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Boys with sex chromosome aneuploidies (SCA) represent an understudied group. We examined parent-reported physical and socio-emotional problems in 25 boys with SCA (Mean age = 11.7 years, SD = 4.5). The majority had no severe physical health problems. One third of the sample had sleep problems and half of them had weekly or monthly pain. Total emotional and behavior problems, as assessed with the Strengths and Difficulties Questionnaire, were at the same level as reported for boys referred to child mental health clinics. Thus, boys with SCA may have the same need for psychological assessment and intervention as clinic-referred boys.

Sex chromosome aneuploidies (SCA) refer to conditions where individuals have an atypical number of sex chromosomes. The most common SCA karyotypes in males are 47,XXY (Klinefelter syndrome, KS), occurring in up to 1:650 males, 47,XYY, occurring in 1:1,000 males, 48,XXYY, occurring in up to 1:18,000 males, and 48,XXXY, occurring in up to 1:17,000 males (Cordeiro, Tartaglia, Roeltgen, & Ross, 2012; Tartaglia, Ayari, Hutaff-Lee, & Boada, 2012). Having (an) extra X and/or Y-chromosome(s) is associated with increased risk for both physical and socio-emotional difficulties, including psychiatric and behavioral disorders.

In terms of physical problems, a previous study of adults with KS found that a third of participants (29 of 87) reported physical health concerns (Herlihy et al., 2011). In a sample of 26 boys with 47,XYY and 82 boys with KS, Ross and colleagues (2012) found that 59% had received occupational and/or physical therapy. A review of studies of adults with SCA showed increased mortality rates due to infectious, nervous, respiratory, and genitourinary diseases for the group (Bojesen & Gravholt, 2011). Decreased bone mineral density with evidence of osteopenia has been found in 44% of 166 adults with SCA (Aksglæde, Skakkebæk, Almstrup, & Juul, 2011).

In terms of socio-emotional problems, many studies have shown a high prevalence of ADHD-symptoms among boys with SCA. Among boys with KS, ADHD prevalence rates have been 31% to 36% (Bruining, Swaab, Kas, & von Egeland, 2009; Tartaglia et al., 2012), as well as 11% to 76% among boys with 47,XYY (Geerts, Steyaert, & Fryns, 2003; Tartaglia et al., 2012) and 72 % among boys with 48,XXYY (Tartaglia et al., 2008; 2012). A Dutch psychiatric evaluation of 51 boys with KS aged 6 to 19 years found that many met criteria for other

emotional difficulties like depressive disorder (12%) and anxiety disorders (7 to 9%; Bruining et al., 2009). In a U.S. sample of boys aged 4 to 15 years, Ross and colleagues (2012) found that parents of boys with SCA reported more behavior problems, attention problems, and anxiety/depression problems on the Child Behavior Checklist (CBCL; Achenbach, 2009), as well as more hyperactivity/attention/impulsivity problems on the Conner Parent Rating scale (CPRS; Conners, Sitarenios, Parker, & Epstein, 1998) for their sons than parents of controls. Boys with SCA have also been described as being shy, withdrawn, anxious, and socially isolated, and as having diminished self-esteem (Cordeiro et al., 2012; Ross et al., 2012). An early study of 12 boys with KS found that these boys were more timid and less self-confident, and had more problems in relating to peers, than controls (Bancroft, Axworthy, & Ratcliffe, 1982). A recent study of 87 adult men aged 19 to 76 years (M = 43 years) with KS found that these men reported lower self esteem, poorer health status, and experienced more psychological distress than controls (Herlihy et al., 2011).

Although increased risk for socio-emotional difficulties seems to apply across SCA variations, there are also some important differences between karyotypes. Extra Y-chromosomes may be associated with more impairing social deficits, irrespective of cognitive abilities (Cordeiro et al., 2012), whereas extra X-chromosome(s) may be associated with more cognitive deficits (Leggett, Jacobs, Nation, Scerif, & Bishop, 2010). In a survey by Ross and colleagues (2012), boys with 47,XYY had more parent-reported problems than boys with KS in several areas (i.e. more thought- and attention-related problems, and elevated levels of aggressive/oppositional behavior, hyperactivity, withdrawal, and social problems; Ross et al., 2012). In a study by Cordeiro and colleagues (2012), severe difficulties in social responsiveness were found for 19.6% of the boys with KS, compared to 50.0% of the boys with 47,XYY and 43.8% of the boys with 48,XXYY.

In summary, there is considerable documentation of increased physical and socio-emotional problems among boys with SCA. Findings also indicate that there are differences between SCA karyotypes. The current study has two main aims. The first is to examine parent-reported physical and socio-emotional problems for boys with SCA (karyotypes 47,XXY [KS], 47,XYY, 48,XXYY, and 48,XXXY). Because recent reviews have shown an association between physical problems like pain and sleep problems among children (Lazaratou, Soldatou, & Dikeos, 2012; Valrie, Bromberg, Palermo, & Schanberg, 2013), we included questions about pain and sleep in the current study. The second aim is to examine the socio-emotional health in boys with SCA compared to boys referred to community child and adolescent mental health clinics, as well as to existing normal population data. Although psychiatric evaluation has been recommended for boys with SCA (Bruining et al., 2009), little is known about their level of socio-emotional

problems. Evaluating if boys with SCA represent a high-risk group in need of psychological screening, prevention, or treatment is an important step forward for the field.

We address the following study questions concerning the SCA sample: First, what is the extent of physical health, pain, and sleep problems among boys with SCA? Second, to what extent are boys with SCA in contact with health services? Third, how many boys with SCA receive testosterone treatment, and what are parents' experiences with this treatment? We have no a priori hypothesis concerning these descriptive data, as little is known in this area for young boys with SCA. The fourth study question is: What is the relation between physical and socio-emotional problems for boys with SCA? We expect these to be related based on previous studies of child populations (Lazaratou et al., 2012; Valrie et al., 2013). Fifth, do boys with KS and 47,XYY differ in their level of socio-emotional problems? Based on earlier studies (Cordeiro et al., 2012; Leggett et al., 2010), we expect to find more problems for boys with 47,XYY. For the second aim, i.e. the comparison between the SCA sample to a clinical sample and to norm data, the study question is: Do boys with SCA have elevated parent-reported socio-emotional problems compared to a clinical sample of boys and/or normal controls? Based on earlier studies documenting the socio-emotional problems of men with SCA (Herlihy et al., 2011), we expect the level of problems for boys with SCA to be within the clinical range.

METHODS

Samples and Procedures

SCA sample

The SCA sample comprised 25 boys who were recruited from one of two settings. Seven participants were recruited from the annual meeting of the Norwegian Klinefelter Syndrome Association in 2012, where information about the study was provided and families were invited to participate. As it is not known how many families were present at the meeting, the exact response rate is unknown. The remaining sample (18 participants) was recruited through the database of Frambu resource center for rare disorders (Frambu). Frambu is a national competence center for rare genetic disorders in Norway. Families can self-refer, and registration in the user database is voluntary. At the time of recruitment, 44 individuals with SCA aged < 18 years were registered in the database. Six of these were among the participants recruited at the KS meeting. Thus, the response rate from the database was 47% (18 of 38 cases new to the study). In both settings, parents were given an envelope with the questionnaires with a stamped return envelope. Analyses are based on responses from one parent (20 mothers and 5 fathers).

The final SCA sample comprised 25 boys (M age = 11.7 years, SD = 4.5, range 2 to 18). In terms of karyotype, the sample comprised 13 boys with KS (M age = 12.4 years, SD = 4.5, range 4 to 18), 6 boys with 47,XYY (M age = 13.0 years, SD =3.2, range 8 to 17), 3 boys with 48,XXYY (M age = 9.3, SD =5.5, range 3 to 13), and 3 boys with 48,XXXY (M age = 8.3, SD =5.7, range 2 to 13). Karyotype details were parent-reported, and double checked in medical records for participants recruited from the resource center (72% of the sample). For these, there were no discrepancies between parent reports and medical records. We did not have access to medical records for participants recruited from the user group meeting.

Clinical sample

The second sample was a clinical sample drawn from a randomized controlled trial (RCT) for childhood anxiety disorders, the Assessment and Treatment—Anxiety in Children and Adults study (ATACA; clinical trial no NCT00586586 [clinicaltrials.gov]). In the ATACA study, 221 children who were regular referrals to community child and adolescent mental health clinics were assessed for inclusion in the RCT. In the current study, we included all the boys assessed for participation in this trial with complete data on the relevant measure, regardless of whether or not they met inclusion criteria for the RCT (i.e. presence of separation anxiety disorder, social phobia, and/or generalized anxiety disorder, as well as absence of mental retardation and/or severe conduct disorder). We chose also to include boys excluded from the RCT, since their problems had been considered severe enough to indicate a need for assessment and treatment in community mental health clinics. Inclusion of these boys therefore gave a more representative clinical comparison sample for the current study. The final clinical sample comprised 98 boys (M age = 10.6 years, SD = 2.0, range 7 to 15).

The mean age of the SCA sample was slightly higher than for the clinical sample ($t = 1.749$, $p < 0.001$). Although this difference was small ($d = 0.15$), age was controlled for in comparisons between the groups. Parent occupational status was classified into five rank ordered socio-economic status classes (SES), in accordance with the Registrar General Social Class coding scheme (Currie, Molcho, Boyce, Holstein, Torsheim, & Richter, 2008), defined by the highest-ranking parent. In the SCA sample, SES was high for 36% of families, medium for 32%, and low for 32%. The majority of parents (72.7% of mothers and 90.6% of fathers) reported to be working outside the home. In the RCT from which the clinical sample is drawn, family SES was high for 31%, medium for 50%, and low for 8% (unknown for 11%). Chi-square analyses indicated that the distribution in the two samples differed for high and medium SES. However, there was no difference between the samples for the low SES distribution. Because low SES is the main factor affecting mental health (Bøe, Øverland, Lundervold, & Hysing, 2012) and

the samples were comparable on this variable, SES was not controlled for in the analyses. Furthermore, matching on age and social class variables was not done, since differences were small and perfect matching would have reduced the SCA sample considerably. Signed informed consent was obtained from parents. Both studies were approved by the regional committees for medical and health research ethics.

Measures

Background information questionnaire

Participants in the SCA sample received a background questionnaire developed for this study. The questionnaire covered 5 main areas: demographic information, SCA diagnostic information, physical health, sleep, and experiences with health professionals. The physical health questions comprised a dichotomous (*yes/no*) question asking parents to indicate if the child experienced health complaints, and (if yes) an open-ended question where parents could describe problem(s) in their own words. The pain question was phrased "*How often does your child experience pain?",* and parents rated this on a 5-point scale from 0 (*never*) to 5 (*every day*). Parents were also asked to indicate pain location (e.g., shoulders, legs), and multiple categories were possible. The pain questions (i.e. frequency and location) were followed by spaces where parents could describe details. The sleep questions comprised a dichotomous (*yes/no*) question (i.e. Does the child have sleep problems?), followed by a detailed question on the type of sleep problems, where multiple response categories were possible (i.e. difficulties falling asleep, difficulties getting up in the morning, reduced/increased sleep need). The question about contact with professionals was phrased, "Which professionals are involved with the boy's care?" Multiple categories were possible (i.e. family doctor, endocrinologist, habilitation services, psychologist, psychiatric nurse, nobody, others [with space to describe details]).

The Strengths and Difficulties Questionnaire (SDQ; Goodman, Ford, Richards, Gatward, & Meltzer, 2000)

The SDQ is a 25-item measure designed to assess socio-emotional functioning in children aged 3 to 16 years. It comprises 5 subscales: emotional difficulties, conduct problems, hyperactivity and inattention, peer difficulties, and pro-social behavior. Participants are required to indicate either 0 (*not true*), 1 (*somewhat true*), or 2 (*certainly true*) for each statement, with higher scores indicative of more significant problems for each subscale, except pro-social behavior where higher scores indicate positive adjustment. The pro-social subscale is not included in the total score. The SDQ has sound psychometric properties for all subscales, adequate test-retest reliability (Vostanis, 2006), concurrent validity and the ability to

distinguish between community and clinical samples (Goodman, 2001; Goodman & Scott, 1999). In the current study, internal consistency was good in the SCA sample ($\alpha = 0.76$) and in the clinical sample ($\alpha = 0.73$).

Data Analysis

SPSS version 20.0 was used for descriptive analyses. When comparing the SCA sample to the clinical sample, independent sample t-tests were calculated (ANOVA). When comparing the SCA sample and the clinical sample to norm data, differences in scores were calculated as effect sizes (Cohen's *d =[M group 1 - M group 2]/pooled SD*), as the norm data are based on previous publications from which we have access to N, mean scores, and standard deviations only. We used Cohen's (1992) criteria to define magnitude of effect sizes (0.10 to 0.29 = small, 0.30 to 0.49 = medium, and >0.50 = large). Due to the small number of participants in the 48,XXXY and 48,XXYY groups, these subsamples were not included in comparison analyses. We used official British norms for the socio-emotional measure as normal controls for both the SCA sample and the clinical sample (SDQ info, 2013).

RESULTS

Description of the SCA Sample

An overview of reported problems related to physical health, pain, and sleep can be found in Table 1.

TABLE 1
Parent-Reported Physical, Pain, and Sleep Problems for 25 Boys with Sex Chromosome Aneuploidies

	Pain problems		
Physical problems	*Frequency*	*Location*[3]	*Sleep problems*
None: n = 10 (40%)	Never: n = 5 (20%)	Back: n = 11	Yes: n = 9 (36%)
Minor[1]: n = 10 (40%)	Rarely: n = 9 (36%)	Knees: n = 11	Sleep problem details[3]:
Possibly major[2]: n = 5 (20%)	Monthly: n = 5 (20%)	Feet: n = 11	Difficulties falling asleep: n = 5
	Weekly: n = 6 (24%)		Reduced sleep need: n = 3
			Difficulties getting up in the morning: n = 3

Note. [1] = e.g., common allergies, asthma, digestion problems. [2] = e.g., pain, epilepsy. [3] = multiple answers possible.

TABLE 2
SDQ Scores, Means and Standard Deviations by Sample

			SDQ scale			
Sample	*Total M (SD)*	*Emotional M (SD)*	*Conduct M (SD)*	*Hyperactivity M (SD)*	*Peer problems M (SD)*	*Pro-social M (SD)*
Total SCA; n = 25	18.77 (7.97)	4.42 (2.56)	3.75 (2.89)	6.24 (2.30)	4.36 (2.75)	6.52 (2.20)
KS; n = 13	17.92 (6.67)	3.85 (2.84)	3.46 (2.30)	6.62 (1.89)	4.00 (2.92)	6.61 (1.39)
47XYY; n = 6	24.00 (7.32)	6.17 (1.72)	5.17 (3.25)	6.67 (2.50)	6.00 (1.79)	5.00 (3.03)
48XXYY; n = 3	23.06 (11.76)	3.17 (1.61)	5.25 (4.21)	6.67 (2.52)	4.00 (3.61)	6.33 (2.08)
48XXXY; n = 3	11.67 (7.77)	4.67 (4.04)	0.67 (0.58)	3.33 (2.31)	3.00 (2.65)	9.33 (0.58)
Clinic sample; n = 98	16.92 (6.92)	6.37 (2.56)	2.41 (1.74)	4.83 (3.01)	3.32 (2.41)	7.12 (2.19)
British SDQ norms*	9.1 (6.0)	1.8 (2.0)	1.7 (1.8)	4.0 (2.7)	1.5 (1.7)	8.4 (1.7)

Note. *based on 5153 boys (www.SDQinfo.com, 2013). SCA = sex chromosome aneuploidy. KS = Klinefelter's syndrome.

Involvement with health services

Parents were asked to report which health professionals were involved with the boys' care. Multiple categories were possible. From most to least frequent, responses included general practitioner/family doctor (n = 7), endocrinologist (n = 6), psychologist (n = 2), and psychiatric nurse (n = 1). Eight participants reported that habilitation services followed them up. In Norway, this term describes services for patients with chronic disorders and/or learning disabilities. Three parents reported that the boys were not followed up.

Medication

Seventeen parents (68%) reported that their boys were taking medications regularly. The most common medications were testosterone replacement therapy (n = 9), asthma medication (n = 4), and ADHD medication (n = 3). The 9 boys who received testosterone replacement therapy were aged 12 to 18 years (*M age* = 15.0, *SD* = 2.2). Of these, 3 (33.3%) reported that an endocrinologist followed them up. The average age of testosterone treatment onset was 12.1 years (SD = 1.5, range 10.0 to 14.0 years).

Comparison of SCA Sample to Normative Samples

SDQ scores for the different samples can be found in Table 2. The effect sizes for all comparisons can be found in Table 3.

TABLE 3
Effect Size of Differences Between Samples, Cohen's d

	Sample						
SDQ scale	*SCA vs norm*	*SCA vs clinical*	*KS vs norm*	*XYY vs norm*	*KS vs clinical*	*XYY vs clinical*	*KS vs XYY*
Total	0.27	0.04	0.24	0.41	0.02	0.15	−0.13
Emotional	0.65	−0.30**	0.59	1.09	−0.40	−0.03	−1.25
Conduct	0.63	0.12*	0.54	1.07	0.31	0.81	−0.25
Hyperactivity	0.31	0.19*	0.36	0.37	0.21	0.21	−0.01
Peer problems	0.98	0.17	0.86	1.56	0.11	0.47	−0.29
Pro-social	−0.65	−0.13	−0.62	−1.17	−0.11	−0.42	0.40

Note. SCA = sex chromosome aneuploidy. KS = Klinefelter's syndrome. * = $p < 0.05$, ** = $p < 0.001$.

Strengths and difficulties

The between group effect size in total SDQ scores for boys with KS and the norm group was small ($d = 0.25$), whereas it was medium for boys with 47,XYY and the norm group ($d = 0.41$). In terms of the SDQ subscales, the effect size differences for the total SCA sample and the norm group were medium to large on all subscales ($d = 0.31$ to 0.98), with the SCA sample scoring higher on all problem subscales and lower on the pro-social scale ($d = -.0.65$).

Comparison of SCA Sample to the Clinical Sample

Strengths and difficulties

When comparing the SCA sample to the clinical sample, there was no difference for SDQ total score ($t = 1.184$, $p = 0.239$, $d = 0.04$). On subscales, the SCA sample had lower scores on emotional symptoms ($t = -3.404$, $p < 0.001$, $d = -0.30$) but higher on the conduct problems ($t = 2.963$, $p < 0.05$, $d = 0.12$) and hyperactivity ($t = 2.192$, $p < 0.05$, $d = 0.19$), compared to the clinical sample. There were no differences on the prosocial ($t = -1.227$, $p = 0.222$, $d = -0.13$) or peer problems subscales ($t = 1.877$, $p = 0.063$, $d = 0.17$). Because there was a significant age difference between the SCA sample and the clinical sample, all analyses were rerun as linear regression models (SCA vs. clinical) on all SDQ scales with age as a covariate. Age was not a significant predictor in any of these models, except for peer problems ($\beta = 0.264$, $p < 0.001$).

TABLE 4
Pearson's r-Correlations Between SDQ Scales in the SCA Sample (N = 25)

	Total	*Emotional*	*Conduct*	*Hyperactivity*	*Peer Problems*
Emotional	0.64**				
Conduct	0.86**	0.26			
Hyperactivity	0.68**	0.06	0.75**		
Peer problems	0.83**	0.58**	0.58**	0.30	
Pro-social	−0.41*	−0.29	−0.42**	−0.28	−0.24

Note. SDQ = Strengths and Difficulties Questionnaire. SCA = sex chromosome aneuploidy. *p < 0.05. **p < 0.001

Associations Between Variables Within the SCA Sample

Independent sample t-tests showed no differences between the KS sample and the XYY sample on the SDQ total scale or on any of the subscales (p-values 0.067 to 0.961, data available upon request).

Correlations between the SDQ total and the different subscales can be found in Table 4. Boys' age was significantly correlated with both total socio-emotional problems ($r = 0.41$, $p < 0.05$) and the emotional problems subscale ($r = 0.48$, $p < 0.05$). Interestingly, there was a large negative correlation between frequency of pain and the SDQ pro-social scale ($r = -0.55$, $p < 0.01$). Parents also reported significantly more frequent pain for boys with confirmed sleep problems (*M diff* -1.0, $t = -2.385$, $p < 0.05$) compared to boys who were not reported to have sleep problems, a large difference ($d = -1.05$). For those cases in the SCA sample where both parents had completed the SDQ (n = 13), there were no significant differences between parents on the SDQ total or any of the subscales.

DISCUSSION

This study had 2 main aims. First, we examined parent-reported physical and socio-emotional problems for boys with SCA, a group about which little is known. The sample mainly comprised boys with karyotypes KS (47,XXY) and 47,XYY but also included individuals with 48,XXYY and 48,XXXY. We addressed physical, pain, and sleep problems. In terms of physical problems, the majority of the sample (80%) reported no major physical health problems. However, a quarter of the sample (24%) was reported to experience pain every week, most frequently specified as pain of the back, knees, and/or feet. A review of studies with both child and adult cohorts has demonstrated deficits in gross and fine motor skills, as well as hypotonia, hand tremor, and poor strength in over half of participants with

KS in studies, as well as motor deficits for many in the 47,XYY group (Leggett et al., 2010). Such difficulties may explain part of the pain problems reported for some of our participants. Over a third of the SCA sample (36%) also reported sleep problems. We are not aware of previous studies examining sleep problems among boys and/or men with SCA. Importantly, boys with confirmed sleep problems had more frequent pain problems than boys without sleep problems in our sample. Because increased sleep problems among children with pain problems is well documented across studies (see Valrie et al., 2013, for review), future studies should examine the extent of pain problems for boys with SCA and their relation to sleep problems.

Socio-emotional problems were assessed with the SDQ (Goodman et al., 2000), a widely used brief measure of socio-emotional functioning. Boys with SCA scored higher on the total scale, on all problem subscales, as well as lower on the pro-social scale, compared to norm groups. The difference was large for peer problems, and medium for the other subscales (emotional problems, conduct problems, hyperactivity, and pro-social functioning), indicating that boys with SCA do have more socio-emotional problems than their peers on several areas of functioning. This is in line with a number of previous studies of boys with SCA (e.g., Bruining et al., 2009; Cordeiro et al., 2012; Geerts et al., 2003; Ross et al., 2012; Tartaglia et al., 2012).

Contrary to our expectations, we found no difference between the boys with KS and the boys with 47,XYY in terms of socio-emotional problems. Given that more problems for individuals with 47,XYY has been consistently reported in the literature (see Cordeiro et al., 2012; Leggett et al., 2010), we believe the main reason for our finding is that we had insufficient sample sizes to detect differences. There was larger effect size differences on several socio-emotional problem scores between boys with 47,XYY and norms than between boys with KS and norms.

The second aim of the present study represents a novel aspect. We compared the socio-emotional problems for the SCA group with a clinical sample of boys referred to mental health services. There was no difference between boys with SCA and the clinical sample on the total SDQ, but there were some differences on subscales. Boys with SCA had more conduct and hyperactivity problems but less emotional problems, compared to the clinical sample. Taken together, our results indicate that the total level of socio-emotional problems among boys with SCA may be comparable to those of boys who are referred to mental health clinics, but that boys with SCA have more externalizing and less internalizing problems than clinically referred boys. Note than the boys in the clinical sample were referred for suspected anxiety problems, and that these patterns may be different for boys referred to mental health services for other problems.

The strengths of the current study include the use of a sample of young boys and the comparison to a clinical sample using a well-validated measure of socio-emotional problems. However, the results need to be regarded in light of some

of the study's limitations. Both the low sample size and the fact that recruitment took place via user groups and a resource center raises questions about the generalizability of results. A large study ($N = 166$) of boys and men recruited from an endocrine outpatient clinic found a low frequency of psychiatric disorders ($n = 8$ for depression, $n \leq 2$ for psychosis, autism, and or medically treated anxiety or ADHD; Aksglæde, 2011). The use of samples recruited from interest groups may overestimate problems among boys and men with SCA. The small sample size also prevented us from matching the SCA sample to the clinical sample and controls. Another issue with regards to generalizability is the fact that SCAs are heavily under-diagnosed. A Danish cohort study indicated that only about 25% of men with KS receive the diagnosis (Bojesen, Juul, Birkebæk & Gravholt, 2004). Our sample of diagnosed boys may not be representative for the undiagnosed SCA population. We can also not be sure that none of the boys in the clinical sample had undiagnosed SCA, although given the low prevalence rates of SCA it is highly unlikely that this would apply to enough individuals to compromise results. Another limitation is that we did not assess intellectual level, and although specific language difficulties are more common for the KS group than general learning difficulties, higher aneuploidies (e.g., 48,XXY, 48.XXXY) tend to be associated with more severe cognitive deficits. We cannot rule out that cognitive problems explain some of the differences found between the SCA sample and comparison samples. In fact, it is likely that this is part of the explanation for differences. Four of our participants were slightly younger or older (≤ 2 years) than the age base for the SDQ norms, so the effect size comparisons between the SCA sample and norms should be considered with caution. Finally, our results are based on parent-report only, and self-report and/or observational data may have increased the validity of our results. Diagnostic SCA status was also based on parent-report only, however we have no reason to assume that parents would inaccurately report their boys' SCA status. In light of these limitations, our results should be interpreted with caution.

IMPLICATIONS FOR PRACTICE

The most important aspect of our findings is that boys with SCA may have the same needs for clinical intervention for socio-emotional problems as boys typically referred to mental health services. The differences that did emerge between norm groups, the clinical sample, and the sample of boys with SCA indicate that at least for some individuals with SCA, there are considerable socio-emotional problems for which the boys do not receive intervention. Only two of the boys with SCA in the current sample were reported to be involved with psychologists, which indicates that these boys may have an unmet need for intervention. Eight participants were involved with habilitation services, but it is not clear to what extent

psychiatric evaluation or treatment is offered through habilitation services. In fact, involvement with habilitation services may sometimes heighten the threshold for contact with other services, such as mental health services. A recent study of several thousand American persons with disabilities showed that receiving habilitation services reduced the likelihood of receiving other regional services, with the likelihood being even lower for persons under 21 years of age (Harrington & Kang, 2008).

Thus, the main implication of our findings is that boys with SCA need to be involved with services that offer psychological screening, prevention, and treatment.

Compared to norm data, boys with 47,XYY appear to be a particularly vulnerable group. Our results indicate that physical and/or pain management therapy should be considered for boys with SCA. Sleep problems occurred in a third of the sample. If future studies also document sleep problems for many in this group, an implication for clinical practice may be that possible sleep problems should be assessed in boys with SCA. To conclude, all boys with SCA may not need referral to mental health services, but screening for emotional, conduct, attention, as well as sleep, pain, and social problems, should be offered as part of standard care for boys with SCA.

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REFERENCES

Achenbach, T. M. (2009). *The Achenbach System of Empirically Based Assessement (ASEBA): Development, findings, theory, and applications*. Burlington, VT: University of Vermont Research Center for Children, Youth and Families.

Aksglæde, L., Skakkebæk, N. E., Almstrup, K., & Juul, A. (2011). Clinical and biological parametres in 166 boys, adolescents, and adults with nonmosaic Klinefelter syndrome: A Copenhagen experience. *Acta Paediatrica*, *6*, 793–806.

Bancroft, J., Axworthy, D., & Ratcliffe, S. (1982). The personality and psycho-sexual development of boys with 47 XXY chromosome constitution. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *23*(2), 169–180.

Bojesen, A., & Gravholt, C. H. (2011). Morbidity and mortality in Klinefelter syndrome (47,XXY). *Acta Paediatrica*, *6*, 807–813.

Bojesen, A., Juul, S., Birkebæk, N., & Gravholt, C. H. (2004). Increased mortality in Klinefelter syndrome. *Journal of Clinical Endocrinology and Metabolism*, *8*, 3830–3834.

Bruining, H., Swaab, H., Kas, M., & von Egeland, H. (2009). Psychiatric characteristics in a self-selected sample of boys with Klinefelter Syndrome. *Pediatrics*, *123*(5), E865–E870.

Bøe, T., Øverland, S., Lundervold, A. J., & Hysing, M. (2012). Socioeconomic status and children's mental health: Results from the Bergen Child Study. *Social Psychiatry and Psychiatric Epidemiology*, *47*, 1557–1566.

Cohen, J. (1992). A power primer. *Psychological Bulletin*, *112*(1), 155–159.

Conners, C. K., Sitarenios, G., Parker, J. D. A., & Epstein, J. N. (1998). The revised Conners' Parent Rating Scale (CPRS-R): Factor structure, reliability, and criterion validity. *Journal of Abnormal Child Psychology*, *26*(4), 257–268.

Cordeiro, L., Tartaglia, N., Roeltgen, D., & Ross, J. (2012). Social deficits in male children and adolescents with sex chromosome aneuploidy: A comparison of XXY, XYY, and XXYY syndromes. *Research in Developmental Disabilities*, *33*(4), 1254–1263.

Currie, C., Molcho, M., Boyce, W., Holstein, B., Torsheim, T., & Richter, M. (2008). Researching health inequalities in adolescents: the development of the Health Behaviour in School-Aged Children (HBSC) family affluence scale. *Social Science & Medicine*, *66*(6), 1429–1436.

Geerts, M., Steyaert, J., & Fryns, J. P. (2003). The XYY syndrome: A follow-up study on 38 boys. *Genetic Counseling*, *14*(3), 267–279. Accession Number: WOS:000185848800002

Goodman, R. (2001). Psychometric properties of the strengths and difficulties questionnaire. *Journal of the American Academy of Child and Adolescent Psychiatry*, *40*(11), 1337–1345.

Goodman, R., Ford, T., Richards, H., Gatward, R., & Meltzer, H. (2000). The Development and Well-Being Assessment: Description and initial validation of an integrated assessment of child and adolescent psychopathology. *The Journal of Child Psychology and Psychiatry*, *41*(5), 645–655.

Goodman, R., & Scott, S. (1999). Comparing the strengths and difficulties questionnaire and the child behavior checklist: Is small beautiful? *Journal of Abnormal Child Psychology*, *27*(1), 17–24.

Harrington, C., & Kang, T. (2008). Disparities in service utilization and expenditures for individuals with developmental disabilities. *Disability and Health Journal*, *1*(4), 84–195.

Herlihy, A. S., McLachlan, R. I., Gillam, L., Cock, M. L., Collins, V., & Halliday, J. L. (2011). The psychosocial impact of Klinefelter syndrome and factors influencing quality of life. *Genetics in Medicine*, *13*(7), 632–642.

Lazaratou, H., Soldatou, A., & Dikeos, D. (2012). Medical comorbidity of sleep disorders in children and adolescents. *Current Opinion in Psychiatry*, *25*(5), 391–397.

Leggett, V., Jacobs, P., Nation, K., Scerif, G., & Bishop, D. V. M. (2010). Neurocognitive outcomes of individuals with a sex chromosome trisomy: XXX, XYY, or XXY: A systematic review. *Developmental Medicine and Child Neurology*, *52*(2), 119–129.

Ross, J. L., Roeltgen, D. P., Kushner, H., Zinn, A. R., Reiss, A., Bardsley, M. Z., . . . Tartaglia, N. (2012). Behavioral and social phenotypes in boys with 47, XYY syndrome or 47, XXY Klinefelter Syndrome. *Pediatrics*, *129*(4), 769–778.

SDQ info. (2013). *British norms for boys*. Retrieved from www.sdqinfo.com/UKNorm.html

Tartaglia, N. R., Ayari, N., Hutaff-Lee, C., & Boada, R. (2012). Attention-deficit hyperactivity disorder symptoms in children and adolescents with sex chromosome aneuploidy: XXY, XXX, XYY, and XXYY. *Journal of Developmental and Behavioral Pediatrics*, *33*(4), 309–318.

Tartaglia, N., Davis, S., Hench, A., Nitnishakavi, S., Beauregard, R., Reynolds, A., . . . Hagerman, R. (2008). A new look at XXYY syndrome: Medical and psychological features. *American Journal of Medical Genetics Part A*, *146A*(12), 1509–1522.

Valrie, C. R., Bromberg, M. H., Palermo, T., & Schanberg, L. E. (2013). A systematic review of sleep in pediatric pain populations. *Journal of Developmental and Behavioral Pediatrics*, *34*(2), 120–128.

Vostanis, P. (2006). Strengths and Difficulties Questionnaire: Research and clinical applications. *Current Opinion in Psychiatry*, *19*(4), 367–372.