Published in final edited form as:

Plast Reconstr Surg. 2012 September ; 130(3): 635–647. doi:10.1097/PRS.0b013e31825dc18b.

Behavioral Adjustment of Toddler and Preschool-Aged Children with Single-Suture Craniosynostosis*

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Abstract

Background—The purpose of this study was to confirm initial reports of elevated behavior problems in children with single-suture craniosynostosis (SSC), using multiple informants, longitudinal analyses and a control group. We hypothesized higher levels of maladjustment for children with SSC than comparison children, particularly at the older age and in selected areas of previously observed vulnerability: attention and social adjustment.

Method—A Child Behavior Checklist (CBCL) was completed when children were ~19 months by 436 mothers (219 with SSC) and 371 fathers (177 with SSC); and at ~37 months by 361 mothers (175 with SSC) and 303 fathers (142 with SSC). A minimum of one caregiver/teacher report was available for 169 of these children (74 with SSC) using the Caregiver-Teacher Report Form (CTRF).

Results—Average CBCL/CTRF externalizing, internalizing and total scores for all informants were consistently higher (worse) for children with SSC than control group children, but most differences were small and statistically non-significant. No differences associated with suture site

*Portions of this paper were presented at the 64th and 65th Annual Meetings of the American Cleft-Palate-Craniofacial Association, Broomfield, Co, April 27, 2007 and Philadelphia, PA, April 18, 2008.

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Conflict of Interest:

The authors have no conflicts of interest to report.

were found. At the oldest age point, both mothers and fathers (but not teachers) generated higher average scores for patients than for controls on scales measuring attention and social problems, with small to medium effects sizes (0.20 to 0.32).

Conclusion—On average toddlers/preschoolers with SSC show behavioral development that is largely indistinguishable from same-aged peers of similar socioeconomic background. The predictive significance of small group differences in attention and social adjustment will be assessed in a follow-up of this cohort at age 7.

Single-suture craniosynostosis (SSC) is the premature fusion of one of the 6 major sutures in the infant calvaria. It has an incidence of approximately 1 in 2000 live births. Infants diagnosed with SSC typically undergo cranial vault surgery in the first year of life, both to minimize skull deformation and to reduce the risk of co-occurring medical problems such as elevated intracranial pressure (ICP) or ocular misalignment.^{1, 2} SSC has been associated with mild delays in development and specific learning disorders in childhood.^{2–4} Although clinical impressions have also suggested elevated rates of mild to moderate behavior problems in this population, there is limited empirical data, with only four previous studies on this topic to our knowledge. In two of these studies, the Child Behavior Checklist (CBCL) was given to children with SSC in hospital-based craniofacial programs.^{5, 6} The third study relied on parent report to assess behavioral problems among 63 children with metopic craniosynostosis evaluated over a 10 year period.⁷ The fourth study featured a population-based cohort in which mothers of 82 children with SSC were interviewed by telephone.⁸ Both CBCL studies found elevated rates of reported behavior problems in the clinical risk range, from 15% to 35% depending on age and CBCL scale. Snyder and Pope⁶ found particular vulnerabilities among children with SSC in social adjustment and attention. Both CBCL studies also found higher rates of problem behaviors among older children, though it is possible that more severely impaired children were more likely to maintain contact with the craniofacial programs from which they were recruited. However, Kelleher et al.,⁷ who retained 96% of their initially identified children, reported a problem rate of 37% including attention deficit disorder, autism, and hyperactivity. They found that 20% of the school age children in their sample required assistance from a classroom aid to manage their behavior. Wong-Gibbons⁸ reported the lowest rate of impairment (13% of mothers reported “emotional or behavioral delays” in children mostly under 5), although no details were provided.

Consistent with prior studies of behavioral adjustment in children with significant medical problems,^{9, 10} these initial studies suggest a modestly higher level of maladjustment among children with SSC. However, several methodological limitations reduce the certainty of this impression. No study of SSC has yet included a control group nor examined children at more than one time point. These are important considerations as behavior problems are correlated with socio-demographic factors¹¹ and are only moderately stable over time.¹² The previous studies relied solely on maternal reports and different informants can provide very different perspectives on child functioning (e.g., mothers versus fathers; teachers versus parents), with moderate correspondence among them.^{13, 14}

The present study examined children with and without SSC who were identified in infancy and whose behaviors were assessed by multiple informants (mothers, fathers, and teachers). Behavioral reports were gathered at ages 19 and 37 months on average (which followed reconstructive surgery for patients), using the CBCL and, for those children in child care or preschool, the Caregiver-Teacher Report Form (CTRF).¹⁵

Based on the previously cited studies, we hypothesized that children with SSC would demonstrate more behavioral and emotional problems than children without SSC, as reported by all informants, and that such differences would increase with age. As suggested

by Snyder and Pope's⁶ school-aged data, we also hypothesized that children with SSC would show more problems than controls on CBCL and CTRF subscales related to attention and social adjustment [captured in this age range by the attention, anxiety/depression and withdrawn syndrome scales and the Diagnostic and Statistical Manual of the Mental Disorders (DSM) attention deficit hyperactivity disorder (ADHD) scale]. The DSM based scale assessing pervasive developmental problems was also of interest given previously cited linkages between autistic traits and craniofacial malformations,¹⁶ particularly infants with isolated fusion of the metopic suture.¹⁷ Finally we conducted exploratory analyses of differences among SSC diagnostic subgroups (e.g., sagittal versus metopic), an issue not addressed by previous investigators.

METHOD

Sample

The participants were 232 patients with SSC and 235 matched controls for whom questionnaire data were available from one or both assessment visits. All participants were recruited through the Infant Learning Project, a multi-site, longitudinal case-control study of neurobehavioral development in children with SSC.³ Participants were enrolled in the study between Jan 2002 and Dec of 2006 after informed consent had been obtained from their parents. The study was approved by the institutional review boards (IRB) from each participating center: Seattle Children's Hospital; Children's Memorial Hospital and Northwestern University in Chicago; Children's Healthcare of Atlanta, St. Louis Children's Hospital; University of Illinois in Chicago (UIC), the University of Chicago (UC) and Children's Hospital of Philadelphia (CHOP). Patients from the UIC and UC and patients and matching control infants from CHOP were referred to the Northwestern University research team for evaluation.

Patients—Infants with SSC were referred to the project at the time of diagnosis by the treating surgeon or pediatrician. Infants were eligible if they: (1) had sagittal, metopic, unilateral coronal, or unilateral lambdoid craniosynostosis confirmed by computed tomography scans; (2) had yet to undergo cranial vault surgery and (3) were 30 months of age or younger at the time of recruitment. Infants were excluded for: 1) prematurity (<34 weeks gestation); 2) presence of major medical or neurological conditions (for example, cardiac defects, seizure disorders, cerebral palsy, or other significant health conditions requiring major surgery); 3) presence of three or more extracranial minor malformations as defined by Leppig and coauthors;¹⁸ or 4) presence of major malformations. Twins were eligible to participate in the study if one of them had SSC. A total of 270 patients were enrolled in the parent study, representing 84% of all those eligible. Four children were later deemed ineligible resulting in a sample of 266 children. Fifty-two families declined actively (n = 29) by expressing lack of interest or passively (n = 23) by not responding to attempts to contact them.

Controls—Infants in the control group had no known craniofacial condition and did not meet any of the exclusionary criteria for patients described above. We recruited control infants who were generally similar to patients, taking into consideration: 1) age, 2) sex, 3) family socioeconomic status within the same Hollingshead 4-factor classification category¹⁹ and 4) ethnicity. A pool of 581 control group participants were recruited through pediatric practices, birthing centers and announcements in newsletters and/or other publications of interest to parents of newborns. The 259 originally enrolled control group participants represented 44% of all those who were eligible. Those not enrolled were mostly infants who "aged out" of the project before they could match to an enrolled case (76% of interested controls). Twelve percent of eligible controls did not respond when contacted after a match

was made. Other reasons for non-participation included: time (4%), distance (3%), lack of interest (3%), and confidentiality concerns (2%).

Measures

Child Behavior Checklist 1½ to 5 (CBCL) and Caregiver-Teacher Report Form (CTRF).¹⁵—The empirically-derived CBCL and CTRF summarize parent or teacher provided information on child behavior problems on two “broadband” scales: Internalizing and Externalizing; seven “syndrome” subscales: Emotionally Reactive, Anxious/depressed, Somatic Complaints, Withdrawn, Sleep problems, Attention problems and Aggressive problems; and five scales that reflect selected diagnostic categories from the DSM-IV:²⁰ Affective, Anxiety, Pervasive Developmental, Attention deficit/hyperactivity and Oppositional Defiant Problems (See Table 1 for a description of scales). The CBCL and CTRF have 99 items that are rated on 3-point rating scales: 0 = not true (as far as you know), 1 = somewhat or sometimes true, and 2 = very true or often true. Items from the CBCL and CTRF are nearly identical, with some rewording of CBCL items on the CTRF to accommodate childcare or preschool situations. A total problem scale provides a summary score for all problems endorsed. On all scales, a higher score indicates more problems. The validity and reliability of both instruments have been well-demonstrated in many previous studies.²¹ In addition, two meta-analyses have assessed agreement on behavior and emotional problems for children based on different reporters including agreement between two parents and agreement between parents and teachers.^{13,14} Both found relatively high correlations between parents (on average $r = 0.60-0.70$), but lower correlations between parents and teachers (on average $r = 0.20-.30$).

Assessment

A CBCL was completed at Time 1 (T1) when children were ~19 months by 436 mothers (219 patients and 217 controls) and 371 fathers (177 patients and 194 controls); and at Time 2 (T2) when children were ~37 months by 361 mothers (175 patients and 186 controls) and 303 fathers (142 patients and 161 controls). Among these participants, 98 children (47 patients and 51 controls) had a CTRF completed by a teacher or daycare provider at T1 and 120 children (48 cases and 72 controls) had a CTRF completed by a teacher or daycare provider at T2.

Procedures

The CBCL was mailed to the parents before the T1 and T2 assessments with a request that they bring their completed questionnaire to the child’s neurodevelopmental assessment. One parent (generally the mother) was interviewed to update the child’s medical and early intervention history and to determine if the child was currently in preschool or cared for by an adult other than parents for any part of the week (or had been since the previous evaluation). Following IRB-approved protocols for each institution, parents of children in preschool or childcare were asked to have the child’s teacher or other caregiver complete the CTRF.

Data Analyses

We used descriptive statistics to summarize demographic characteristics separately for children with and without SSC. To examine for attrition bias, we compared the demographic characteristics of participants and non-participants at T1 (i.e., those who were enrolled in the study, but lost to follow-up before completing T1 questionnaires). We also examined the demographics and T1 behavioral outcomes of participants versus those lost to follow-up between T1 and T2. Finally, we examined the correlation between informants at both visits using Pearson’s r for the Externalizing, Internalizing, and Total Problems scores.

Group differences on broadband and total scores—Means and standard deviations were calculated separately by group for all measures. We used linear regression analyses to compare outcomes for children with and without SSC, adjusting for study site, children's age, sex, race/ethnicity, and family socioeconomic status.¹⁹ In addition to *p*-values, we estimated the magnitudes of group differences using standardized mean difference effect sizes (ES).

To examine the effects of missing data, we repeated these analyses using inverse probability weighting (IPW).²² These analyses place extra weight on participants who are retained in the study who have similar characteristics to those lost to follow-up. We first identified demographic and clinical predictors of attrition, case status, and behavioral outcomes and then used these variables to predict the probability of being observed (i.e. participating). Group comparisons were then re-run for each outcome, with analyses weighted by the inverse of the probability of being observed to account for dropout.

To evaluate changes in the magnitude of group differences across the two age points, we examined the interaction between SSC status and age using generalized estimating equations (GEE),²³ which accounts for repeated observations within subjects, adjusting for age at each visit as a time-varying covariate. An advantage of GEE, relative to analysis of variance, is that GEE retains subjects who have missing data at one of the two time points. Due to limited data and variability in the informants on the CTRF at T1 versus T2 (e.g., children changing teachers or daycare providers), we only conducted these analyses for parent report on the CBCL.

We also examined differences among patients as a function of diagnostic subgroup (i.e., based on location of suture fusion), using linear regression analyses with diagnosis as an independent variable and the same covariates listed previously to control for demographic confounds. Children with sagittal synostosis were treated as the reference group, and we estimated overall *p*-values for diagnostic group using a Wald statistic.

We also used logistic regression to calculate odds ratios (OR) to determine whether patients were more likely than controls to score above established clinical cut-offs on the CBCL and CTRF broadband and total scores (defined as T-scores ≥ 60) based on the reports of any single informant (mother, father or teacher), either parent, or the combination of all three informants.

Exploratory analyses of group differences on syndrome scales—Finally, to examine group differences in specific behavioral domains, we used adjusted linear regression to calculate ES and *p*-values for the CBCL and CTRF syndrome and DSM subscales. Given the exploratory nature of these analyses and the potential for increased Type I errors due to multiple comparisons, we examined ES and *p*-values descriptively, rather than viewing *p*-values as dichotomous outcomes.

Analyses were completed by using the STATA SE 10.0 software package.²⁴

RESULTS

Sample demographic characteristics are summarized in Table 1. Partial or complete data were available for 223 children with SSC and 221 unaffected controls at T1, representing 84% and 86% of the original cohorts, respectively. At T2, partial or complete data were available for 180 children with SSC and 190 unaffected controls (70% and 74% of the original cohorts, respectively). Approximately one third of patients and controls were female and >70% were of white, non-Hispanic race/ethnicity. Patients were less likely to come from

upper socioeconomic (SES) backgrounds compared to controls (Hollingshead categories I-II; 61% cases, 79% controls). Among patients, 102 had sagittal synostosis, 53 had metopic synostosis, 56 had right or left unilateral coronal synostosis, and 12 had lambdoid synostosis.

Compared to participants, non-participants (i.e., children who were enrolled in the study but lost to follow-up prior to T1) were less likely to be white (61% non-participants, versus 74% participants) and less likely to be from a middle to upper SES family (46% non-participants, versus 71% participants). Differences were negligible based on gender (64% non-participants were male, versus 65% participants). Across study sites, the rate of non-participation at T1 ranged from 14% to 19%. Similarly, at T2 non-participants were less likely to be white (65% non-participants, versus 74% participants) and less likely to be from a middle to upper SES family (52% non-participants versus 73% participants). Differences were again negligible based on gender (65% non-participants were male, compared to 61% participants) and study site (non-participation rate at T2 ranged from 22% to 40%). Differences in CBCL scores between T2 participants and non-participants were small (differences in T-scores = 0.0 to 0.8 on broad band scales). Compared to participants, non-participants received higher scores at T1 based on teacher report on the CTRF (differences in T-scores = 1.3 to 2.8 on broad band scales). At T1 and T2, correlations between mother and father reports were moderate ($r = 0.54$ to 0.62 at T1; 0.60 to 0.61 at T2). Correlations between parent and teacher reports were generally low at both assessments ($r = 0.11$ to 0.21 at T1; 0.14 to 0.38 at T2).

Unadjusted mean standard scores and standard deviations from the CBCL and CTRF for children with and without single suture craniosynostosis are provided in Table 3. All mean standard scores are within the average range for both groups.

Group differences on broadband and total behavior problem scores

Mothers' reports—Compared to controls, children with SSC received higher CBCL Internalizing scores reported by mothers at T1 ($ES = 0.19$, $p = .046$) (Table 3). Differences on the 18 month Externalizing and Total Problems scales were minimal, with wide confidence intervals. At T2, mothers of children with SSC again reported slightly more behavior problems than mothers of controls, though these differences were variable and small in magnitude (Table 3). These findings were virtually unchanged with the application of IPW (Internalizing: $ES = 0.19$, $p = 0.048$; Externalizing: $ES = 0.02$, $p = 0.841$; Total: $ES = 0.08$, $p = 0.450$). Interactions between group (SSC vs. control) and age (19 vs. 37 months) were small and not statistically significant (p -values = 0.217 to 0.815). Differences by SSC diagnostic sub-group were small and were not statistically significant at T1 ($p = 0.552$ to 0.688) or T2 ($p = 0.383$ to 0.731).

Fathers' reports—Group differences based on fathers' report at T1 were negligible on all global scales. At T2 children with SSC had slightly more behavior problems on all scales, though these differences were small and variable (Table 4). The magnitude of these group differences was slightly larger at T2 after applying IPW (Internalizing: $ES = 0.16$, $p = 0.126$; Externalizing: $ES = 0.02$, $p = 0.814$; Total: $ES = 0.04$, $p = 0.711$). Group $\times$ time interactions were small in magnitude and not statistically significant ($p = 0.690$ to 0.961). Differences by diagnostic subgroup were small and were not statistically significant at either time point (T1: $p = 0.488$ to 0.680 ; T2 $p = 0.100$ to 0.258).

Teacher or caregiver reports—Few children received out-of-home childcare at either age point, and CTRF data were only available for a subset of children in both groups (47 patients and 51 controls at T1; 48 patients and 72 controls at T2; 21 patients and 26 controls

at both time points). At T1 children with SSC had more behavior problems than unaffected controls on all scales of the CTRF (ES = 0.32 to 0.43), though these differences were imprecise with p-values ranging from 0.063 to 0.133 (Table 3). All group differences at T2 were negligible. Differences by location of suture fusion were negligible and were not statistically significant at either time point (T1: $p = 0.291$ to 0.452 ; T2: $p = 0.446$ to 0.557).

Group differences in scores above clinical threshold—Relatively few children in either group scored above the established clinical cut-off based on scores from any of the three reporters (Table 5). After adjusting for matching factors, patients were more likely than controls to score above the clinical threshold on the CTRF Externalizing scale (6.4% versus 0%; because there were no controls above the threshold, an OR could not be calculated) at T1. At T2, patients were more likely than controls to score above the clinical cut-offs on the CBCL Internalizing and Externalizing scales generated by fathers [OR = 2.37 to 2.58, $p = 0.028$ to 0.065] and on the Internalizing, Externalizing, and Total scales when considering the report of either parent (OR = 1.82 to 2.07, $p = 0.047$ to 0.091). Differences were small and were not statistically significant based on caregiver/teacher report at T2 (OR = 0.76 to 1.96, $p = 0.266$ to 0.768).

Group differences on syndrome and DSM scales

Mothers' reports—At T1 children with SSC showed more frequent somatic complaints than did controls (ES = 0.31, $p = 0.001$; see Figure 1). At T2, group differences were most apparent on the attention problems scale (ES = 0.20, $p = 0.063$) and DSM attention deficit hyperactivity disorder scale (ES = 0.31, $p = 0.006$), and for the DSM pervasive developmental problems scale (ES = 0.20, $p = 0.053$).

Fathers' reports—Group differences at T1 were negligible in nearly all domains, though children with SSC were somewhat less likely than controls to have sleep problems (ES = -0.20 , $p = 0.055$; see Figure 1). At T2, findings were more consistent with mothers' report: fathers of children with SSC reported that their children had more problems than controls on the following syndrome and DSM scales, respectively: anxiety/depression (ES = 0.24, $p = 0.037$) and attention problems (ES = 0.21, $p = 0.079$); DSM anxiety (ES = 0.21, $p = 0.073$), DSM attention deficit hyperactivity disorder (ES = 0.32, $p = 0.007$), and DSM pervasive developmental problems (ES = 0.21, $p = 0.078$).

Teachers or daycare reports—Children with SSC had more problems than controls across several domains at T1, though these differences were variable and had large confidence intervals. The largest differences were observed on the withdrawn scale (ES = 0.43, $p = 0.063$; see Figure 1), and on the attention problems (ES = 0.41, $p = 0.059$) and DSM attention deficit hyperactivity disorders scale (ES = 0.41, $p = 0.048$). At T2, all differences were small and statistically non-significant (p -values = 0.286 to 0.938).

DISCUSSION

Recent studies have suggested that children with SSC have elevated risk for emotional and behavioral problems, based on comparisons of these children with behavior checklist norms.^{5, 6} However, the present study, which is the first to include a demographically-matched control group, found little support for this hypothesis, at least among very young children. Although average CBCL/CTRF broadband and total scores for all informants were consistently higher for children with SSC, these differences were small and unreliable. The percentages of children falling into the "clinical range" defined by the CBCL and CTRF (T scores ≥ 60) were also generally higher for patients than controls, but OR were mostly imprecise and group differences statistically non-significant. A notable exception was the

relative percentage of children with high externalizing scores from either parent at T2, with nearly twice as many patients as controls receiving scores in this range (14.5% vs. 7.6%, respectively).

We also found little evidence for the hypothesis that behavior problems for children with SSC would worsen over time in relation to controls. This finding may be specific to the narrow age range we examined (toddler to preschool years), in which there is relatively little change in social and academic expectations. Similar to recent findings for children with congenital heart disease, the preschool years may represent a 'silent period' with regard to significant psychological problems for children with SSC.²⁵ In the previously reviewed studies more problems were seen at elementary school age, a time in which there is usually a significant increase in the social and academic demands placed on children.

Exploratory analyses of diagnostic subgroups among children with SSC found no evidence of behavioral differences associated with location of the isolated cranial suture.

The picture generated by these findings--of overall good adjustment for children with SSC -- is slightly altered by examination of two specific areas of functioning (social and attention problems), which we targeted because of findings from previous research.^{5-7, 16, 17} CBCL and CTRF items that capture social difficulties are found on two internalizing syndrome scales (withdrawal and anxiety/depression) and two DSM-IV scales (anxiety and pervasive developmental problems; PDD). These items reference eye contact, reciprocal language, and fearfulness in interpersonal situations. Attention problems on both instruments are indexed by a syndrome scale of the same name and the DSM-IV attention deficit hyperactivity (ADHD) scale; both scales describe behaviors commonly associated with ADHD (e.g., can't concentrate, restless or hyperactive). There were few meaningful differences on these scales at T1, but by T2 both mothers and fathers (but not teachers) were reporting higher average scores for patients than did parents of controls on the scales related to anxiety and attention, with generally small to medium effects sizes (.20 to .31). The predictive significance of these small differences is presently unclear, but may relate to the sensitivity and specificity of these scales for detecting subtle maturational differences in attention and socialization that typically occur during this time frame. These issues will be addressed in a follow-up assessment of this cohort at age 7, which is currently underway.

Methodologically, this study represents an advance over previous work in that it included a well-matched control group, longitudinal data points and multiple informants. A significant limitation is the differential loss of participants across time from lower SES backgrounds and from minority groups, not unusual in longitudinal studies.²⁶ However, we used inverse probability weighting to determine whether this bias substantially altered our findings; there was no evidence that it did so. Another limitation is the relatively few children in our sample who attended out-of-home daycare or preschool. This constrained our ability to examine nonparent caregivers' reports of behavioral adjustment, which tend to have better predictive validity.²⁷

The overall results of this study suggest that children with SSC on average show behavioral and emotional development that is largely indistinguishable from same-aged peers of similar socioeconomic background, at least during the very earliest years in which behavioral adjustment can be meaningfully assessed. Although this is reassuring for parents, these findings, based on average case-control group differences, should not obscure preventative opportunities for the minority of children who are struggling. For example, by age 3 nearly 18% of our children with SSC exceeded the clinical cutoff on the internalizing or externalizing problem scale. Given the potential persistence of untreated behavior problems,^{28, 29} the effectiveness of behavioral interventions in early life,³⁰ and the ease of

developmental surveillance for children already followed closely by craniofacial teams, young children with SSC should be routinely screened with a measure like the CBCL, which is a low-cost method of identifying high risk children.

Acknowledgments

We thank the families who have graciously participated in this research. We also thank Sharman Conner, Rebecca Gaither, and Claudia Crilly Bellucci for project coordination and data collection, Kristen Daniels for data analysis; and Diana Prise for data entry and validation.

Sources of Funding:

This work was supported by a grant from the National Institute of Dental and Craniofacial Research (NIDCR grant # R01 DE 13813 awarded to Dr. Speltz).

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Figure 1.

Forest plot presenting adjusted mean differences and effect sizes with 95% confidence intervals (CI) for Child Behavior Checklist (CBCL) and Caregiver-Teacher Report Form (CTRF) syndrome and DSM scores at Time (T) 1 and T2. Analyses adjusted for study site, age (months), socioeconomic status (composite score from the Hollingshead¹⁹, entered as a continuous score), sex, and race/ethnicity (white, non-Hispanic versus non-white or Hispanic)

Table 1

Description of Scores from Child Behavior Checklist^{*} and Caregiver-Teacher Report Form (CTRF)^{*} for Ages 1½ to 5

Composite Scales	Summary Scores
Internalizing Problems	Total of Emotionally Reactive, Anxious/Depressed, Somatic Complaints, and Withdrawn Syndrome Scales
Externalizing Problems	Total of Attention Problems and Aggressive Behavior Syndrome Scales
Total Behavior Problems	Total of all 7 (6 for CTRF) Syndrome Scales
Syndrome Scales	Provide empirically based summary scores of symptoms that tend to occur together
Emotionally Reactive	Mood instability, difficulty handling change, whiny
Anxious/Depressed	Problems with separation, self-consciousness, fearfulness
Somatic Complaints	Problems with eating, bowels, nausea, aches and pains
Withdrawn	Lack of interest in age appropriate behaviors, unresponsive to affection
Sleep Problems ^{**}	Resists bed, frequent nighttime waking, nightmares
Attention Problems	Doesn't focus, wanders away, shifts from one activity to another quickly
Aggressive Behavior	Defiant, gets into frequent fights, hits and bites, temper tantrums
DSM-IV Scales	Symptoms regrouped to fit major diagnostic categories from the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV)
Affective Problems	Symptoms associated with Major Depressive Disorder and Dysthymic Disorder
Anxiety Problems	Symptoms associated with General Anxiety Disorder, Social Anxiety Disorder and Specific Phobia
Pervasive Developmental Problems	Symptoms associated with Autism Spectrum Disorders including Asperger's Syndrome
Attention Deficit/ Hyperactivity Problems	Symptoms associated with inattentive and hyperactive types of attention disorders
Oppositional/Defiant Problems	Symptoms associated with aggression, anger, temper tantrums

^{*} A higher score on each scale indicates more problems

^{**} Not included on CTRF

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Characteristic	Time 1											
	Controls			SSC			Sagittal			Metopic		
	N	%		N	%		N	%		N	%	
Total	191	100.0%		180	100.0%		83	100.0%		41	100.0%	
Sex												
Female	69	36.1%		60	33.3%		19	22.9%		9	22.0%	
Male	122	63.9%		120	66.7%		64	77.1%		32	78.0%	
Months of Age (median, SD)	37.6, 1.0			37.5, 0.8			37.4, 0.9			37.2, 0.6		
Race												
Non-white	54	28.3%		41	22.8%		18	21.7%		10	24.4%	
White	137	71.7%		139	77.2%		65	78.3%		31	75.6%	
SES category¹⁹												
I (high)	56	29.3%		42	23.3%		21	25.3%		8	19.5%	
II	98	51.3%		69	38.3%		31	37.3%		20	48.8%	
III	24	12.6%		42	23.3%		16	19.3%		7	17.1%	
IV	7	3.7%		17	9.4%		9	10.8%		5	12.2%	
V (low)	3	1.6%		8	4.4%		4	4.8%		1	2.4%	
Parent's Marital Status[*]												
One Parent	9	4.7%		13	7.2%		9	10.8%		1	2.4%	
Two Parent	180	94.2%		167	92.8%		74	89.2%		40	97.6%	
Site												
Seattle	70	36.6%		60	33.3%		28	33.7%		13	31.7%	
Chicago	80	41.9%		75	41.7%		23	27.7%		20	48.8%	
St. Louis	18	9.4%		23	12.8%		15	18.1%		3	7.3%	
Atlanta	23	12.0%		22	12.2%		17	20.5%		5	12.2%	

* Parents' marital status data missing for 2 controls and 1 case

Unadjusted T-score means and standard deviations (SD) from Child Behavior Checklist^a and Caregiver/Teacher Report Form^a for children with single suture craniosynostosis (SSC) and controls at Time 1 and Time 2.

Table 3

	Mother			Father			Teacher/Caregiver		
	SSC	Control	SSC	SSC	Control	SSC	SSC	Control	Control
	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean
Time 2 (18 months)									
Composite Scales^b	n = 219	n = 217	n = 177	n = 194	n = 47	n = 51			
Internalizing	44.4 (9.6)	41.8 (9.2)	43.4 (9.3)	41.6 (9.2)	48.4 (8.9)	45.5 (7.7)			
Externalizing	47.0 (9.2)	46.2 (9.3)	45.8 (8.9)	45.1 (9.8)	52.1 (7.9)	49.7 (7.6)			
Total	46.1 (9.6)	44.5 (9.4)	44.8 (9.4)	43.9 (9.8)	51.1 (8.6)	48.2 (8.2)			
Syndrome Scales^c									
Emotionally Reactive	52.2 (4.4)	51.9 (4.1)	52.0 (4.1)	52.0 (4.2)	53.6 (5.6)	52.6 (3.8)			
Anxious/Depressed	51.9 (4.0)	51.3 (3.5)	51.6 (3.4)	51.2 (3.0)	54.3 (5.9)	53.1 (4.2)			
Somatic Complaints	52.5 (4.6)	51.3 (3.1)	52.0 (4.6)	51.5 (3.3)	51.6 (4.2)	50.6 (2.0)			
Withdrawn	52.5 (5.0)	51.9 (4.5)	52.1 (4.9)	51.8 (3.8)	53.0 (5.0)	51.3 (2.1)			
Sleep Problems	53.1 (5.7)	53.3 (5.8)	52.3 (4.4)	53.1 (4.9)	NA	NA			
Attention Problems	53.4 (5.0)	52.9 (4.9)	52.8 (4.5)	52.8 (4.7)	53.6 (5.3)	52.3 (3.5)			
Aggressive Behavior	52.4 (4.3)	52.4 (4.8)	52.0 (3.9)	52.1 (4.9)	54.7 (5.5)	53.4 (5.4)			
DSM-IV Scales^c									
Affective Problems	52.9 (4.7)	52.9 (5.1)	52.4 (4.2)	53.0 (4.9)	53.2 (5.1)	53.3 (4.3)			
Anxiety Problems	52.2 (5.1)	51.6 (4.1)	51.6 (4.3)	51.4 (3.3)	55.1 (6.4)	53.8 (5.3)			
Pervasive Developmental Problems	52.6 (5.3)	51.8 (4.5)	52.2 (4.8)	52.0 (4.3)	53.3 (5.1)	52.1 (3.3)			
Attention Deficit/Hyperactivity Problems	53.5 (4.3)	53.1 (4.9)	53.2 (4.6)	53.1 (4.8)	54.1 (4.9)	52.7 (3.8)			
Oppositional/Defiant Problems	52.1 (3.9)	51.9 (4.0)	51.7 (3.6)	51.9 (4.1)	54.4 (5.5)	53.2 (5.1)			
Time 3 (36 months)									
Composite Scales^b	n = 175	n = 185	n = 142	n = 160	n = 48	n = 71			
Internalizing	45.1 (9.6)	43.6 (9.7)	44.9 (10.5)	43.0 (9.0)	46.4 (10.1)	48.7 (10.9)			
Externalizing	47.4 (9.4)	45.4 (9.8)	46.5 (9.8)	44.4 (9.4)	49.2 (10.3)	49.6 (9.0)			

	Mother				Father				Teacher/Caregiver			
	SSC		Control		SSC		Control		SSC		Control	
	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)
Total	47.0	(9.5)	44.6	(9.5)	46.0	(10.2)	43.8	(9.4)	47.4	(11.5)	48.4	(11.1)
Syndrome Scales^c												
Emotionally Reactive	52.4	(4.4)	52.4	(4.8)	52.6	(4.9)	51.8	(3.7)	53.1	(4.9)	53.7	(6.6)
Anxious/Depressed	51.9	(4.2)	51.4	(3.6)	52.1	(4.1)	51.2	(3.1)	52.9	(4.7)	54.0	(5.2)
Somatic Complaints	52.9	(5.2)	52.4	(4.5)	52.6	(4.9)	51.9	(4.1)	52.0	(4.6)	52.3	(5.3)
Withdrawn	53.0	(4.7)	52.4	(4.4)	53.3	(5.7)	52.8	(4.3)	53.1	(5.2)	53.9	(6.0)
Sleep Problems	54.6	(7.0)	54.0	(5.6)	54.4	(7.9)	53.9	(5.6)	NA	NA	NA	NA
Attention Problems	53.1	(4.3)	52.4	(4.8)	52.5	(3.9)	51.9	(3.6)	53.6	(7.6)	53.6	(5.9)
Aggressive Behavior	52.8	(4.5)	52.2	(5.0)	52.7	(5.5)	52.0	(4.2)	54.1	(6.2)	53.5	(5.1)
DSM-IV Scales^c												
Affective Problems	52.9	(4.4)	53.3	(5.1)	53.2	(4.7)	53.0	(5.1)	53.0	(4.8)	54.4	(6.8)
Anxiety Problems	52.6	(5.5)	51.7	(4.3)	52.9	(5.6)	51.9	(4.1)	53.0	(5.2)	53.7	(5.3)
Pervasive Developmental Problems	53.5	(6.0)	52.6	(5.0)	53.9	(6.1)	52.6	(4.5)	53.2	(5.2)	54.5	(7.3)
Attention Deficit/Hyperactivity Problems	53.2	(4.7)	51.9	(4.0)	52.9	(4.6)	51.7	(3.6)	53.5	(6.5)	53.2	(5.1)
Oppositional/Defiant Problems	52.9	(4.6)	52.7	(4.5)	52.9	(5.1)	52.3	(4.1)	53.6	(5.0)	54.1	(5.7)

^a A higher T Score indicates more problems on all CBCL and CTRF scales. Composite T scores >59, and Syndrome and DSM scores >64 are clinically meaningful.

^b Composite Scale T Scores have a mean of 50 and standard deviation of 10.

^c Syndrome and DSM Scale T Scores are truncated at 50 and do not reflect variation in scores below 50; raw scores were used for statistical analysis as recommended by scale authors.

Table 4

Adjusted group differences^a in raw scores on the Child Behavior Checklist (CBCL) and Caregiver-Teacher Report Form (CTRF) scores for children with single suture craniosynostosis (SSC) versus controls at Time 1 and Time 2.

Time 1			
Measure	Adj. Diff (95% CI)	EffectSize (95% CI)	p-value
CBCL- Mother			
<i>N = 219 SSC, 217 Controls</i>			
Internalizing	0.87 (0.02, 1.73)	0.19 (0.00, 0.38)	0.046
Externalizing	0.19 (-1.10, 1.48)	0.03 (-0.16, 0.22)	0.772
Total Problems	1.28 (-1.73, 4.29)	0.08 (-0.11, 0.27)	0.405
CBCL- Father			
<i>N = 177 SSC, 194 Controls</i>			
Internalizing	0.54 (-0.36, 1.43)	0.12 (-0.08, 0.32)	0.242
Externalizing	0.16 (-1.21, 1.54)	0.02 (-0.18, 0.23)	0.814
Total Problems	0.29 (-2.98, 3.56)	0.02 (-0.18, 0.22)	0.863
CTRF			
<i>N = 47 SSC, 51 Controls</i>			
Internalizing	2.13 (-0.09, -0.09)	0.43 (-0.02, 0.89)	0.063
Externalizing	2.90 (-0.85, -0.85)	0.32 (-0.09, 0.73)	0.133
Total Problems	6.21 (-0.72, -0.72)	0.38 (-0.04, 0.80)	0.082
Time 2			
Measure	Adj. Diff (95% CI)	EffectSize (95% CI)	p-value
CBCL - Mother			
<i>N = 175 SSC, 186 Controls</i>			
Internalizing	0.64 (-0.43, 1.72)	0.12 (-0.08, 0.33)	0.243
Externalizing	1.21 (-0.27, 2.69)	0.17 (-0.04, 0.39)	0.111
Total Problems	3.38 (-0.09, 6.84)	0.21 (-0.01, 0.42)	0.057
CBCL - Father			
<i>N = 142 SSC, 161 Controls</i>			
Internalizing	1.07 (-0.11, 2.26)	0.21 (-0.02, 0.44)	0.076
Externalizing	1.30 (-0.35, 2.95)	0.18 (-0.05, 0.42)	0.123
Total Problems	3.58 (-0.40, 7.56)	0.21 (-0.02, 0.44)	0.079
CTRF			
<i>N = 48 SSC, 72 Controls</i>			
Internalizing	-0.73 (-3.17, -3.17)	-0.11 (-0.49, 0.26)	0.561
Externalizing	0.41 (-3.64, -3.64)	0.04 (-0.35, 0.42)	0.842
Total Problems	-0.08 (-8.30, -8.30)	0.00 (-0.39, 0.38)	0.985

^aAnalyses adjusted for study site, age (months), socioeconomic status (composite score from the Hollingshead¹⁹, entered as a continuous score), sex, and race/ethnicity (white, non-Hispanic versus non-white or Hispanic).

Table 5

Proportion of children with single suture craniosynostosis (SSC) versus controls scoring in the “borderline” or “clinical” range^a on the Child Behavior Checklist (CBCL) and Caregiver-Teacher Report Form (CTRF) at Time 1 and Time 2.

	Time 1		Adj. OR ^b (95% CI)	p-value
	SSC	Control		
CBCL- Mother				
<i>N = 219 SSC, 217 Controls</i>				
Internalizing	17 (7.8%)	10 (4.6%)	1.55 (0.63, 3.81)	0.343
Externalizing	17 (7.8%)	17 (7.8%)	0.85 (0.39, 1.86)	0.683
Total Problems	16 (7.3%)	18 (8.3%)	0.77 (0.34, 1.71)	0.518
CBCL- Father				
<i>N = 177 SSC, 194 Controls</i>				
Internalizing	10 (5.6%)	9 (4.6%)	1.08 (0.41, 2.84)	0.875
Externalizing	11 (6.2%)	18 (9.3%)	0.59 (0.25, 1.36)	0.214
Total Problems	11 (6.2%)	13 (6.7%)	0.85 (0.35, 2.10)	0.728
CBCL - Either Parent				
<i>N = 221 SSC, 221 Controls</i>				
Internalizing	20 (9.0%)	18 (8.1%)	1.06 (0.52, 2.16)	0.883
Externalizing	22 (10.0%)	27 (12.2%)	0.75 (0.40, 1.43)	0.387
Total Problems	21 (9.5%)	24 (10.9%)	0.87 (0.44, 1.73)	0.698
CTRF				
<i>N = 47 SSC, 51 Controls</i>				
Internalizing	3 (6.4%)	0 (--)	--	--
Externalizing	10 (21.3%)	7 (13.7%)	1.82 (0.55, 6.04)	0.328
Total Problems	8 (17.0%)	6 (11.8%)	1.74 (0.48, 6.33)	0.401
Parent or Teacher				
<i>N = 223 SSC, 221 Controls</i>				
Internalizing	22 (9.9%)	18 (8.1%)	1.21 (0.60, 2.43)	0.595
Externalizing	31 (13.9%)	34 (15.4%)	0.89 (0.51, 1.54)	0.667
Total Problems	29 (13.0%)	29 (13.1%)	1.06 (0.58, 1.92)	0.853
	Time 2		OR ^b (95% CI)	p-value
	SSC	Control		
CBCL - Mother				
<i>N = 175 SSC, 186 Controls</i>				
Internalizing	16 (9.1%)	11 (5.9%)	1.45 (0.64, 3.29)	0.369
Externalizing	18 (10.3%)	10 (5.4%)	1.78 (0.75, 4.21)	0.189
Total Problems	17 (9.7%)	12 (6.5%)	1.58 (0.71, 3.53)	0.263
CBCL- Father				
<i>N = 142 SSC, 161 Controls</i>				
Internalizing	18 (12.7%)	9 (5.6%)	2.59 (1.12, 6.02)	0.026

	Time 1		Adj. OR ^b (95% CI)	p-value
	SSC	Control		
Externalizing	15 (10.6%)	8 (5.0%)	2.38 (0.96, 5.93)	0.062
Total Problems	14 (9.9%)	9 (5.6%)	2.02 (0.82, 4.97)	0.127
CBCL - Either Parent				
<i>N = 179 SSC, 186 Controls</i>				
Internalizing	26 (14.5%)	16 (8.6%)	1.85 (0.95, 3.63)	0.071
Externalizing	26 (14.5%)	14 (7.5%)	2.08 (1.01, 4.27)	0.046
Total Problems	25 (14.0%)	16 (8.6%)	1.83 (0.91, 3.65)	0.089
CTRF				
<i>N = 48 SSC, 72 Controls</i>				
Internalizing	5 (10.4%)	9 (12.5%)	0.76 (0.21, 2.78)	0.676
Externalizing	8 (16.7%)	10 (13.9%)	1.17 (0.41, 3.32)	0.768
Total Problems	9 (18.8%)	8 (11.1%)	1.96 (0.60, 6.40)	0.266
Parent or Teacher				
<i>N = 180 SSC, 191 Controls</i>				
Internalizing	30 (16.7%)	23 (12.0%)	1.45 (0.80, 2.64)	0.224
Externalizing	33 (18.3%)	21 (11.0%)	1.75 (0.95, 3.23)	0.074
Total Problems	31 (17.2%)	22 (11.5%)	1.64 (0.89, 3.03)	0.114

^a A higher T Score indicates more problems on all CBCL and CTRF scales. Composite T scores >59 are borderline or clinically significant.

^b Analyses adjusted for study site, age (months), socioeconomic status (composite score from the Hollingshead¹⁹, entered as a continuous score), sex, and race/ethnicity (white, non-Hispanic versus non-white or Hispanic)