	4.07	3.70	3.73	3.31	2.80	3.40
Positive symptom total	Mean	49.88	56.20	49.64*	58.60	49.18	57.38
	Std error	5.59	4.91	4.10	2.98	3.12	6.40

*Significantly different from same-sex controls ($p \leq .05$).

special education assistance in the course of their elementary school education [Bender et al., 1991]. In adolescence this group had the lowest level of educational achievement and the highest incidence of psychiatric disturbance [Bender et al., 1995; Harmon et al., 1998]. Again in adulthood, their average GAF score was the lowest among all karyotype groups, and they reported increased psychiatric symptoms on the SCL-90-R. Additionally, both the propositae and psychiatric interviewer found social adjustment to be largely decreased in this group.

The transition from adolescence to early adulthood among 47,XXX females has been remarkably varied

within this group. Five of the eleven graduated from high school, with an additional subject receiving a graduate equivalency degree. Two of the five graduates attended college, and both achieved bachelor's degrees. Eight of these young women have been pregnant. Five have married, and all but one have been divorced. Work histories have ranged from employment in a fast-food restaurant to a self-owned small business, but most frequently involve unskilled labor.

45,X The 45,X women demonstrated lower IQs and greater psychological dysfunction, as reflected in lower GAF scores, than female controls. While this pattern appears to be similar to that of the 47,XXX group, it is

TABLE IV. Social Adjustment Scale Ratings of Propositi

		45,x (n = 9)	47,xXx (n = 11)	47,xxY (n = 11)	Mosaics (n = 6)	Female siblings (n = 11)	Male siblings (n = 10)
Self-Ratings							
Social/leisure	Mean	2.35*	2.16**	2.09	2.07	1.73	1.75
	Std error	0.22	0.16	0.19	0.10	0.13	0.13
Work	Mean	1.17	1.52	1.74	2.57**	1.47	2.03
	Std error	0.09	0.14	0.34	0.78	0.13	0.59
Extended family	Mean	1.64	2.05**	1.81	1.78	1.61	1.64
	Std error	0.20	0.24	0.21	0.11	0.11	0.21
Overall	Mean	1.89	1.99**	1.79	2.05	1.63	1.80
	Std error	0.15	0.12	0.11	0.22	0.09	0.19
Psychiatrist ratings							
Social/leisure	Mean	2.88**	3.78**	2.64	2.00	1.82	2.50
	Std error	0.55	0.55	0.31	0.00	0.23	0.38
Work	Mean	3.20**	4.00**	2.67	1.33	1.57	1.86
	Std error	0.86	0.77	0.50	0.33	0.20	0.14
Extended family	Mean	2.63	3.78	2.91	2.00	2.45	3.00
	Std error	0.68	0.68	0.37	0.55	0.55	0.68
Overall	Mean	3.00	3.78*	2.82	2.00	2.00	2.50
	Std error	0.65	0.43	0.30	0.00	0.30	0.42

* $p \leq .01$.

**Significantly different from same-sex controls ($p \leq .05$).

not identical. The 45,X women and the psychiatric interviewer rated their social adaptation during leisure pursuits as less satisfying than that of female controls; the psychiatric interviewer additionally assigned lower ratings to their work and overall social adaptation. SCL-90-R self-ratings included significantly greater phobic anxiety, or anxiety about specific situations, and trends toward increased distress in a variety of areas. In contrast to the 47,XXX group, the 45,X group in adolescence demonstrated few specific instances of psychiatric disorder [Bender et al., 1995].

Several additional findings characterize the personal adaptation of this group. Most were later to begin dating than their chromosomally normal siblings. Three young women from this group were married by age 25, and, of these, one has divorced. The 45,X women achieved relative educational success, in that eight of the nine were high school graduates, and five have college degrees. One of these young women is a nurse, another is a social worker with a graduate degree, and a third has continually advanced in the military.

47,XXY. 47,XXY men in this study demonstrated a lower mean IQ than male controls. This finding is similar to that reported during their childhood, when most had learning disabilities [Bender et al., 1986, 1993; Decker and Bender, 1988; Pennington et al., 1982]. Difficulties with socialization did not emerge on the SAS, whether completed by the propositi or psychiatric interviewer. Strikingly, the 47,XXY men rated themselves as experiencing less psychiatric symptoms than controls on the SCL-90-R. This finding stands in contrast to their mean GAF score, which, although not significantly different from that of controls, was suggestive of decreased psychological adaptation. This same group in adolescence was found to have decreased psychological resources, and about half were diagnosed with mild to moderate psychiatric disorders [Bender et al., 1995].

The 47,XXY group appears overall to have met the demands of early adulthood with fair success, although slightly less well than did their siblings. The 47,XXY boys began dating at a mean age of 15 1/2 years, approximately a year later than the male sibling controls, although not outside of the normal range of their male peer group. Of the 11 young men, four married, and one divorced and remarried. Eight of these young men graduated from high school, and three received college degrees. Three other young men entered the military; all received injuries and were subsequently discharged. Currently, all 11 are employed (one skilled, four semi-skilled, six unskilled).

Mosaics. The mosaic women were generally not different from female controls, with mean IQ and GAP scores that were very similar. Despite this, the mosaic group tended to be much more self-critical. This group alone rated themselves more poorly than the psychiatric interviewer on one scale from the SAS, suggesting a high level of self-criticism that stands in contrast to results obtained with the less self-critical nonmosaic propositi. Throughout childhood and adolescence, scores from the mosaic group have not differed from those of controls on tests of intelligence, achievement, language skill, motor ability, and psychological adap-

tations [Bender et al., 1986, 1989, 1993, 1995; Linden et al., 1988; Robinson et al., 1979].

The mosaic group demonstrated unremarkable psychosocial adaptation from adolescence to young adulthood. The number of pregnancies, marriages, and divorces is similar to that of the control group. Educationally, the females have also achieved similar success in that all of them graduated from high school, and four of the five proceeded to college.

Self-Rating Discrepancy

The tendency among nonmosaic propositi to underreport psychiatric symptoms and problems of social adjustment is striking and has not been previously reported in this population. All three nonmosaic groups viewed their social adaptation as better than that perceived by the interviewing psychiatrist. This finding suggests that studies of psychosocial adaptation in this population will underestimate pathological findings if based exclusively upon self-report questionnaires, a methodology widely employed. The opposite tendency characterized members of the mosaic group, who were at times more self-critical but generally consistent with the psychiatrist when evaluating their social adaptation. The psychiatrist/self-rating discrepancy may be attributable to several possible factors, including a negative bias by the interviewing psychiatrist. However, the discrepancy is most probably due to either subject's failure to comprehend the nature of this self-assessment or a distorted perception of one's social failings. Statistical modeling of the psychiatrist/self-discrepancy was performed while adjusting for the two factors that address their competency explanations, IQ and GAP. The discrepancy was not related to IQ and thus cannot be explained as a consequence of insufficient understanding of the questionnaire items. Rather, it was directly related to the degree of psychopathology present. The discrepancy increases with severity of psychopathology; more disturbed individuals are more likely to underreport their symptoms. Symptom denial, or a tendency to minimize the severity of one's own difficulties, remains the most probable explanation.

This phenomenon is not unique to individuals with SCA. The tendency in the two sibling control groups to underreport problems in social adjustment was similarly associated with degree of maladjustment but not IQ. The apparently smaller psychiatrist/self-rating discrepancy in controls is explained by their overall higher level of psychological adjustment. Although seemingly not widely recognized, the finding that ability to evaluate shortcomings diminishes as pathology increases has been reported in research with other populations. The validity of self-reported symptoms deteriorates at the more "distressed" end of the mental health continuum in the general population [Shedler et al., 1993] as well as among patients with physical illness [Derogatis et al., 1979]. This finding, while frequently ignored in investigations of psychopathology, strongly suggests that conclusions based solely upon self-reported psychological adaptation may be appropriate in mainstream populations but inappropriate in maladjusted populations.

CONCLUSIONS

This report on early adult SCA adjustment indicates increased psychological and social problems relative to chromosomally normal sibling controls. Personal adaptation is variable; some nonmosaic propositi have dated, married, attended college, and pursued careers, while others failed to complete high school, had difficulty achieving economic independence, and demonstrated more psychological difficulty. In personal relationships and educational or vocational achievements, many SCA propositi have not fared as well as their siblings, although in a few families SCA adjustment has exceeded that of siblings. Within-karyotype variability reflects the fact that these individuals' chromosomal abnormality does not singularly override all other developmental determinants but rather interacts with an array of other genetic and environmental influences. The complete adult SCA behavioral phenotype has not been determined. It is not known, for example, whether many of the individuals who have experienced frustration and failure individuating from their families, forming satisfying social relationships, and achieving educational and vocational success will become increasingly positively adapted, or whether the incidence of psychopathology in this group will grow over time. Further investigation into adult development in the SCA population is essential to complete the psychological picture associated with these conditions and must include evaluation by psychosocial clinicians not relying solely upon self-report measures.

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