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Psychosocial outcomes in children with and without non-syndromic craniosynostosis: findings from two studies

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Abstract

Objective—To evaluate the hypothesis that children with craniosynostosis and their parents have differences in psychosocial outcomes, as compared with an unaffected control group.

Design—Two studies were conducted, both which followed children born with and without craniosynostosis. Study 1 ascertained affected children from clinics and Study 2 ascertained affected children from a population-based study of birth defects.

Participants—Study 1 included 22 children with single-suture craniosynostosis and 18 controls, ages 4–5 years. Study 2 included 24 children with non-syndromic craniosynostosis and 124 unaffected controls, ages 5–9 years.

Main Outcome Measures—Outcome measures included the Child Behavior Checklist (CBCL), Social Competence Scale (SCS), Pediatric Quality of Life Inventory (PedsQL™), and Parenting Stress Index (PSI).

Results—We observed lower scores on measures of health-related quality of life in cases versus controls, with adjusted effect sizes ranging from −0.72 to −0.44 ($p<0.05$) on summary measures. Small but statistically non-significant increases in behavioral problems were observed in cases versus controls, with no apparent differences in social competence or parenting stress.

Conclusions—Results provide preliminary evidence suggesting that children with non-syndromic craniosynostosis may have elevated risk for psychosocial difficulties, particularly health-related quality of life. Continued follow-up through pre-adolescence and adolescence is warranted.

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Keywords

Craniosynostoses; Quality of Life; Psychosocial; National Birth Defects Prevention Study

Craniosynostosis refers to the premature fusion of the sagittal, metopic, coronal, or lambdoidal cranial sutures in the perinatal period. One or multiple sutures may be involved, and craniosynostosis may occur with other structural malformations or in isolation. Treatment includes surgical excision of the fused suture(s), which for most cases of isolated craniosynostosis is performed within the first year of life, with continued follow-up throughout childhood (Mccarthy et al., 2011). Surgical and non-surgical management of craniosynostosis ideally includes follow-up throughout childhood and adolescence by a multidisciplinary craniofacial team.

The importance of outcomes research for understanding long-term morbidity in children with craniosynostosis was recently highlighted by a report from the Centers for Disease Control and Prevention (Rasmussen et al., 2008), which noted the few studies comparing children with and without craniosynostosis and the need to clarify behavioral and psychosocial outcomes in this population. Previous studies have generally had methodological limitations such as small sample sizes (Kapp-Simon and Mcguire, 1997; Virtanen et al., 1999; Ozgur et al., 2006), and variable ages, including infants and adults (Sidoti et al., 1996; Boltshauser et al., 2003; Becker et al., 2005). Samples often included heterogeneous craniofacial anomalies, with relatively few craniosynostosis cases (Krueckeberg and Kapp-Simon, 1993; Speltz et al., 1993; Kapp-Simon and Mcguire, 1997), or did not include a control group (Sidoti et al., 1996; Bottero et al., 1998; Becker et al., 2005; Kelleher et al., 2006; Ozgur et al., 2006; Wong-Gibbons et al., 2009). In addition, standardized psychosocial measures were often not used (Bottero et al., 1998; Kelleher et al., 2006; Ozgur et al., 2006; Wong-Gibbons et al., 2009). Moreover, prior studies have mainly evaluated neurocognitive problems rather than psychosocial outcomes (Arnaud et al., 1995; Speltz et al., 1997b; Kapp-Simon, 1998; Panchal et al., 2001; Arnaud et al., 2002; Magge et al., 2002; Cohen et al., 2004; Speltz et al., 2004; Bellew et al., 2005; Starr et al., 2007; Van Der Meulen et al., 2008).

Parenting behaviors may be influenced by the experience of having an infant with a birth defect (e.g. stress due to diagnosis, surgery, possible infant mortality, and concerns regarding the child's future). Furthermore, there is evidence of higher stress and care-giving difficulties in mothers of children with craniofacial anomalies than among parents of children with no craniofacial anomalies (Barden et al., 1989; Speltz et al., 1990; Speltz et al., 1994), factors which likely affect children's psychosocial adaptation.

We present two studies in which we examined behavioral adjustment, health-related quality of life (HRQoL) and social competence in 4 to 9 year-old children with craniosynostosis, as compared with children without craniofacial anomalies. Reports of HRQoL were taken from both mothers and the children themselves. We also compared maternal stress in families of affected and unaffected children. Study 1 included participants recruited from an ongoing follow-up study of children with and without isolated single-suture craniosynostosis (Speltz et al., 2007; Starr et al., 2007). Study 2 included cases with non-syndromic craniosynostosis and a comparison group of unaffected children identified through the Massachusetts Center of the National Birth Defects Prevention Study (NBDPS) (Yoon et al., 2001).

METHODS

Sample

Study 1—The current cross-sectional analysis includes a sample of children who have been followed longitudinally since infancy as part of a multi-center study of neurodevelopment in children with and without single-suture craniosynostosis (Speltz et al., 2007; Starr et al., 2007). The two study groups included cases with isolated single-suture craniosynostosis (confirmed by computed tomography), and a comparison group without major congenital anomalies. Controls were initially frequency matched to cases by sex, race/ethnicity, socioeconomic status (SES) and study center. At the time of enrollment into the original study, cases had not yet undergone surgery. Because of the potential differences in psychosocial and neurobehavioral outcomes among children who do versus do not receive surgery, participation in the original study was limited to those planning to undergo surgery as part of their clinical care. The vast majority of affected children undergo surgery in infancy to improve cosmesis, and all cases in the current sample did have surgical treatment. Exclusion criteria for all participants included the presence of major malformations or ≥3 minor anomalies (Leppig et al., 1987); age >30 months at enrollment; age at delivery < 34 weeks; and major medical or neurological conditions (e.g., seizure disorders).

For the current cross-sectional analysis, participants at one of four study centers (Seattle Children's Hospital) were invited for follow-up in 2007 and 2008, between the ages of 4 to 5 years. We attempted to contact 69 families from this cohort. Of these, 22 (61%) cases and 18 (55%) controls were enrolled and provided complete data. Non-participants included 4 active decliners, 17 passive non-responders, and 8 families who did not complete study questionnaires. Overall, non-participating families had lower SES based on the Hollingshead Index than did participating families.

Study 2—Mothers of subjects were originally identified and interviewed through the Massachusetts Center of the NBDPS, a population-based case-control study of selected structural anomalies that began in 1997 (Yoon et al., 2001). Controls were randomly selected from Massachusetts birth records during the same time interval, and included children born without major structural anomalies.

Cases selected for inclusion in the current study were children with craniosyostosis born between October 1997 and December 2002, after excluding those with known syndromes or chromosomal anomalies (as described in the NBDPS)(Rasmussen et al., 2008). Cases with both single and multiple suture fusions were included, as were children with other malformations. Follow-up data were collected for all subjects in 2007. Among eligible individuals, 24 of 37 (65%) cases and 124 of 225 (55%) controls participated. On average, non-participating mothers were younger, less-educated and less likely to be white as compared with participants.

Data Collection

Study 1—Families were contacted by phone when their child was between the ages of 4 to 5 years to determine study interest and to complete a brief phone interview. Interested families were mailed a consent form and study measures, which included the Child Behavior Checklist (CBCL) (Achenbach and Rescorla, 2000; Achenbach and Rescorla, 2001) and Social Competence Scale (SCS) (Corrigan A, 2002). Sociodemographic data collected at baseline included each child's birthdate, sex, and race/ethnicity. Data updated as part of the interview included maternal age and household SES (Hollingshead Four Factor Index) (Hollingshead, 1975).

Study 2—Study packets sent to mothers included an introductory letter, consent form, and measures of psychosocial functioning, which included the CBCL, SCS, Pediatric Quality of Life Inventory (PedsQL™), and Parenting Stress Index (PSI). Sociodemographic variables were available from the NBDPS, and included each child's birthdate and maternal race/ethnicity, age and education level at delivery. Mothers were telephoned by study staff one week after the initial mailing. After four weeks, non-responders were recontacted by telephone, with a follow-up letter two weeks later.

Each study was reviewed and approved by an institutional review committee. Parents of participating children provided written informed consent.

Measures

The Child Behavior Checklist (CBCL) is a norm-referenced parent-report measure of behavior problems, with versions for ages 1½ to 5 years (CBCL/1½–5) (Achenbach and Rescorla, 2000) and 6 to 18 years (CBCL/6–18) (Achenbach and Rescorla, 2000; Achenbach and Rescorla, 2001). Parents rate the frequency of behavior problems on a 3-point Likert-type scale (0='not true' to 2='very true or often true'). The CBCL/1½–5 includes seven scales: emotionally reactive, anxious/depressed, somatic complaints, withdrawn, sleep problems, attention problems, and aggressive behavior. The CBCL/6–18 includes the following sub-scales: anxious/depressed, withdrawn/depressed, somatic complaints, social problems, thought problems, attention problems, rule-breaking behavior, and aggressive behavior. Summary scores are derived for internalizing problems (e.g., anxiety, depression), externalizing problems (e.g., aggression, acting out), and an overall score. T-scores with a normative mean of 50 [standard deviation (sd) 10] are generated, with higher scores reflecting more severe behavior problems. Summary results for both versions have been combined and from this point forward will simply be referred to as 'CBCL.'

The Social Competence Scale (SCS) (Corrigan, 2002) includes 12 items describing scenarios commonly encountered by young children in social situations, and has been validated in community-based samples and in children at high-risk for conduct problems (Corrigan, 2002; Gouley et al., 2008; CPPRG, 1995). The parent rates each item based on how well it describes the child, selecting from a five-point Likert scale ranging from 'not at all' to 'very well.' Scores summarize pro-social/communication skills, emotional regulation, and overall social competence. Low scores are suggestive of poor social competence.

Health-related quality of life (HRQoL) was assessed using both the parent and youth report scales of the Pediatric Quality of Life Inventory, Ages 5 to 7 years (PedsQL™ 4.0) (Varni et al., 1999; Varni et al., 2001). The PedsQL™ has been validated in samples of healthy and chronically ill children, and provides summary measures for different aspects of HRQoL, including physical, psychosocial and total health scores. Within the psychosocial composite, sub-scale scores can be derived for emotional, social, and school functioning. Mother and child each respond to items based on frequency of occurrence. Response options range from 'never' to 'almost always' on a three-point scale for children, and a five-point scale for parents. Low scores indicate poor HRQoL.

The Parenting Stress Index (PSI) (Abidin, 1983) was selected to evaluate the parent-child relationship and family functioning. Parents are presented with 89 statements for which they respond using a five-point Likert scale ranging from 'strongly agree' to 'strongly disagree.' Twelve additional multiple choice items with 4 or 5 options are given. The PSI Child Domain includes the following subscales: distractibility/hyperactivity, adaptability, demandingness, mood, and reinforces parent. The Parent Domain subscales include competence, social isolation, attachment to child, health, role restriction, acceptability, depression, and relationship with spouse. A Total Stress Domain combines the Child and

Parent scores. Parents are also asked to identify stressful life events occurring in the 12 months prior to completing the questionnaire, selecting from a list of 19 events (e.g. divorce, promotion at work). Good reliability and predictive validity have been demonstrated previously, including in other craniofacial populations (Speltz et al., 1997a). High scores indicate elevated levels of stress.

Statistical Analyses

Sociodemographic characteristics of children with and without craniosynostosis were descriptively summarized. We additionally calculated the number and proportion of cases and controls scoring in the recommended 'borderline' and 'clinical' ranges on the CBCL (borderline >84th percentile; clinical >92nd percentile) and PSI (clinical >85th percentile).

Linear regression was used to compare mean scores in the case versus control groups. When comparing two groups (i.e. case versus control), results from linear regression are equivalent to those from standard t-tests of two independent samples. However, linear regression is more flexible, and allows for the estimation of case-control differences in the outcome variable (e.g. PSI Total Score) after adjusting for potential confounders. Adjusted models included sex and age (continuous) as covariates. SES [I(high)=55–66; II=40–54; III–V=8–39] (Hollingshead, 1975) was additionally included as a covariate for Study 1, whereas maternal education (<16; ≥16 years) was included for Study 2 analyses. Standardized effect sizes (Hedge's g) were additionally calculated for each measure (Durlak, 2009); absolute values of 0.2 or less are said to reflect a "small" association, 0.3 to 0.8 reflect a "moderate" association, and those 0.8 or greater reflect a "large" association (Cohen, 1988). Case-control differences are presented with 95% confidence intervals (CI) to show their relative stability. There was no adjustment for multiple comparisons.

Sensitivity Analyses—We additionally conducted several restricted analyses: excluding cases noted to have mutations (Study 1); excluding cases with multiple suture involvement (Study 2); and excluding children with additional malformations (Study 2). Case-control differences were virtually unchanged for each sensitivity analysis, and are not reported.

RESULTS

Participant Characteristics

The mean age of Study 1 participants was 5.3 (sd 0.4) years in both study groups. Among cases and controls, 15 (68%) and 11 (61%) were male, respectively (Table 1). The sample was non-Hispanic white (>80%) or of mixed racial and ethnic backgrounds (<20%). Household SES was categorized as Hollingshead categories I or II for most cases (77%) and controls (94%). By design, all Study 1 cases had single-suture craniosynostosis. The largest subgroup included 10 (45%) sagittal cases (Table 2). One sagittal case had a novel genetic mutation and one unicoronal case had Meunke Syndrome (FGFR mutation).

In Study 2, cases were somewhat younger (mean 6.2 years, sd 0.8) than controls (mean 6.7 years, sd 1.1), and were more likely to be male (Table 1). The majority (>90%) of participants were non-Hispanic white. Maternal education level at the time of the study child's birth was ≥16 years for approximately two-thirds of participants. Among cases, the most common diagnosis was single-suture sagittal synostosis (50%), with multiple suture involvement in 2 (8%) participants. (Table 2) Three metopic cases had additional malformations (diaphragmatic hernia, cardiac and limb defects, hypospadias).

Child Behavior Checklist (CBCL)

In Study 1, mean CBCL T-scores ranged from 44.6 to 45.7 in cases, and 41.1 to 42.3 in controls, with adjusted differences of approximately 3.5 points for each comparison (aES 0.38 to 0.41; $p>0.05$) (Table 3). One case and one control scored above the 84th percentile on at least one CBCL summary measure. Of these two children, only the control scored above the 92nd percentile (not shown).

In Study 2, mean CBCL T-scores were consistently higher in cases (range 48.3 to 49.3) than controls (range 45.3 to 47.7). Differences were accentuated after adjustment for age, sex and maternal education (aES 0.29 to 0.51), and were statistically significant for the CBCL total score (Table 3). Four (17%) cases and 8 (7%) controls scored above the clinical cutoff (>92nd percentile) on at least one CBCL summary measure, although comparisons were not statistically significant (not shown).

Social Competence Scale (SCS)

In Study 1, mean SCS total scores were 2.7 (sd 0.5) and 2.6 (sd 0.5) in cases and controls, respectively (aES 0.32; $p>0.05$) (Table 3). In Study 2, average SCS total scores were lower in the case (mean=2.3, sd=0.9) versus control groups (mean=2.6, sd=0.7) (aES −0.36), though differences were not statistically significant.

Pediatric Quality of Life Inventory (PedsQL™)

On average, Study 1 cases scored 6.3 to 6.5 points lower on PedsQL™ Child Report summary measures as compared with controls (aES −0.59 to −0.44, $p< 0.05$) (Table 4). Mean summary scores by parent report were 9.0 to 10.5 points lower in cases versus controls (aES −l0.72 to −0.64, $p<0.05$). Case-control differences were particularly notable for school functioning (child aES −0.79; parent aES −0.71; $p<0.05$), with statistically significant differences for parent-reported social functioning (aES −0.53, $p<0.05$).

Parenting Stress Index (PSI)

On average, PSI total stress scores were somewhat elevated in cases (208) versus controls (198) (aES 0.23). This appeared to be driven by increased child domain scores (96 versus 87 in cases and controls, respectively; aES 0.43), with negligible difference on the parent domain (Table 4). However, none of the comparisons were statistically significant. Seven (29%) case-parents scored above the clinical cutoff on at least one PSI domain, as compared with 28 (23%) control-parents ($p>0.05$). Measures of life stress did not differ according to group status (not shown).

DISCUSSION

Among the various psychosocial constructs assessed in this research, the measure of HRQoL used in Study 2 provided the clearest discrimination of cases and controls. On average, the mothers of children with craniosynostosis reported lower HRQoL than did the mothers of unaffected controls, and children's reports paralleled this difference. Differences were particularly evident in school functioning, potentially reflecting previously reported neurodevelopmental differences and elevated risk for learning problems (Becker DB et al., 2005; Bellew M, et al., 2005; Cohen SR et al., 2004; Kapp-Simon KA, 1998; Kelleher MO et al., 2006; Magge SN et al., 2002; Starr JR et al., 2007). Furthermore, the magnitude of the observed differences suggests that they are likely to be clinically significant (i.e., absolute effect sizes greater than 0.5), with implications for clinical screening and monitoring of patients with craniosynostosis. However, as with any parent report measure, it is possible that these differences reflect in part mothers' concerns about the quality of their children's lives as well as their observations of how their children function. Children's reports of their

own HRQoL cannot be considered fully independent of their mothers' reports, as parental instructions and help were probably required for children's completion of the PedsQL™ at home. Confirmation of these HRQoL findings is therefore needed, ideally using teacher reports of school and social problems as is suggested by the PedsQL™.

With regards to reported behavior problems among Study 2 participants, group differences were statistically significant only for the total behavior score. Although children with non-syndromic craniosynostosis had consistently higher behavior problem scores than controls, it is unlikely that such differences are clinically significant. Overall, the majority of children with and without craniosynostosis scored within the normative range on behavior measures, and on average did not show meaningful differences in social competence.

Study 1 cases also had higher average scores on the CBCL broad domains than controls, but very few cases or controls in Study 1 had behavioral scores which would be considered clinically significant. The magnitude of group differences was similar to those observed in Study 2. However, in Study 2, children with craniosynostosis were more than twice as likely as controls to score within the clinically significant range. As behavior problems tend to be inversely correlated with socio-demographic factors (Pike et al., 2006). This shift in the distribution of scores among Study 1 participants, as compared with participants in Study 2, likely reflects the relatively low social risk (e.g. high SES) in participating Study 1 families. Yet, even in this lower-risk sample, differences between cases and controls were observed.

Two recent studies of clinical samples containing older children with non-syndromic craniosynostosis reported elevated levels of emotional and behavioral problems in relation to CBCL norms (Becker et al., 2005; Snyder and Pope, 2010). However, we found little support for this impression of elevated psychosocial risk, at least among younger children in the present study, which is one of the first to include a demographically-matched control group. It is possible that the marginally elevated problem scores reported here among cases become more pronounced with age and academic advancement, a possibility that we will examine in a longitudinal follow-up of the Study 1 cohort at age 7.

Some investigators and clinicians have raised the possibility of association between autistic traits and craniofacial malformations (Tripi et al., 2008), including infants with isolated suture fusions (Ijichi and Ijichi, 2002). The magnitude of observed group differences in this study suggest that this is highly unlikely, although individual diagnostic evaluations would be required to rule this out with certainty.

In addition to a control group, this study extends previous work in other ways: it includes a broad assessment battery that evaluates behavior problems, both parent- and child-reported HRQoL, social competence, and parents' stress and it replicates key outcomes in two independent samples. The use of a population-based sample in Study 2 makes this study unique in the literature, and helps to overcome some of the limitations of studies that had recruited participants through clinical programs (e.g., potential ascertainment bias, with more complicated or impaired cases more likely to require ongoing medical care). Our results are further strengthened by a series of sensitivity analyses, in which we excluded cases with characteristics that might be expected to affect psychosocial functioning, such as additional malformations, genetic mutations, and multiple suture involvement.

Both studies had limitations that could have affected results. Participation was higher for cases than controls, and varied according to demographic variables that may also affect psychosocial outcomes (e.g., SES). Individuals who were at highest risk for adverse psychosocial outcomes may have therefore been under-represented. Verification of our findings in future longitudinal studies with expanded effort to retain 'high-risk' families remains a priority.

CONCLUSION

Our report addresses research goals identified by a panel of experts on craniosynostosis research by specifically addressing scientific gaps with respect to psychosocial functioning in school-aged children. Observed differences in HRQoL persisted regardless of the presence of additional malformations, analytic restrictions based on sutural involvement, and across two studies with differing sampling frames. Healthcare practitioners should be aware that children with non-syndromic craniosynostosis may have elevated risk for psychosocial sequelae that affect quality of life. Research in the field is most likely to be advanced by longitudinal studies that track psychosocial development from pre-school to early adolescence and simultaneously seek to identify predictive and risk factors associated with poor psychosocial functioning among children with non-syndromic craniosynostosis.

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TABLE 1

Sociodemographic Characteristics of Study 1 and Study 2 Participants, by Case versus Control Status

Characteristic	STUDY 1		STUDY 2	
	Cases (N = 22) N (%)	Controls (N = 18) N (%)	Cases (N = 24) N (%)	Controls (N = 124) N (%)
Sex				
female	7 (32)	7 (39)	9 (38)	66 (53)
male	15 (68)	11 (61)	15 (63)	58 (47)
Age at Ascertainment, *years*				
4–4.9	6 (27)	6 (33)	--	--
5–5.9	16 (73)	12 (67)	13 (54)	40 (32)
6–6.9	--	--	5 (21)	33 (27)
7–6.9	--	--	5 (21)	29 (23)
8–8.9	--	--	1 (4)	21 (17)
≥9	--	--	0 (0)	1 (1)
Race/Ethnicity				
Hispanic Caucasian	--	--	1 (4)	4 (3)
Non-Hispanic Caucasian	18 (82)	15 (83)	23 (96)	114 (92)
Other or Mixed Race/Ethnicity	4 (18)	3 (17)	0 (0)	6 (5)
Maternal Education (at time of Delivery)				
≤12yrs	--	--	5 (21)	18 (15)
13–15yrs	--	--	2 (8)	24 (19)
16+yrs	--	--	17 (71)	82 (66)
Socioeconomic Status[a]				
I (High)	5 (23)	4 (22)	--	--
II	12 (55)	13 (72)	--	--
III–IV (Low)	5 (23)	1 (6)	--	--

[a]Hollingshead 4-factor index of social status:(Hollingshead, 1975) I=55–66; II=40–54; III=30–39; IV=20–29; V=8–19

TABLE 2

Sutural Involvement of Craniosynostosis Cases in Study 1 and Study 2

	STUDY 1	STUDY 2
Suture Involvement	**N (%)**	**N (%)**
Sagittal	10 (45)	12 (50)
Metopic	4 (18)	7 (29)
Right Unicoronal	3 (14)	2 (8)
Left unicoronal	2 (9)	0 (0)
Lambdoidal[a]	3 (14)	1 (4)
Multiple[b]	0 (0)	2 (8)

[a] Lamboidal cases are single-suture

[b] Includes bicoronal cases

TABLE 3

Results from linear regression analyses with accompanying effect size estimates (Hedge's G) comparing mean Child Behavior Checklist (CBCL) and Social Competence (SCS) scores in craniosynostosis cases versus controls in Study 1 and Study 2

	Study 1				Study 2			
Measure	**Case Mean (sd)**	**Control Mean (sd)**	**Adjusted Case-Control Difference (95% CI)[a]**	**Hedge's G**	**Case**	**Control**	**Adjusted Case-Control Difference (95% CI) [b]**	**Hedge's G**
Child Behavior Checklist (CBCL)								
Internalizing	45.7 (7.6)	42.3 (10.2)	3.5 (−2.1, 9.1)	0.38	49.3 (13.1)	47.7 (10.2)	3.1 (−2.5, 8.6)	0.29
Externalizing	44.7 (7.4)	41.2 (9.1)	3.5 (−1.7, 8.8)	0.40	48.3 (11.8)	45.4 (10.4)	4.5 (−0.5, 9.5)	0.44
Total	44.6 (7.6)	41.1 (9.9)	3.6 (−1.7, 9.0)	0.41	49.1 (12.2)	45.3 (10.6)	5.4 (0.3, 10.4) *	0.51
Social Competence Scale (SCS)								
Total	2.7 (0.5)	2.6 (0.5)	0.2 (−0.1, 0.5)	0.32	2.3 (0.9)	2.6 (0.7)	−0.3 (−0.7, 0.1)	−0.36

* Likelihood Ratio Test p-value < 0.05

[a] Adjusted for sex, age (continuous), and SES

[b] Adjusted for sex, age (continuous), and maternal education (<16, ≥16 years)

TABLE 4

Results from linear regression analyses with accompanying effect size estimates (Hedge's G) comparing mean Pediatric Quality of Life Inventory (PedsQL™) and Parenting Stress Inventory (PSI) scores in craniosynostosis cases versus controls (Study 2 Only)

Measure	Case	Control	Adjusted Case-Control Difference (95% CI) [a]	Hedge's G
PedsQL™ Child Report				
Emotional	73.8 (22)	74.5 (19.6)	−1.8 (−11.5, 7.9)	−0.09
Social	75.5 (16)	80.5 (16.6)	−5.2 (−12.2, 1.7)	−0.32
School	71.3 (24.6)	82.7 (15.5)	−13.6 (−23.5, −3.6) *	−0.79
Psychosocial Summary	73.5 (18.0)	79.1 (14.1)	−6.7 (−14.4, 1.0) *	−0.44
Physical Summary	82.8 (14.4)	88.6 (9.6)	−6.3 (−12.3, −0.4) *	−0.59
Total	76.8 (15.2)	82.4 (11.4)	−6.5 (−12.9, −0.1) *	−0.53
PedsQL™ Parent Report				
Emotional	68.3 (19.3)	74.5 (15.6)	−6.0 (−14.1, 2.1)	−0.37
Social	75.9 (22.4)	84.7 (15.6)	−9.0 (−18.3, 0.2) *	−0.53
School	71.9 (19.7)	82.3 (16.2)	−11.9 (−19.9, −3.8) *	−0.71
Psychosocial Summary	72.0 (17.1)	80.5 (13.0)	−9.0 (−16.2, −1.8) *	−0.64
Physical Summary	77.5 (21.0)	87.7 (13.9)	−10.5 (−18.9, −2.0) *	−0.69
Total	73.9 (16.5)	83.0 (12.2)	−9.5 (−16.4, −2.7) *	−0.72
Parenting Stress Inventory (PSI) [b]				
Child Domain	96.3 (34.8)	86.9 (21.2)	10.5 (−4.0, 24.9)	0.43
Parent Domain	111.6 (31.1)	111.0 (24.5)	0.3 (−12.3, 12.9)	0.01
Total	208.0 (61.9)	198.0 (41.4)	10.6 (−14.3, 35.6)	0.23

* Likelihood Ratio Test p-value < 0.05

[a] Adjusted for sex, age (continuous), and maternal education (<16, ≥16 years)

[b] PSI Child Domain score missing for 1 control; PSI Parent Domain and PSI Total missing for 3 controls