MEMORY AND RESPONSE INHIBITION IN YOUNG CHILDREN WITH SINGLE-SUTURE CRANIOSYNOSTOSIS

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Abstract

Using two versions of the A-not-B task, memory and response inhibition were assessed in 17- to 24-month-old children with surgically corrected single-suture craniosynostosis (cases) and unaffected children (controls). Children's development and language were initially assessed on average at 6–7 months of age and again at this second visit. Cases and controls performed at equivalent levels on average, with cases performing slightly better than controls on several of the variables measured. However, fewer cases than controls were able to complete the more challenging of the two tasks, which may have predictive significance for later functioning. Children's age and cognitive ability were related to successful performance on the A-not-B task. Among cases, age of cranioplastic surgery was unrelated to performance. Our findings suggest that children with single-suture craniosynostosis show normal development of visual memory and response inhibition in the age range studied here.

Keywords

single-suture craniosynostosis; neuropsychological function; visual attention; memory; inhibitory control

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INTRODUCTION

Single-suture craniosynostosis (SSC) is a congenital anomaly in which there is premature fusion of a single cranial suture: metopic, sagittal, right or left coronal, or right or left lambdoid. The prevalence of any one of these fused sutures is approximately 1 in 2,000 live births (Shuper, Merlob, Grunebaum, & Reisner, 1985; Singer, Bower, Southall, & Goldblatt, 1999). One hypothesized correlate or consequence of SSC is brain deformation with associated neurodevelopmental impairment (Kapp-Simon, Speltz, Cunningham, Patel, & Tomita, 2007; Speltz, Kapp-Simon, Cunningham, Marsh, & Dawson, 2004). The possibility of such impairment is one of several reasons for surgically releasing the fused suture as early as possible in infancy (Marsh, Jenny, Galic, Picker, & Vannier, 1991; Marsh & Vannier, 1986; Renier, Lajeunie, Arnaud, & Marchac, 2000).

On global measures of development (e.g., Bayley Scales of Infant Development-Second Edition [BSID-II]; Bayley, 1993), infants and young children with SSC have shown mild delays, about a quarter to a half standard deviation lower than matched controls (Speltz et al., 2007; Starr et al., in press). Age of surgery has not consistently shown the hypothesized inverse association with neurodevelopmental outcomes (due to the presumed mediating effects of earlier reduction of intracranial pressure; Renier & Marchac, 1988), and there is little evidence for improving neurodevelopmental status following surgery (Kapp-Simon, 1994, 1998; Kapp-Simon, Figueroa, Jocher, & Schafer, 1993; Mathijssen, Arnaud, Lajeunie, Marchac, & Renier, 2006; Speltz, Endriga, & Mouradian, 1997; Starr et al., in press).

Despite having average or near average global IQ, a sizable proportion of older children with SSC (35% to 50%) has shown some type of neurocognitive or neurobehavioral impairment, such as a learning disability, language impairment, or attention deficit (Becker et al., 2005; Bottero, Lajeunie, Arnaud, Marchac, & Renier, 1998; Kapp-Simon, 1998; Rozelle, Marty-Grames, & Marsh, 1995; Shimoji, Shimabukuro, Sugama, & Ochiai, 2002; Shipster et al., 2003). This suggests that the global delays found among infants and toddlers with SSC may develop into more specific forms of impairment in later years, such as a learning/language disability. Previous studies of infants and young children with SSC have focused exclusively on global measures, however, with no assessment, to our knowledge, of more specific areas of functioning (e.g., memory, attention/planning, inhibitory control). Thus, there may be specific functional deficits during infancy that have yet to be identified and, unlike global development, are related to surgery age.

It is reasonable to hypothesize that the effects of SSC on brain development are relatively specific. Preliminary evidence from neuroimaging studies of infants with SSC suggests that single-suture fusions are associated with morphologic abnormalities in brain structure including small frontal lobes, displacement of the lateral ventricles, and compressed corpus callosum (Aldridge et al., 2005; Aldridge, Marsh, Govier, & Richtsmeier, 2002; Bottero et al., 1998; Shimoji et al., 2002). In children without SSC, these neuroanatomical regions have been implicated in the development of learning, language, and attention disorders (Castellanos et al., 2002; Hynd et al., 1995; Leonard et al., 2002; Shaywitz et al., 2002). For example, frontal lobe abnormalities have been linked to deficits in executive functions that, in preliminary studies, have been associated with SSC in school-age children (Da Costa et al., 2006; Magge, Westerveld, Pruzinsky & Persing, 2002).

The current study assessed specific neuropsychological functions in 17- to 24-month-old children with SSC using two versions of the delayed response “A not B” (AB) paradigm. The AB task was originally developed by Piaget (1954) and has been used with both typically developing infants (e.g., Bjork & Cummings, 1984; Diamond & Goldman-Rakic, 1989) and those with developmental delays (Dawson, Meltzoff, Osterling, & Rinaldi, 1998;

Dawson et al., 2002; Diamond, Prevor, Callender, & Druin, 1997; Yerys, Hepburn, Pennington, & Rogers, 2006). Although believed to tap a number of neuropsychological functions (see Smith, Thelen, Titzer, & McLin, 1999, for a review), success on the task depends primarily on two early emerging skills: (1) visual working memory, and (2) inhibition of a prepotent response (Diamond, 1985, 1988, 1990; Diamond, Crittenden, & Neiderman, 1994; Munakata, 1998; Munakata, McClelland, Johnson, & Siegler, 1997). Typically developing infants can solve the AB task successfully by 10–12 months of age. However, under certain task conditions, such as moving a hidden object (called "invisible displacement"), longer delays, highly similar AB locations, and increasing number of A trials, typical children up to 3 years of age will continue to show perseverative reaching to the A (first) location (called the "AB error"; Smith et al., 1999).

This study tested the hypothesis that 17- to 24-month-old children with SSC would perform more poorly than similarly aged, unaffected children on both the AB task and a more difficult version featuring invisible displacement (ABID). We also explored whether task performance would vary as a function of the specific suture fused (e.g., sagittal vs. metopic). To address the hypothesis that earlier surgery might reduce the risk of deficit in specific neuropsychological functions, we examined associations between age of surgery and postsurgery performance on the AB and ABID tasks. Finally, given the clinical significance of young children's test-interfering behaviors (Mantynen, Poikkeus, Ahonen, Aro, & Korkman, 2001; Roth, Eisenberg, & Sell, 1984; Speltz, DeKlyen, Calderon, Fisher, & Greenberg, 1999), the test behaviors of participants were coded to assess for case-control differences.

METHODS

Participants

Participants included two groups of 17- to 24-month-old toddlers being followed in a longitudinal study of SSC (Speltz et al., 2007; Starr et al., in press): 200 with SSC and 149 unaffected children. Families were referred at the time of diagnosis by the treating physician. Infants were given a battery of neuropsychological tests after diagnosis and before cranioplasty, called the "Time 1" (T1) assessment. The AB and ABID tasks were administered as part of a second "Time 2" (T2) assessment, typically scheduled at 18 months of age. However, for children who were not diagnosed until after age 12 months, the T2 assessment was scheduled approximately 6 months after the T1 assessment (to ensure an adequate time interval between assessments). Nineteen children who were too old (>25 mos.) due to a delay in their T2 assessment were not included in the present study (see Table 1).

Children and their families were tested at one of four centers: Children's Hospital and Regional Medical Center in Seattle; The Cleft Lip and Palate Institute and Northwestern University in Chicago; Children's Health Care of Atlanta; and St. Louis Children's Hospital. Each center obtained independent Institutional Review Board approval, and informed consent was obtained from each family prior to enrollment in the study. This research is in full compliance with Health Insurance Portability and Accountability Act (HIPAA) standards.

Cases—Children were eligible if they had SSC (sagittal, metopic, left or right unilateral coronal synostosis, or unilateral lambdoid synostosis), confirmed by computed tomography (CT) scans. Exclusion criteria for cases included: (1) premature birth (before 34-weeks gestation); (2) presence of major medical or neurological conditions (e.g., cardiac defects, seizure disorders, cerebral palsy); (3) presence of three or more extracranial minor

malformations as defined by Leppig and colleagues (1987); or (4) presence of extracranial major malformations.

Controls—Children were eligible as controls if they had no known craniofacial anomaly and did not meet any of the exclusionary criteria for cases (described above). Control group participants were recruited through pediatric practices, birthing centers, and announcements in publications for parents of newborns.

Measures

AB Task—In the training phase of this task, the child watched as a small toy was hidden under a washcloth. If the child was able to find the hidden object, the examiner then hid the toy under an inverted cup while the child watched. If the child successfully retrieved the toy, the child proceeded to the test phase. If the child was unsuccessful, the task was discontinued. During the test phase, two identical cups were inverted and placed to the right and left of the child, with approximately 16 inches between cups. While the child observed, a toy was placed under one cup (starting side varied randomly across children within groups). After a 5-second delay, during which the cups were hidden from view by an opaque screen, the child was encouraged to find the toy. If incorrect, the child was shown the location of the toy ("it was over here") but not permitted to retrieve it. After two consecutive correct trials at location A, the location of hiding was reversed to the opposite side, B. After two consecutive correct trials at B, the location reversed again. After the second reversal followed by two consecutive correct trials, the delay increased to 12 seconds. The task ended after two reversals followed by two consecutive correct trials at 12-second delay, or after 24 trials. Dependent variables included percent correct overall, percent correct on reversal trials, and the proportion of children making a correct response on the first B trial (Marcovitch & Zelazo, 1999; Wellman, Cross, & Bartsch, 1986).

ABID Task—In the training phase of the ABID task, the child watched as the examiner placed a toy in a box in the center of the table. The examiner used an attached cover on the box to hide the toy from view, and the box was then hidden behind an opaque screen. After 1–2 seconds, the child was prompted to "find the toy." Two additional training trials were administered, with the box moved (invisible displacement) to the right (or left) while the child watched (the order of these two trials, right then left or left then right, was counterbalanced across participants within groups, with the training trials ending on the start side for the test phase). After the third training trial, the test phase began. During the test phase, once the box was moved to location A and hidden by the screen (5-second delay), an identical empty box was placed on the other side (location B), with approximately 14 inches between the boxes. After the delay, the child was prompted to find the toy. If the child chose incorrectly, the child was shown the location of the toy ("it was over here") but not permitted to retrieve it. After two consecutive correct trials at location A, the location of hiding reversed to the opposite side, B. After two consecutive correct trials at B, the location reversed again. The task ended after three reversals followed by two consecutive correct trials, or after 14 trials. Dependent variables included percent correct overall, percent correct on reversal trials, and the proportion of children making a correct response on the first B trial.

Examiners categorized the child's test behavior as follows: (1) "acceptable" (little or no test interfering behavior); (2) "questionable" (e.g., occasional noncompliance/fussiness, less than optimal motivation as evidenced by slowed response time) or (3) "unacceptable" (e.g., clear refusals to perform, leaving the table).

Measures of Global Development, Language, and Maternal Intelligence— Details of these measures, as well as group comparisons, are reported by Speltz et al. (2007). The BSID-II (Bayley, 1993) measured global cognitive and psychomotor status, yielding a Mental Development Index (MDI) and a Psychomotor Development Index (PDI). The Behavior Rating Scale (BRS; Bayley, 1993) from the BSID-II assessed participants' behavior during test administration (e.g., attention/arousal, engagement, motor quality). The Pre-school Language Scale – Third Edition (PLS-3; Zimmerman, Steiner, & Pond, 1991) yielded auditory comprehension (AC), expressive communication (EC), and total language scores. Maternal intelligence was assessed using the Wonderlic Personnel Test (WPT; Wonderlic, 2000), a brief (12-minute) timed test that correlates highly with IQ scores from comprehensive standardized test batteries (Dodrill & Warner, 1988).

Examiner Training and Reliability—All measures were administered by psychometrists and videotaped for reliability. Before testing study participants, examiners provided two tapes of the BSID-II and PLS-3 for review by the third author (Kapp-Simon), and two tapes of the AB and ABID tasks for review by the first author (Toth). Approximately 10% of all subsequent assessments were reviewed to ensure reliability. Average interrater agreement for the AB task was 98.3% and for the ABID task 95.5%. Interrater reliability for the BSID-II and PLS-3 are reported elsewhere (Speltz et al., 2007).

Procedure

The BSID-II and the PLS-3 were administered first and then, after a short break, the AB and ABID tasks. The Wonderlic Personnel Test (WPT) was completed independently by mothers in a quiet room.

Statistical Analyses—We excluded participants with "unacceptable" or "questionable" test behavior, as defined above, except for analyses of the test behavior variable itself (e.g., group comparisons of test behavior classifications). Pairwise correlations were calculated between the AB and ABID tasks and each of the following variables: BSID-II MDI and PDI scores; PLS-3 AC and EC scores; BRS Total score, WPT score, child age, and surgery age.

For the AB and ABID tasks, we calculated the percent correct responses of the total number of trials. To test for mean case-control differences, we fit a series of linear regression analyses with test scores regressed versus the case indicator. Since the number of possible reversal trials was few, the percent correct on all reversal trials was nonnormally distributed. Thus, for AB and ABID reversal trials, we categorized the percent correct across trials as either <50% or ≥50%. For these outcomes, as well as the outcome of the first reversal trial for each set of tasks, we assessed case-control differences by fitting a series of logistic regression models, again regressing test outcomes versus the case indicator. We adjusted all linear and logistic regression models by including as covariates: age at testing, site, gender, maternal IQ, socioeconomic status (SES), and white ethnicity. We estimated p values by calculating likelihood ratio (LR) tests, adjusting p values for multiple comparisons by conducting a stepdown Bonferroni procedure for 12 comparisons (Hochberg, 1988).

We also tested mean differences between the two largest diagnostic subgroups: sagittal (n=83) and metopic (n=47). As with the case versus control analyses, we fit a series of regression analyses with test scores regressed versus the case indicator, adjusting for all the covariates listed above.

To assess whether cases' AB and ABID scores were related to surgery age, we fit linear and logistic regression models as described above. These models differed in that instead of including a case indicator, we included age at surgery (in months). The adjustment variables and LR test procedure were otherwise the same.

To assess the case-control difference in proportions with acceptable test behavior, we fit logistic regression models in which the acceptability of test behavior was regressed versus the case indicator, with the same covariate adjustments and LR tests as described above. To examine potential differences between participants who were able to complete the ABID tasks versus those with unacceptable or questionable behavior, we compared BSID-II, PLS-3, and BRS scores. Specifically, we fit the same logistic regression models with ABID-test acceptability as the outcome, including as an additional covariate (in separate models) either BSID-II, PLS-3, or BRS scores. These models included the case indicator as a covariate.

To explore potential biases, we performed several subanalyses: we reanalyzed the data by including data for participants with "questionable" as well as "acceptable" test behavior and, in separate analyses, by excluding (1) children above 20 months of age at testing (n=16 cases and 15 controls); (2) five cases in whom sequencing of exons in craniosynostosis syndrome-causing genes detected mutations (Seto et al., 2007); (3) three cases who had not had surgery by the time of the first testing visit; (4) and participants who had intervention, such as speech therapy, between the first and second visits (n=24 cases and 6 controls).

RESULTS

Because of frequency-matching, the case and control groups were very similar with respect to sex, age, and ethnicity (see Table 1). Both SES (Hollingshead, 1975) and maternal IQ, however, were somewhat lower among cases than controls, most likely reflecting recruitment bias; that is, parents of higher SES status and maternal IQ were more likely to volunteer to participate.

On the AB task, 93% of cases and 96% of controls demonstrated acceptable test behavior as defined above. On the ABID task, 82% of cases and 92% of controls were classified as having acceptable test behavior (covariate-adjusted p=.013, stepdown Bonferroni-adjusted p=.143).

Association between AB and ABID Task Performance and Other Abilities

We observed modest correlations between performance on the AB task at 5-second delay and various measures of cognitive ability (Table 2). Both cases and controls showed positive associations between age and performance on AB at the 12-second delay.

Group and Subgroup Comparisons on AB and ABID Tasks

Cases and controls showed nearly equivalent levels of performance on the AB and ABID tasks (Table 3). This was true for measures of memory (percent correct overall; case-control average adjusted differences ranged from –1.0 to 2.4; $p > .25$ and corrected p=1.0 for all comparisons) and response inhibition (percent correct on reversal trials): case-control average adjusted odds ratios (ORs) ranged from 0.9 to 1.4, $p > .15$ and corrected p=1.0 for all comparisons; percent correct on first reversal trials: ORs were 0.7 (p=.02; corrected p=.230) and 1.8 (p=.63; corrected p=1.0) for AB and ABID, respectively. These odds ratios indicated that cases performed slightly better than controls on 5 of the 8 AB and ABID measures (Table 3).

Among cases, those with sagittal and metopic synostosis showed nearly equal levels of performance across all measures of AB and ABID performance (data not shown). Cases' AB and ABID performance were virtually unrelated to surgery age (data not shown).

As compared with cases with acceptable AB or ABID test behavior, cases with unacceptable or questionable test behavior scored lower on the BSID-II, PLS-3, and BRS (data not

shown). The decrease in odds of having unacceptable ABID performance associated with a 5-point increase in test scores was 13% for the BSID (p=.05; corrected p=.45), 30% for the PLS (p=.06; corrected p=.48), and 10% for the BRS (p=.005; corrected p=.06).

Results did not differ in any meaningful way when we performed subanalyses relating to questionable (vs. acceptable) responses; age at testing; novel mutations; cases' lack or lateness of surgery; and participants' use of intervention services.

DISCUSSION

The study of neuropsychological characteristics in infants and children with SSC is important for several reasons, including the potential to illuminate complex interrelationships between the developing brain and cranium (Kjaer, 1995) and to identify children with elevated risk for subsequent learning and behavior problems (Kapp-Simon et al., 2007). Neuropsychological research will also help to clarify the basis upon which recommendations for cranioplasty are made, a procedure that has a mortality rate of nearly 1% and morbidity rate of nearly 7% (Sloan, Wells, Raffel, & McComb, 1997). The assertion that cranioplastic surgery prevents or mitigates neurobehavioral delays or deficits (e.g., Arnaud, Renier, & Marchac, 1995) has sparked considerable debate among surgeons and other health providers, raising questions of whether meaningful neurodevelopmental problems are widespread and lasting among infants with SSC, and whether surgery has only aesthetic or functional benefits as well (Bellew, Chumas, Mueller, Liddington, & Russell, 2005; Hayward, Jones, & Evans, 1999; Kapp-Simon, 1994, 1998; Mathijssen et al., 2006; Posnick, 1998; Rozelle et al., 1995). In the absence of clear answers to these questions, parents are often confused about the justification for this potentially life-threatening surgical procedure and its effects on neurodevelopment (Speltz et al., 2004).

In the current study, we sought to extend knowledge about the effects of SSC on global development to more specific measures of memory and response inhibition, using two versions of the well-known A-not-B (AB) task. The hypothesis that 17- to 24-month-old children with SSC would perform more poorly on these tasks than unaffected children was rejected. Cases and controls performed at roughly equivalent levels on both the AB and ABID tasks. In fact, cases performed slightly better than controls on several tasks, including the first reversal trial for the AB task, which is likely the best single indicator of perseverative behavior in the AB paradigm (Marcovitch & Zelazo, 1999).

There are several explanations for the absence of case-control group differences. First, it may simply be that differences in visual memory and response inhibition between children with and without SSC are minimal or nonexistent. Second, it may be that the executive function impairments found in studies of older children with SSC (Da Costa et al., 2006; Magge et al., 2002) are unrelated or only weakly related to the skills assessed by the AB tasks during late infancy. It is also possible that the deficits found among older children with SSC in the two studies cited are not representative of most children with SSC, as both studies contained very small samples. We are re-administering the ABID task to cases and controls at age 3 and planning school-age assessments of this relatively large cohort. This will allow for examination of whether school-age executive function deficits are widely apparent in this population and, if so, at what age they can be first detected.

Another factor that may have contributed to our findings is the broader assessment situation in which the AB and ABID were administered. These tasks were the last two in a lengthy battery of cognitive, language, and motor tasks, making them perhaps more challenging than normal because of extraordinary demand for sustained motivation and attention in the context of fatigue. Although these factors should have affected both groups equally, cases

were less likely than controls to show acceptable test behavior during the more challenging ABID task: Nearly 20% of cases were excluded from analyses of this task due to significant test-interfering behavior. This finding has two implications: (1) relative group performance on the ABID task may have been different had these cases been able to participate fully; and (2) cases' higher frequency of poor test behavior may itself have predictive significance for later functioning. Indeed, findings from studies of other high-risk populations suggest that young children's refusals and interfering behaviors during testing situations can be as important as test performance in predicting later developmental outcomes (Mantynen et al., 2001; Roth et al., 1984). It is possible that the difficulties experienced by cases with questionable/unacceptable test behavior presage later problems, either in the functions measured by the tasks (memory, response inhibition) or the behaviors required to demonstrate them (e.g., attention, task persistence, motivation to perform).

Among cases, we chose to compare only the two largest diagnostic subgroups (sagittal vs. metopic) in order to have adequate statistical power for this analysis. Although these suture fusions produce quite different abnormalities in skull shape and subcortical morphology (Aldridge et al., 2002; Speltz et al., 2004), the sagittal and metopic groups performed similarly on the tasks given in this study.

Associations between neuropsychological performance and surgery age have been of interest because they provide a test of the hypothesis that later surgeries are associated with more prolonged exposure to intracranial pressure and, consequently, compromised brain development (Bristol, Lekovic, & Rakate, 2004; Gault, Renier, Marchac, & Jones, 1992; Renier et al., 2000). An inverse relation between surgery age and task performance would support this hypothesis, a finding obtained in some studies (e.g., Arnaud et al., 1995; Bottero et al., 1998; Speltz et al., 1997), but not others (e.g., Kapp-Simon, 1998; Gewalli et al., 2001). In previous analyses of this cohort, we found no associations between surgery age and cognitive, motor, and language scores (Starr et al., in press). In the present study, none of the eight measures of AB and ABID task performance showed association with surgery age, further supporting the impression that neither surgery, nor the age at which it is performed, is related to the neuropsychological status of young children with SSC (Starr et al., in press).

In conclusion, our findings suggest that toddlers with SSC show normal development of visual memory and response inhibition at 17 to 24 months of age, even though they had lower scores on global measures of development than controls at this same age (Starr et al., in press). At this early stage of research on the neurodevelopmental correlates of SSC, global measures of development provide the strongest evidence of delayed functioning during the early and late infancy periods (Bellew et al., 2005; Gewalli et al., 2001; Kapp-Simon et al., 2007; Speltz et al., 2007; Starr et al., in press).

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Table 1

Participant characteristics: 17- to 24-month-old children with SSC (“cases”) and unaffected children (“controls”).

					Cases			Controls	
Characteristic	**Sagittal**	**Metopic**	**Right Unicoronal**	**Left Unicoronal**	**Lambdoid**	***n***	**%**	***n***	**%**
n	94	51	24	19	12	200	57	149	43
Child Gender									
Female	21	14	14	16	4	69	34	54	36
male	73	37	10	3	8	131	66	95	64
Child Age, months									
Mean (*SD*)	18.6 (1.2)	18.8 (1.3)	18.7 (.7)	19.6 (2.4)	19.1 (1.0)	18.8 (1.4)		18.7 (1.4)	
Child Ethnicity									
Caucasian	76	37	20	12	10	155	78	121	81
Asian/Pac Islander	0	1	0	2	1	4	2	3	2
Black/African Amer	2	3	0	1	0	6	3	5	3
Hispanic/Latino	6	6	2	2	1	17	8	5	3
Other/Multiracial	10	4	2	2	0	18	9	15	11
SES Score									
I (high)	23	9	6	6	4	48	24	42	28
II	37	21	8	6	5	77	38	77	52
III	16	10	8	4	1	39	20	22	14
IV	15	8	1	2	1	27	13	4	3
V (low)	3	3	1	1	1	9	5	4	3
Bayley Scores mean (*SD*)						Cases		Controls	
MDI	92.5 (12.2)	90.3 (15.3)	91.0 (18.2)	87.8 (12.9)	82.8 (11.3)	90.7 (14.0)		94.7 (12.2)	
PDI	82.8 (10.9)	81.9 (14.9)	81.5 (13.1)	80.7 (14.8)	79.2 (12.9)	82.0 (12.7)		85.1 (9.7)	
BRS	56.9 (25.1)	50.2 (23.7)	55.0 (30.2)	49.9 (31.9)	46.6 (28.7)	53.7 (26.3)		58.3 (24.0)	
PLS-3 Scores mean (*SD*)									
AC	87.8 (14.1)	87.8 (16.5)	85.5 (15.4)	89.3 (13.1)	80.8 (7.0)	87.3 (14.5)		90.8 (15.0)	
EC	89.0 (14.6)	90.1 (16.3)	87.4 (14.3)	89.3 (16.5)	80.9 (6.9)	88.6 (14.9)		92.5 (15.1)	
Maternal IQ	106.3 (13.6)	105.1 (16.0)	106.6 (11.4)	103.8 (16.9)	104.2 (9.6)	105.7 (14.0)		110.4 (11.4)	

Bayley Scales of Infant Development, 2nd Edition; MDI – Mental Development Index; PDI – Psychomotor Development Index. PLS-3=Preschool Language Scales, 3rd Edition; AC – Auditory Comprehension; EC – Expressive Communication.

Table 2

Correlations among AB and ABID task performance and cognitive, motor, and language abilities, test behavior, maternal intelligence, age, and age at surgery for 17- to 24-month-old children with SSC (“cases”) and unaffected children (“controls”).

	BSID-II		PLS-3					
Cases	**MDI**	**PDI**	**AC**	**EC**	**BRS Total**	**WPT**	**Age**	**Age at Surgery**
AB-5s	0.185**	0.156*	0.041	0.118	0.116	−0.023	0.214**	0.079
AB-5s rev	0.160*	0.145*	0.078	0.079	0.078	−0.002	0.017	0.013
AB-12s	0.141	0.154	0.028	0.115	0.122	0.009	0.250**	0.124
AB-12s rev	0.060	0.032	−0.046	0.005	0.047	0.111	0.044	−0.048
ABID	−0.009	0.074	−0.047	−0.066	−0.026	0.041	0.055	0.031
ABID-rev	−0.002	0.020	0.013	−0.056	0.040	−0.018	0.010	−0.011
Controls								
AB-5s	0.240**	0.127	0.072	0.114	0.067	−0.040	0.067	–
AB-5s rev	0.203*	−0.069	0.152	0.123	0.058	0.027	−0.154	–
AB-12s	0.047	0.102	0.063	0.049	−0.036	0.107	0.215*	–
AB-12s rev	−0.042	0.131	0.124	−0.054	0.036	0.047	0.195*	–
ABID	0.092	0.118	−0.028	0.000	−0.074	0.006	0.102	–
ABID-rev	−0.091	−0.055	0.009	−0.079	−0.015	0.130	0.051	–

AB 5s=% correct overall; AB 5s rev=% correct reversal trials.

AB 12s=% correct overall; AB 12s rev=% correct reversal trials.

ABID=% correct overall; ABID-rev=% correct reversal trials.

BSID-II=Bayley Scales of Infant Development, 2nd Edition.

MDI = Mental Development Index.

PDI = Psychomotor Development Index.

BRS=Behavior Rating Scale.

PLS-3=Preschool Language Scales, 3rd Edition.

AC = Auditory Comprehension.

EC = Expressive Communication.

WPT=Wonderlic Personnel Test.

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* $p < .05$.

** $p < .01$.

Table 3

AB and ABID task performance: 17- to 24-month-old children with SSC ("cases") vs. unaffected children ("controls").

	Mean								
	Cases	**Controls**	**Cases**	**Controls**	**Difference[1]**	**95% CI[2]**	**Effect Size**	***p*[3]**	***p*[4]**
Overall score (% correct)									
A-not-B with 5-second delay	186	140	61.3	59.9	2.4	(−2.1, 6.8)	0.06	0.292	1.00
A-not-B with 12-second delay	186	140	58.2	59.5	−1.0	(−5.9, 3.9)	−0.02	0.686	1.00
A-not-B with Invisible Displacement	154	129	46.5	46.8	0.46	(−4.1, 5.0)	0.01	0.842	1.00
	n		Proportion of participants						
	Cases	Controls	Cases	Controls	Odds Ratio[4]	95% CI[2]		*p*[3]	*p*[4]
Score on reversal trials (≥50% correct vs. <50% correct)									
A-not-B with 5-second delay	186	140	0.54	0.50	1.4	(0.7, 2.0)		0.179	1.00
A-not-B with 12-second delay	186	140	0.46	0.47	1.1	(0.5, 1.6)		0.750	1.00
A-not-B with Invisible Displacement	149	124	0.32	0.35	0.9	(0.4, 1.3)		0.629	1.00
Correct on first reversal trial									
A-not-B with 5-second delay	178	136	0.33	0.23	1.8	(0.9, 2.8)		0.023	0.23
A-not-B with Invisible Displacement	130	109	0.33	0.38	0.7	(0.3, 1.2)		0.288	1.00

[1] "Difference" is the average case-control difference in the percent correct between cases and controls, adjusted for age at testing in months, site, gender, maternal IQ, SES (Hollinsghead scale, continuous) and white ethnicity.

[2] "CI" is confidence interval.

[3] *p* values were calculated by using likelihood-ratio tests with one degree of freedom and are two-sided.

[4] Corrected *p* values are corrected for multiple comparisons by using a stepdown Bonferroni correction procedure.

[5] The odds ratio estimating the average increase or decrease in cases' vs. controls' odds of having ≥50% correct on reversals, adjusted for age at testing in months, site, gender, maternal IQ, SES (Hollinsghead scale, continuous), and white ethnicity.