Journal of the International Neuropsychological Society (2004), **10**, 536–548.

DOI: 10.1017/S1355617704104116

Bimanual coordination in alcohol-exposed children: Role of the corpus callosum

TRESA M. ROEBUCK-SPENCER,[1] SARAH N. MATTSON,[2] SARAH DEBOARD MARION,[3] WARREN S. BROWN,[3] AND EDWARD P. RILEY[2]

[1]National Rehabilitation Hospital, Washington, DC 20010
[2]Center for Behavioral Teratology, San Diego, CA 92120
[3]Travis Research Institute, Fuller Graduate School of Psychology, Pasadena, CA

(RECEIVED July 10, 2003; REVISED December 2, 2003; ACCEPTED December 6, 2003)

Abstract

The corpus callosum (CC) is one of several brain structures affected in children prenatally exposed to alcohol. This structure plays a major role in coordinating motor activity from opposite sides of the body, and deficits in bimanual coordination have been documented in individuals with agenesis of or damage to the CC, particularly when the task is performed without visual feedback. The Bimanual Coordination Test was used to assess speed and accuracy on a task where both hands must coordinate to guide a cursor through angled pathways providing measures of interhemispheric interaction or the ability of the two hemispheres to coordinate activity *via* the corpus callosum. Twenty-one children with fetal alcohol spectrum disorders (FASD) and 17 non-exposed control children (CON), matched closely in age, sex, and ethnicity were tested. For trials with visual feedback (WV), children with FASD were slower than CON children but were equally accurate. Although statistically significant group differences were not observed on most trials completed without visual feedback (WOV), accuracy of the FASD group on WOV trials was highly variable. Group differences in accuracy on WOV angles approached significance after accounting for performance on the WV angles, and children with FASD were significantly less accurate on an individual angle believed to be particularly sensitive to interhemispheric interaction. These results indicate that children with FASD are slower than CON children but equally accurate on basic visuomotor tasks. However, as task complexity and reliance on interhemispheric interaction increases, children with FASD demonstrate variable and inaccurate performance. Preliminary analyses suggest that inaccurate performance on the bimanual coordination task, and presumably impaired callosal functioning, may be related to the attention and problem solving impairments commonly reported in children with FASD. (*JINS*, 2004, *10*, 536–548.)

Keywords: Fetal alcohol syndrome, Prenatal alcohol exposure, Corpus callosum, Interhemispheric interaction, Bimanual coordination, Fetal alcohol spectrum disorders

INTRODUCTION

A distinct pattern of anomalies related to prenatal alcohol exposure was first documented in 1968 by French researchers who described 127 children of alcoholic parents (Lemoine et al., 1968). Independently, a group of researchers in the United States made similar observations (Jones & Smith, 1973; Jones et al., 1973) and named the characteristic pattern the Fetal Alcohol Syndrome (FAS). The criteria for receiving a diagnosis of FAS has generally remained the same since that time (Stratton et al., 1996) and consist of the following three characteristics: (1) a specific pattern of craniofacial anomalies (e.g., small palpebral fissures, flattened midface, smoothed philtrum, and thin upper lip); (2) pre and/or postnatal growth deficiency; and (3) central nervous system (CNS) dysfunction (e.g., learning disability, mental retardation).

Children born to mothers who consumed heavy amounts of alcohol during pregnancy demonstrate a wide array of cognitive and behavioral impairments. For many of these children, cognitive impairments tend to be global in nature and include deficits in the areas of general intellectual functioning, language, visual-spatial skills, verbal learning and memory, executive functioning, and fine-motor dexterity

Reprint requests to: Edward P. Riley, Ph.D., Director, Center for Behavioral Teratology, San Diego State University, 6363 Alvarado Court #209, San Diego, CA 92120. E-mail: eriley@mail.sdsu.edu

(for a comprehensive review see Mattson & Riley, 1998). Behaviorally, alcohol-exposed children have been described as having poor judgment, difficulty perceiving social cues, increased levels of activity, increased distractibility and difficulty regulating attention (Aronson et al., 1985; Janzen et al., 1995; Landesman-Dwyer et al., 1981; Streissguth et al., 1989, 1996). Qualitatively similar but sometimes less severe impairments in cognitive and behavioral functioning are also seen in children prenatally exposed to heavy amounts of alcohol who do not meet full criteria for a diagnosis of FAS (Mattson & Riley, 2000; Mattson et al., 1997, 1998; Roebuck et al., 1999).

Given the devastating effects of alcohol on the developing brain, it is likely that the behavioral and cognitive impairments seen in alcohol-exposed individuals are related to underlying structural or functional changes in the brain. Early autopsy reports documented wide-spread structural anomalies and high rates of microencephaly, hydrocephalus, and holoprosencephaly (for review, see Mattson & Riley, 1996; Roebuck et al., 1998). Structural magnetic resonance imaging (MRI) studies of surviving children with heavy prenatal alcohol exposure have documented overall reduced brain size and specific anomalies in the caudate nucleus (Mattson et al., 1994, 1996c) and the anterior vermis of the cerebellum (Sowell et al., 1996). Disproportionate volume reductions are also observed in white matter relative to gray matter, with the most severe volume reductions seen in the parietal white matter (Archibald et al., 2001; Sowell et al., 2001b).

Specific to the current study, structural anomalies of the corpus callosum have been reported in alcohol-exposed children (Bookstein et al., 2001, 2002a; Clarren et al., 1978; Coulter et al., 1993; Johnson et al., 1996; Kinney et al., 1980; Peiffer et al., 1979; Riley et al., 1995; Sowell et al., 2001a; Swayze et al., 1997; Wisniewski et al., 1983), and the incidence of agenesis of this structure is higher in alcohol-exposed children (Mattson et al., 1992; Riley et al., 1995) than in other developmentally disabled groups (Jeret & Serur, 1991). In alcohol-exposed children without agenesis, prenatal alcohol exposure is related to thinning and spatial displacement of the corpus callosum, particularly in the posterior regions (Riley et al., 1995; Sowell et al., 2001a).

The corpus callosum is a large white matter tract that connects the two cerebral hemispheres and facilitates effective interhemispheric interaction. Individuals born without a corpus callosum, who are otherwise neurologically asymptomatic, display subtle cognitive and behavioral difficulties, including poor bimanual coordination, impaired processing of complex information, poor psychosocial functioning, and decreased interhemispheric transfer of learning (Brown et al., 1999; Brown & Paul, 2000; Ferriss & Dorsen, 1975; Fischer et al., 1992; Jeeves et al., 1988a; Paul et al., 2003, 2004; Preilowski, 1972, 1975; Sauerwein & Lassonde, 1994; Schieffer et al., 2000; Solursh et al., 1965). However, the functional implications of corpus callosum anomalies in alcohol-exposed children are unclear. Sowell et al. (2001a) recently reported that in alcohol-exposed children the corpus callosum is located more anterior and inferior in the posterior regions. This displacement was correlated with decreases in verbal learning ability, even after controlling for verbal intellectual ability. In contrast, when FSIQ was used as a covariate, visuospatial functioning was not specifically related to corpus callosum anatomical measures.

Using morphometric methods, Bookstein et al. (2002b) recently demonstrated associations between cognitive functioning and callosal midline shape. These authors documented a significant amount of variability in callosal shape in adult males with heavy prenatal alcohol exposure and found that this shape variation was associated with two different profiles of neurobehavioral functioning, which were independent of relationships with Full Scale IQ. Executive dysfunction was associated with a relatively thick callosum, and motor dysfunction was associated with a thin callosum.

Although these studies confirm alcohol's teratogenic effect on the corpus callosum and its relation to cognitive function, few studies have examined tasks sensitive to interhemispheric transfer of information. Because complex tasks such as problem solving and social interaction require rapid transfer and integration of information across the two cerebral hemispheres, documentation of performance on tasks requiring interhemispheric transfer provide insight into the integrity of corpus callosum functioning. Finger localization tasks have frequently been used to investigate interhemispheric transfer of tactile information in normally developing children and in a range of clinical groups. In normal adults, accuracy of localization on crossed (interhemispheric) conditions is 7% poorer than on uncrossed conditions. Patients with a full commissurotomy were 82% worse on cross-localization trials and those with the trunk of the corpus callosum sectioned were 28% worse (Geffen et al., 1985). Recently, we demonstrated that alcohol-exposed children made more errors than age-matched controls on trials of a finger localization task that required transfer of information across the corpus callosum (Roebuck et al., 2002). An increase in errors on trials that required information to cross the corpus callosum was significantly correlated with smaller size of anterior and posterior portions of the corpus callosum, taken from midsagittal MR images. Callosal size was related only to components of the finger localization task that required interhemispheric transfer (i.e., trials completed without visual aid). Full Scale IQ was not correlated with area of the corpus callosum in alcohol-exposed children, indicating that the observed neuroanatomical/behavioral correlations were not explained by general reductions in intellectual functioning.

The corpus callosum plays a major role in coordinating motor activity from opposite sides of the body. Deficits on various tests of bimanual coordination have been documented in patients with commissurotomy and callosal agenesis (Eliassen et al., 1999, 2000; Gott & Saul, 1978; Preilowski, 1972, 1975; Silver & Jeeves, 1994; Zaidel &

Sperry, 1974). On a bimanual coordination task requiring individuals to navigate diagonal pathways with one hand controlling vertical movement and the other hand controlling horizontal movement, Preilowski (1972, 1975) demonstrated that the anterior forebrain commissures are necessary for rapid and precise bilateral motor coordination. On Preilowski's task, patients with surgically sectioned anterior forebrain commissures displayed slower and less accurate overall performance, diminished improvement after practice relative to controls, and strikingly poor performance when denied visual feedback. Jeeves et al. (1988a) reported similar results on Preilowski's task with acallosal individuals. Unlike control subjects, who, after practice, performed well on this task without visual aid, acallosal individuals were dependent on visual aid to perform effectively, particularly on angles requiring asymmetric contribution of hand speed. A recent study by Larson et al. (2002) measured bimanual coordination in patients with multiple sclerosis using a modified version of Preilowski's task. Patients with evidence of callosal dysfunction (*via* cross-callosal evoked potentials) demonstrated impaired bimanual coordination, whereas patients without evidence of callosal dysfunction did not.

Functional imaging studies also provide support for the role of the corpus callosum in bimanual tasks (Andres et al., 1999; Gerloff & Andres, 2002). For instance, interhemispheric functional coupling between the premotor and sensorimotor areas was seen during an early stage of bimanual coordination learning (Andres et al., 1999; Gerloff & Andres, 2002). Such coupling was not seen for unimanual tasks. However, interhemispheric coupling was reduced once the task was adequately learned, indicating the corpus callosum plays an important role in bimanual movements with a certain degree of conscious control, but a lesser role in overlearned bimanual actions.

Further analysis of corpus callosum functioning in alcohol-exposed children is warranted given that the corpus callosum has been implicated in attention (Banich, 1998; Hines et al., 2002; Roeltgen & Roeltgen, 1989), learning disabilities (Davidson et al., 1990; Moore et al., 1995; Njiokiktjien et al., 1994), behavioral functioning (Brown & Paul, 2000; O'Brien, 1994; Paul et al., 2004), and auditory verbal learning and memory (Geffen et al., 1994a). Although our recent findings from a test of finger localization suggest inefficient transfer from one hemisphere to the other, they do not provide information about how well the two hemispheres interact to perform a task.

In the current study, a computerized version of the Bimanual Coordination Test (cBCT) (Brown, 1991; Marion et al., 2003) was used to measure basic visuomotor ability and interhemispheric interaction in a representative sample of children with fetal alcohol spectrum disorders (FASD) believed to exhibit the range of corpus callosum anomalies described in the literature review above (Riley et al., 1995; Sowell et al., 2001a). The cBCT was adapted from Preilowski's task used to document patterns of unusual performance in individuals with agenesis and partial commisurotomy (Jeeves et al., 1988a; Preilowski, 1972, 1975) and is a computerized version of the task used by Larson and colleagues (2002) to document impairment in patients with multiple sclerosis and corpus callosum compromise. The cBCT assesses speed and accuracy when one or both hands must move a cursor through narrow angled paths presented on a computer screen when one hand controls vertical movement and the other controls horizontal movement. Performance on individual angled paths is grouped according to type of movement required, reflecting three functional domains (Marion et al., 2003; Steese-Seda et al., 1995). Performance on unimanual angles reflects simple motor speed. Performance on angled paths requiring symmetrical hand speed reflects basic visuomotor skill (i.e., the ability to make accurate motor adjustments based on visual feedback). Lastly, performance on asymmetrical paths (i.e., those that demand relative speed adjustment between the two hands) and performance on paths completed without visual feedback reflect interhemispheric functioning as these two conditions require subtle ongoing adjustments between the two hands for successful completion and are specifically impaired in individuals with agenesis or anterior section of the corpus callosum (Jeeves et al., 1988a; Preilowski, 1972, 1975). Children with FASD were expected to perform poorly on all measures compared to matched controls with relatively poorer performance on asymmetric angles and on angles performed without visual feedback. Ancillary correlational analyses were conducted to determine whether selected cBCT variables were correlated with performance on cognitive and behavioral measures.

METHODS

Research Participants

Two groups of children and adolescents between the ages of 10 and 19 participated in this study. One group included individuals with known exposure to large amounts of alcohol during their prenatal development. The second group included non-exposed, normally developing individuals. All participants were drawn from a larger group of individuals followed at the Center for Behavioral Teratology (CBT) at San Diego State University and had similar histories regarding exposure to previous neuropsychological testing as part of their participation in this larger ongoing study. Using similar samples of children, studies from the CBT have documented a wide range of neurobehavioral (Mattson et al., 1996a, 1996b, 1997, 1998, 1999; Mattson & Riley, 1999; Mattson & Roebuck, 2002) and neuroanatomical anomalies (Archibald et al., 2001; Mattson et al., 1992, 1996c; Sowell et al., 1996, 2001a, 2001b) in children with heavy prenatal alcohol exposure.

All alcohol-exposed individuals were evaluated by a pediatric dysmorphologist, Dr. Kenneth Lyons Jones. A diagnosis of FAS was made for those children who met the criteria described earlier ($N = 13$). Those children with

https://doi.org/10.1017/S1355617704104116 Published online by Cambridge University Press

documented histories of heavy prenatal alcohol exposure, but who lacked the growth deficiency and facial dysmorphology to receive a diagnosis of FAS, were identified as having Prenatal Exposure to Alcohol (PEA; $N = 8$). Although detailed histories of actual levels and patterns of exposure were not typically available, in all cases mothers were known, through maternal report or medical or social service records, to have abused substantial amounts of alcohol throughout their pregnancy. Both the FAS and PEA groups fall under the umbrella label of Fetal Alcohol Spectrum Disorders (FASD; O'Malley & Nanson, 2002; Streissguth & O'Malley, 2000). These groups were combined because there is substantial evidence that children with FAS and PEA show qualitatively similar cognitive impairments (Mattson et al., 1997, 1998, 1999; Roebuck et al., 1999), psychosocial problems (Mattson & Riley, 2000; Mattson et al., 1997, 1998; Roebuck et al., 1999) and brain anomalies (Mattson et al., 1994, 1996c; Riley et al., 1995; Sowell et al., 2001a). The distribution of intellectual functioning within this sample is consistent with that seen in other studies of FASD with approximately 29% of children with IQ scores below 70.

Non-exposed control children (CON) were recruited from the community and were screened for prenatal exposure to alcohol and other potentially teratogenic substances *via* a phone screen and parent questionnaire. Individuals were not included in the CON group if there was report of prenatal exposure to any known behavioral teratogen. Parents or caregivers of children in the CON group reported minimal or no alcohol consumption during pregnancy. To insure a normally developing sample with no undetected psychiatric or neurologic disorders, exclusion criteria for the CON group were prenatal exposure to any potentially teratogenic substances, Full Scale IQ scores below 75, history of significant psychiatric or physical disability that might interfere with ability to complete testing, and diagnosis of Attention Deficit Hyperactivity Disorder (ADHD). Individuals with ADHD were specifically excluded due to reports suggesting that ADHD may be related to anomalies of the corpus callosum (Giedd et al., 1994; Hynd et al., 1991).

In all, 38 individuals were tested as part of this project: 17 in the CON group and 21 in the FASD group. The CON and FASD groups were closely matched on the basis of age, sex, and ethnicity. See Table 1 for demographics. Socioeconomic status was measured using the Hollingshead Four Factor Index of Social Status. Scores represent social strata indices, with higher scores representing higher socioeconomic status.

Table 1. Demographic information for total sample of children with fetal alcohol spectrum disorders (FASD) and controls (CON)

	FASD ($n = 21$)	CON ($n = 17$)	
Sex (*n*)			
Males	11	6	*ns*
Females	10	11	
Age			
M (*SD*)	13.4 (2.71)	14.6 (2.73)	*ns*
Range	10.0–19.8	10.4–19.9	
Diagnosis			
FAS	13		
PEA	8		
Hollingshead[a]			
M (*SD*)	3.2 (1.12)	4.1 (1.03)	$p < .05$
Handedness (*n*, %)			
Right-handed	17 (81.0%)	17 (100%)	*ns*
Left-handed	4 (19.0%)	0 (0%)	
Mixed	0 (0%)	0 (0%)	
Ethnicity (*n*, %)			
White	13 (61.9%)	13 (76.5%)	*ns*
African American	7 (33.3%)	2 (11.7%)	
Hispanic descent	0 (0.0%)	1 (5.9%)	
Other	1 (4.8%)	1 (5.9%)	
Full Scale IQ[b]			
M (*SD*)	78.6 (16.24)	107.8 (11.83)	$p < .001$
Range	45–110	90–127	

[a]Data were not available for two children in the CON group. Hollingshead data analyzed by chi-square.
[b]IQ was assessed using the Wechsler Intelligence Scale for Children–Third Edition. Data were not available for four children in the CON group.

Measures

The Bimanual Coordination Test

The computerized version of the Bimanual Coordination Test (cBCT) was used to measure cooperation and coordination between the two hands (Brown, 1991; Marion et al., 2003). This task assesses speed and accuracy when both hands must coordinate the movement of a cursor through narrow pathways presented on a computer screen. Subjects were asked to draw a line through a demarcated path using two knobs, the right controlling vertical movement and the left controlling horizontal movement. The task comprised a series of unimanual and bimanual angled paths. The unimanual angled pathways test simple motor speed with the right and left hand individually. Trials included a 90° pathway requiring only the right hand and a 0° pathway requiring only the left hand. The bimanual pathways consisted of three right-facing angled paths (22.5°, 45°, and 67.5°) and three left-facing angled paths (112.5°, 135.5°, and 157.5°). See Figure 1 for examples of angled paths. To control for practice effects, the presentation of the trials were randomized within the right and left angles. The unimanual trials were randomized separately from the bimanual trials and were always presented first. The bimanual angled paths were tested in two ways: (1) with visual feedback (WV) and (2) without visual feedback (WOV) for the last half of the target path (i.e., the cursor disappeared from view and the subject was required to finish traversing the target path without the ability to see where the cursor was going). Each angle was tested twice and performance measures were averaged for data analysis.

https://doi.org/10.1017/S1355617704104116 Published online by Cambridge University Press

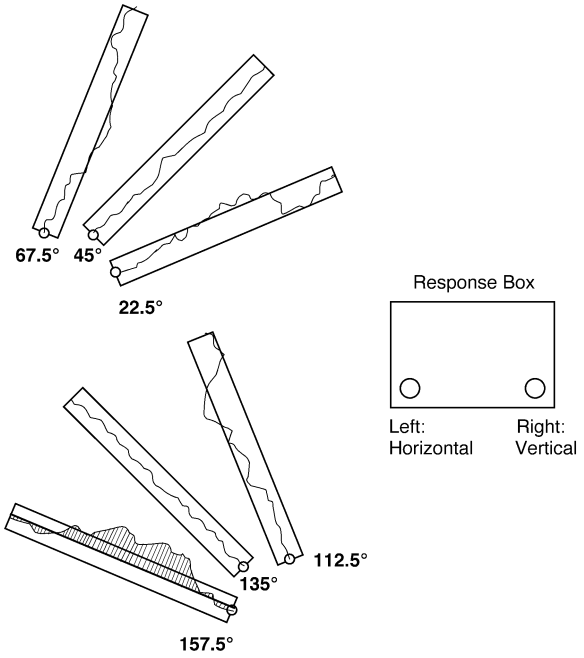

Fig. 1. Illustration of angles used in the Bimanual Coordination Test (cBCT).

Measures of behavioral and cognitive functioning

Given the corpus callosum's potential relation with behavioral and cognitive functioning (Banich, 1998), associations were examined between selected cBCT variables and available cognitive and behavioral measures selected *a priori* from a pre-existing database. Measures were selected to reflect both general and specific cognitive domains (e.g., global cognitive function, motor function) or based on previous studies that documented relationships between behavioral function and interhemispheric interaction (Banich, 1998; O'Brien, 1994). Specific measures included were: Full Scale IQ (FSIQ) from the Wechsler Intelligence Scale for Children–Third Edition (Wechsler, 1991), Beery Buktenica Developmental Test of Visuomotor Integration (VMI; Beery, 1997), dominant hand performance from the Grooved Pegboard Test (PEGS; Spreen & Strauss, 1998), percentage of perseverative responses from the Wisconsin Card Sorting Test (WCST; Heaton et al., 1993), time to complete Part B of the Trailmaking Test (Trails B; Spreen & Strauss, 1998), short (SDF) and long delay free recall (LDF) scores from the California Verbal Learning Test–Children's Version (CVLT-C; Delis et al., 1994), and the Attention, Delinquency, and Aggression subscales from the Child Behavior Checklist (CBCL; Achenbach, 1991). In all cases, standardized variables derived from published norms were used to correct for age effects.

General Procedures

All participants were tested at the CBT at San Diego State University. Informed consent and assent were obtained prior to participation. Two examiners completed all testing and were blind to diagnosis when possible. Both examiners tested a similar percentage of individuals from the CON and FASD groups. All children understood task directions without problem regardless of global intellectual level. A small incentive to participate was provided following testing. As part of other ongoing evaluations of these individuals at the CBT, data from neuropsychological testing, including IQ testing, were available for all but 4 CON subjects. With the exception of one person in each group, all subjects received this testing prior to participation in the current study. This testing was always conducted prior to age 17 and all individuals received the same test protocol. Average time between testing sessions was approximately 2 years (range 0–4 years). A subset of children ($N = 9$) with testing interval less than 1.5 years was also examined.

Handedness was assessed by asking the person to demonstrate performance of simple tasks (e.g., writing with a pencil; using a spoon; using a comb; using a hammer; using a toothbrush; picking up a coin; and throwing a ball). Handedness was determined by demonstration of 5 of 7 items with that hand. Four individuals (1 female, 3 males) in the FASD group were left-handed.

General Analyses

Time to complete path and accuracy of performance were measured for each variable by computer. For data reduction purposes, angles were averaged across trials according to the type of movement required, resulting in the following variables: unimanual angles (0° and 90°), bimanual angles (45°, 67.5°, 22.5°, 135°, 157.5°, and 112.5°), symmetric bimanual angles (45° and 135°), asymmetric bimanual angles (67.5°, 22.5°, 157.5° and 112.5°), right-hand facilitation angles (67.5° and 112.5°), and left-hand facilitation angles (22.5° and 157.5°). These variables are similar to those analyzed in other studies using the cBCT (Gladstone et al., 1989; Marion et al., 2003; Moore et al., 1995). Speed was measured in seconds to complete each path. Accuracy was calculated based on the amount of deviation from the line of best fit (as illustrated in Figure 1) expressed as area under the curve. Speed and accuracy measures from angles contributing to WOV variables were log transformed due to significant violations of normality. Since the homogeneity of variance assumption was met for all variables, pooled variance estimates were used in the analyses. There were no significant main or interactive effects of sex, and therefore, the variable of sex was dropped from the final analyses. Further, there is no evidence of sex differences based on previous literature using this task with children and with adults (Oakes et al., 2002; Steese-Seda et al., 1995). No differences in performance were seen as a function of tester or handedness. Specifically, none of the below results changed if left-handers were excluded from the analysis. Given that left-handers are over-represented in alcohol-exposed children, they were not excluded from the final analysis to insure that our sample was representative of the

https://doi.org/10.1017/S1355617704104116 Published online by Cambridge University Press

overall FASD population. To control Type II errors that might result from small sample sizes, an alpha level of .05 was considered to be statistically significant in all analyses.

RESULTS

Analysis of Speed Variables on the cBCT

Speed to complete pathways was compared by *t* tests, which revealed significant group differences in favor of faster response times for the CON group compared to the FASD group on the following WV variables: unimanual angles [$t(36) = -3.1$, $p = .004$]; bimanual angles [$t(36) = -2.1$, $p = .04$]; and symmetrical angles [$t(36) = -3.2$, $p = .003$]. A marginally significant difference was seen on right-hand facilitation angles ($p = .08$). The groups did not differ on asymmetric angles or left-hand facilitation angles, although absolute differences were indicative of slower performance times in the FASD group. Surprisingly, no group differences were observed for WOV angles (ps $> .05$). See Figure 2 for a summary of these results. In order to examine group differences on WOV angles after accounting for performance on WV trials, a ratio score was calculated by dividing the average of all WOV angles by the average of all WV angles. Results of a between-group *t* test examining this variable revealed significantly higher scores in the CON group ($p = .012$). These results were not unusual given that the CON group demonstrated slower performance on WOV angles and the FASD children did not adjust their speed between WV and WOV angles.

Analysis of Accuracy Variables on the cBCT

Accuracy was also tested by *t* tests, which revealed no significant differences ($.36 < p$s $< .94$) between accuracy scores for the CON and FASD groups on WV variables. Although group differences did not reach statistical significance for WOV variables ($.07 < p$s $< .20$), inspection of absolute differences reveals a general trend for persons with FASD to be less accurate than CON individuals (Figure 3). A small number of outliers, in the direction of extremely deficient performance (i.e., > 3 *SD*s from the mean) were observed in both the CON and FASD groups. Because there was no reason to exclude these subjects, they were retained in the final analyses. Notably, the results did not differ when these outliers were excluded. As described above, a ratio score was calculated by dividing the average accuracy score for all WOV angles by the average accuracy score of all WV angles. Results of a between group *t* test examining this variable were marginally significant ($p = .08$) suggesting a trend for the FASD group to demonstrate specific impairment on WOV angles after controlling for WV performance.

Because large group differences were observed on the WOV variable but were not found to be statistically significant, *post hoc* analyses were conducted to determine whether

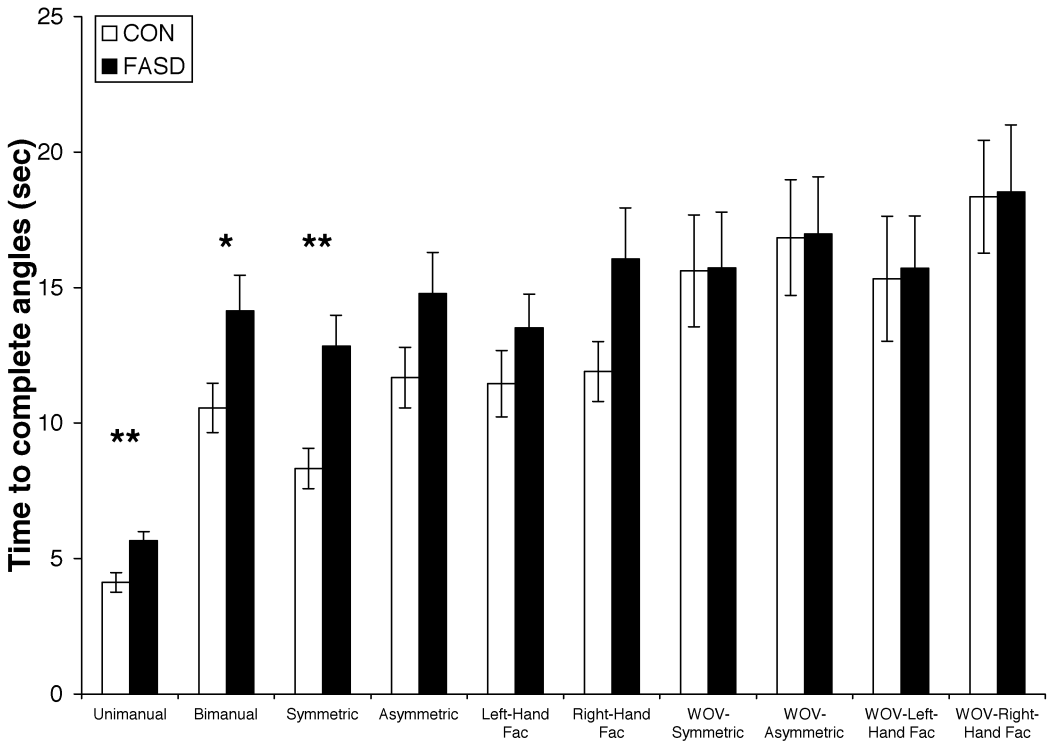

Fig. 2. Average time to complete angles on cBCT task in children with fetal alcohol spectrum disorders (FASD) and controls (CON).
*$p < .05$; **$p < .01$.

https://doi.org/10.1017/S1355617704104116 Published online by Cambridge University Press

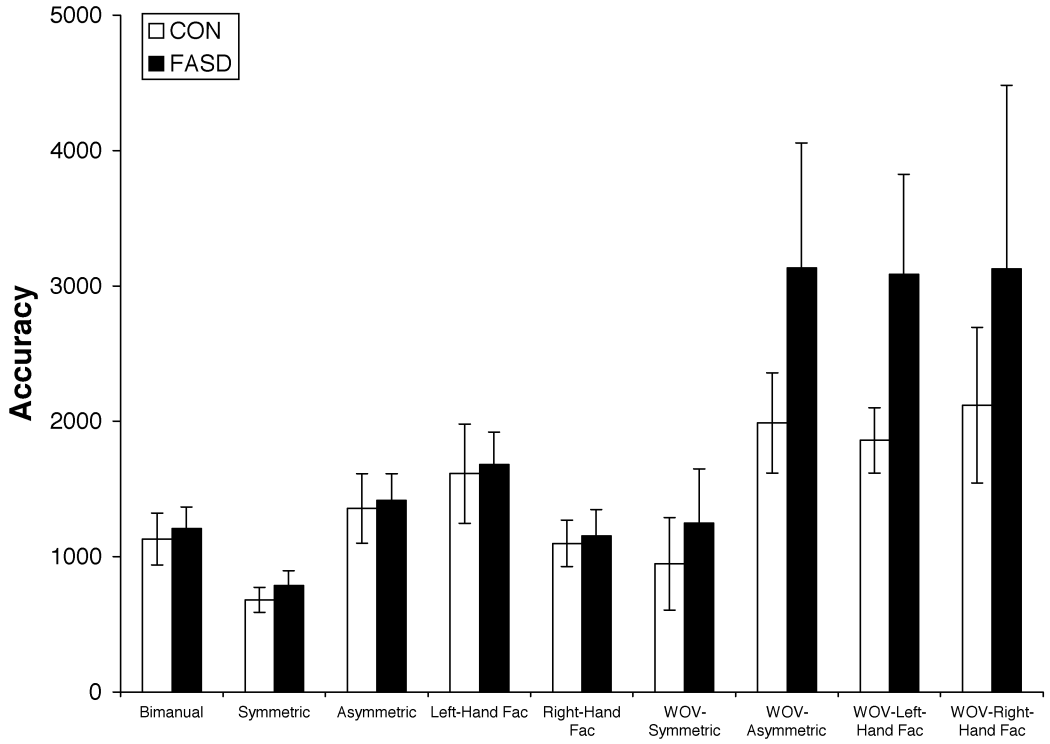

Fig. 3. Accuracy on combined angles of the cBCT task in children with fetal alcohol spectrum disorders (FASD) and controls (CON). Greater accuracy scores correspond to poorer performance (i.e., greater area under the curve).

there were significant group differences on individual WOV angles. For each angle, log transformed accuracy scores were analyzed with *t* tests using pooled variance estimates. These *t* tests revealed a statistically significant group difference on the WOV 157.5° angle [$t(36) = -2.44$, $p = .02$; Figure 4]. This difference remained significant after controlling for performance on the average of all angles completed with visual aid [$F(1,35) = 5.7$, $p = .02$], and performance on symmetric angles [$F(1,35) = 4.8$, $p = .04$]. Group differences on the other individual angles were not significant ($.14 < p\text{s} < .63$).

cBCT and Age

Due to the wide range of age in the sample and the fact that several studies have documented age-related improvement in bimanual performance (Fagard et al., 1985; Jeeves et al., 1988b; Marion et al., 2003; Steese-Seda et al., 1995), the above analyses of speed and accuracy were examined with age as a covariate. In no case were the findings different when age was covaried. However, trends toward significance emerged on the following speed variables: WV Asymmetric Angles [$F(2,35) = 3.4$, $p = .072$] and WV Right-Hand Facilitation Angles [$F(2,35) = 4.0$, $p = .053$]. Trends toward significance were also seen on the following accuracy variables when age was used as a covariate: WOV Asymmetric Angles [$F(2,35) = 3.5$, $p = .07$] and WOV Left-Hand Faciliation Angles [$F(2,35) = 3.0$, $p = .092$]. Correlations between age and cBCT performance for all speed and accuracy variables revealed no significant correlations in either the CON or FASD groups ($.13 < p\text{s} < .96$).

Correlations Between cBCT and Cognitive and Behavioral Measures

For data reduction purposes and to reduce chance of Type I errors, only cBCT variables believed to be most reflective of interhemispheric functioning (e.g., WOV symmetric, WOV asymmetric, and WOV 157.5° angles) based on the current and previous studies (Jeeves et al., 1988a; Preilowski, 1972, 1975) were included in this analysis (see Table 2). Likewise, a limited number of variables were selected *a priori* from available cognitive tests and behavior rating scales in order to represent specific domains of interest (i.e., general intellectual functioning, visual–motor integration, fine-motor skills, verbal learning, executive functioning, and behavioral adjustment). In all cases, these variables were corrected for age using published norms. For consistency purposes, standardized scores on the CBCL, Grooved Pegboard, and Trail Making tests were transposed so that higher scores reflected better functioning. Two-tailed Pearson product-moment correlation coefficients between cBCT and cognitive and behavioral measures are presented in Table 2 for all available individuals in the FASD group. The FASD group was examined alone in order to rule out the possibility that group differences in general functioning were contributing to observed correlations. Negative correlations were expected for all variables, as it was expected that

https://doi.org/10.1017/S1355617704104116 Published online by Cambridge University Press

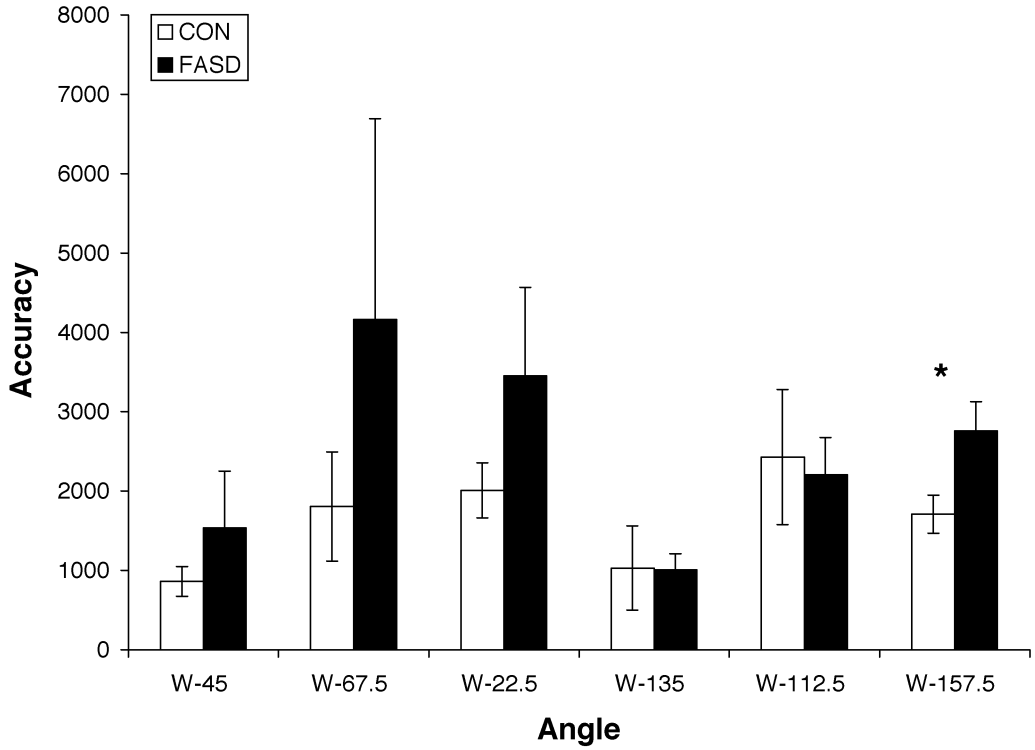

Fig. 4. Accuracy on individual angles completed without visual aid in children with fetal alcohol spectrum disorders (FASD) and controls (CON). Greater accuracy scores correspond to poorer performance (i.e., greater area under the curve).
*$p < .05$.

difficulty on cBCT (indicated by higher speed and accuracy scores) would be related to poorer cognitive and behavioral scores. Associations were seen between accuracy on WOV symmetric angles and the WCST and the Attention subscale of the CBCL. Associations seen in the FASD group between cBCT variables and the WCST and the Attention subscale of the CBCL were not observed in the control group. Instead when the CON group was examined alone marginally significant and significant associations in the expected directions were seen between the WOV symmetric angles and the Grooved Pegboard test ($r = -.506$, $p = .07$) and the VMI ($r = -.495$, $p = .08$). The WOV symmetric angles were significantly associated with the Aggression subscale of the CBCL ($r = -.709$, $p = .007$). Positive associations were seen between WOV Symmetric Angles and LDF from the CVLT-C ($r = .719$, $p = .006$). Associations in the expected direction were also seen between the WOV Asymmetric Angles and Trails B ($r = -.574$, $p = .04$) and the VMI ($r = -.666$, $p = .03$).

DISCUSSION

Geffen et al. (1994b) suggest that the corpus callosum plays an important role in bimanual tasks *via* inhibitory and excitatory transfer of motor commands between the two cerebral hemispheres. The current study used the cBCT (Brown, 1991) to assess how well the hands work together to draw lines through a series of angled pathways presented on a computer screen. Acallosal individuals and individuals with surgically sectioned anterior portions of the corpus callosum are impaired on similar measures of bimanual coordination, particularly during novel acquisition of the task and execution of the task without visual feedback (Jeeves et al., 1988a; Preilowski, 1972, 1975). Furthermore, recent studies have shown that patients with multiple sclerosis and known evidence of inefficient callosal transfer perform more poorly on this task than those without callosal impairment (Larson et al., 2002).

In the current study, angled pathways from the cBCT were combined to measure simple motor speed (i.e., unimanual angles), visuomotor integration (bimanual and symmetric angles with visual feedback), and interhemispheric interaction (i.e., asymmetric angles and all angles completed without visual feedback). It was expected that the FASD group would exhibit slower and less accurate performance compared to the performance of the CON group on all measures, particularly on those most heavily dependent on interhemispheric interaction.

The FASD group consistently took longer than the CON group to complete angles with visual feedback, displaying slowed simple motor speed and visuomotor integration skills. These results are consistent with earlier studies demonstrating impaired fine-motor speed in children with heavy prenatal alcohol exposure on traditional neuropsychological

https://doi.org/10.1017/S1355617704104116 Published online by Cambridge University Press

Table 2. Pearson product moment correlations between cBCT and traditional measures for the FASD group ($N = 21$)

	cBCT accuracy variables completed without visual assistance		
Cognitive and behavioral measures	Symmetric	Asymmetric	157.5°
General intellectual functioning			
FSIQ	−.352	−.169	.054
Visual motor integration			
VMI	−.359	−.351	−.103
Fine motor skills			
Pegs	−.068	.064	.012
Executive functioning			
WCST	−*.609***	−.379	−.256
Trails B	−.014	.137	−.021
Verbal learning (CVLT–C)			
SDF	−.348	−.315	−.123
LDF	−.244	−.078	−.055
Behavioral functioning (CBCL)			
Attention	−*.599***	−.402	−.292
Aggression	−.151	−.110	−.001
Delinquency	−.099	.059	.249

***$p < .01$.

tests (Mattson & Riley, 1998b; Mattson et al., 1998). Surprisingly, the FASD group did not differ from the CON group in terms of speed on angles completed without visual feedback and performed better than CON children on a ratio score of time to complete WOV angles after controlling for timed performance on WV angles. Whereas the CON group performed progressively slower as trials increased in complexity, the children in the FASD group did not. These findings indicate differences in strategy and speed accuracy trade-offs between the two groups. Specifically, children in the FASD group did not adjust their strategy as the task became more complex.

When accuracy of performance was examined, the FASD group performed similarly to the CON group on angles completed with visual feedback. The FASD group also performed similarly to the CON group on WOV angles, despite the fact that, unlike the CON group, the FASD group did not slow their response speed on these trials. Visual inspection of the data, however, revealed large group differences in WOV accuracy scores that did not reach statistical significance, most likely due to highly variable performance in the FASD group. When age was included as a covariate, trends toward significance were seen on WOV Asymmetric Angles on WOV Left-hand Facilitation Angles. Furthermore, there was a trend for the FASD group to demonstrate selectively worse accuracy on WOV angles compared to the CON group when a ratio score controlling for performance on WV angles was examined.

To more specifically examine potential group differences on measures of accuracy, the CON and FASD groups were compared to one another on individual WOV angles. This analysis revealed that the FASD group was less accurate than the CON group on the WOV 157.5° angle. This specific finding is suggestive of subtle callosal dysfunction, given that this angle is particularly dependent on interhemispheric communication. This angle not only requires performance without the aid of visual feedback, a condition that has been shown to be specifically impaired in individuals with callosal agenesis (Jeeves et al., 1988a; Preilowski, 1972, 1975), but is also leftward facing (requires mirror movements of the hands) and requires faster left than right hand response speed for successful completion, both conditions proposed to place a relatively greater demand on interhemispheric interaction (Jeeves et al., 1988a; Moore et al., 1995). Similar results were found in studies of children and adults with dyslexia (Gladstone et al., 1989; Moore et al., 1995), a condition believed by some to be related, in part, to callosal anomalies (Hynd et al., 1995; Njiokiktjien et al., 1994). Furthermore, developmental studies have shown that Left-hand Facilitation and WOV angles are specifically related to age and presumably corpus callosum maturation (Marion et al., 2003). Finally, current findings of inefficient interhemispheric transfer are consistent with our earlier work demonstrating impaired performance on aspects of a finger localization task that required interhemispheric transfer (Roebuck et al., 2002).

Several studies have demonstrated improved performance on bimanual coordination tasks related to age (Fagard et al., 1985; Jeeves et al., 1988b; Marion et al., 2003; Steese-Seda et al., 1995), with older children performing faster and more accurately and younger children performing similarly to adults with commisurotomy. Age-related

https://doi.org/10.1017/S1355617704104116 Published online by Cambridge University Press

improvement on the cBCT mirrors that expected from developmental myelination of the corpus callosum and appears to be most evident on asymmetric angles and on angles that require greater left than right hand contribution. However, the current study found no associations between age and any of the examined cBCT variables. Additionally, with a few exceptions, results generally did not differ when age was included as a covariate. The absence of significant correlations with age is most likely attributable to the fact that the age range in our sample was older than the age ranges used in previous developmental studies, increasing the possibility that individuals in our study had reached a plateau with respect to age-related changes on the cBCT task.

The corpus callosum has been implicated in the regulation of attention (Banich, 1998; Hines et al., 2002; Hynd et al., 1990, 1991, 1995; Roeltgen & Roeltgen, 1989), learning and memory (Geffen et al., 1994a), reading and learning disabilities (Davidson et al., 1990; Moore et al., 1995, 1996; Njiokiktjien et al., 1994), and behavioral/social disturbance (Brown & Paul, 2000; O'Brien, 1994; Paul et al., 2004). Therefore, inefficient functioning of this structure may contribute to the myriad of cognitive and behavioral deficits observed in alcohol-exposed children. To test this hypothesis, associations between cBCT variables shown from past research to be most dependent on interhemispheric functioning and performance on standardized behavioral and cognitive measures were examined. Specifically, accuracy on symmetric WOV trials, asymmetric WOV trials, and the WOV 157.5° angle were chosen for these analyses. Results indicated that within the FASD group inaccurate performance on the cBCT was related to parental report of attention difficulties and novel problem solving skills. These findings are consistent with a study by Brown and Paul (2000) demonstrating that deficits in novel problem solving are basic to the symptomatology of individuals with agenesis of the corpus callosum. Similarly, it has been shown that individuals with callosal agenesis have deficits in spatial attention (Hines et al., 2002).

Because the time interval between testing sessions was quite large for several individuals, the above correlational analyses were conducted with a subset of individuals ($N = 9$) with testing intervals less than 1.5 years, and the results were unchanged. Although the gap between normative scores on traditional neuropsychological tests might be expected to widen between FASD and CON groups over time given potential reduced developmental gains in FASD children, there is no reason to expect that their absolute performance on cognitive or motor tests would decline over time. There remains the possibility that large inter-test intervals may have attenuated our ability to detect associations between cBCT variables and other measures. Future studies with larger sample sizes should further examine associations between cBCT variables and traditional neuropsychological measures, while also examining the association of each with neuroimaging data.

A limitation of the current study is that neuroimaging data was not available to document the presence of corpus callosum anomalies in the individuals with FASD or to correlate with the behavioral measures. The lack of neuroimaging data precludes us from knowing what percentage and to what degree the current sample of alcohol-exposed individuals demonstrated an absent, reduced, or displaced corpus callosum. If individuals without CC anomalies are included in the sample, it would serve to attenuate the current findings for those persons who are more severely affected by alcohol exposure, thus making our current findings of subtle interhemispheric interaction deficits more conservative. This possibility may also explain the high degree of variability seen in FASD group performance on the cBCT task as this variability increased with greater task complexity and presumed greater reliance on efficient callosal functioning. It is likely that the current findings would be greater in magnitude and less variable if we were able to limit our sample to those individuals known to have quantifiable anomalies of the corpus callosum. Further study is warranted assessing the association between bimanual coordination with neuroanatomical measures of the corpus callosum in alcohol-exposed individuals.

In sum, these results indicate that individuals with FASD are slower than controls, but equally accurate on measures of basic visuomotor ability (i.e., angles performed with visual feedback). The lack of group differences in speed on angles completed without visual feedback suggests that individuals with FASD did not adjust their strategy in the face of greater task complexity. This may account for the high degree of variability seen in the FASD group's ability to accurately complete angles without visual feedback. Specifically, the FASD group was less accurate than the CON group on WOV angles when performance on WV angles was accounted for and on one specific angle (i.e., WOV 157.5°) believed to be the most heavily dependent on interhemispheric interaction. These results are consistent with earlier findings of impaired interhemispheric transfer in this group of children (Roebuck et al., 2002). Finally, preliminary correlational analyses between selected cBCT and neuropsychological variables in children with FASD revealed that inaccurate performance on cBCT variables believed to reflect interhemispheric interaction was related to impaired novel problem solving and attention. These results suggest that impaired callosal functioning may be contributing to the behavioral deficits commonly reported in these functional domains.

ACKNOWLEDGMENTS

This manuscript was supported in part by the National Institute on Alcohol Abuse and Alcoholism Grants AA10417 to E.P.R. and AA10820 to S.N.M. These data were presented at the 2001 Meeting of the International Neuropsychological Society.

REFERENCES

Achenbach, T.M. (1991). *Manual for the Child Behavior Checklist/4-18 and 1991 Profile*. Burlington, VT: University of Vermont Department of Psychiatry.

Andres, F.G., Mima, T., Schulman, A.E., Dichgans, J., Hallett, M., & Gerloff, C. (1999). Functional coupling of human cortical sensorimotor areas during bimanual skill acquisition. *Brain*, *122*, 855–870.

Archibald, S.L., Fennema-Notestine, C., Gamst, A., Riley, E.P., Mattson, S.N., & Jernigan, T.L. (2001). Brain dysmorphology in individuals with severe prenatal alcohol exposure. *Developmental Medicine and Child Neurology*, *43*, 148–154.

Aronson, M., Kyllerman, M., Sabel, K.G., Sandin, B., & Olegard, R. (1985). Children of alcoholic mothers. Developmental, perceptual and behavioural characteristics as compared to matched controls. *Acta Paediatrica Scandinavica*, *74*, 27–35.

Banich, M.T. (1998). The missing link: The role of interhemispheric interaction in attentional processing. *Brain and Cognition*, *36*, 128–157.

Beery, K.E. (1997). *The Visual-Motor Integration Test: Administration, scoring and teaching manual* (Rev. 4th ed.). Parsippany, NJ: Modern Curriculum Press.

Bookstein, F.L., Sampson, P.D., Connor, P.D., & Streissguth, A.P. (2002a). Midline corpus callosum is a neuroanatomical focus of fetal alcohol damage. *Anatomical Record*, *269*, 162–174.

Bookstein, F.L., Sampson, P.D., Streissguth, A.P., & Connor, P.D. (2001). Geometric morphometrics of corpus callosum and subcortical structures in the fetal-alcohol-affected brain. *Teratology*, *64*, 4–32.

Bookstein, F.L., Streissguth, A.P., Sampson, P.D., Connor, P.D., & Barr, H.M. (2002b). Corpus callosum shape and neuropsychological deficits in adult males with heavy fetal alcohol exposure. *NeuroImage*, *15*, 233–251.

Brown, W.S. (1991). *The Bimanual Coordination Test: Version 1*. Pasadena, CA: The Travis Institute.

Brown, W.S., Jeeves, M.A., Dietrich, R., & Burnison, D.S. (1999). Bilateral field advantage and evoked potential interhemispheric transmission in commissurotomy and callosal agenesis. *Neuropsychologia*, *37*, 1165–1180.

Brown, W.S. & Paul, L.K. (2000). Cognitive and psychosocial deficits in agenesis of the corpus callosum with normal intelligence. *Cognitive Neuropsychiatry*, *5*, 135–157.

Clarren, S.K., Alvord, E.C., Sumi, S.M., Streissguth, A.P., & Smith, D.W. (1978). Brain malformations related to prenatal exposure to ethanol. *Journal of Pediatrics*, *92*, 64–67.

Coulter, C.L., Leech, R.W., Schaefer, G.B., Scheithauer, B.W., & Brumback, R.A. (1993). Midline cerebral dysgenesis, dysfunction of the hypothalamic-pituitary axis, and fetal alcohol effects. *Archives of Neurology*, *50*, 771–775.

Davidson, R.J., Leslie, S.C., & Saron, C. (1990). Reaction time measures of interhemispheric transfer time in reading disabled and normal children. *Neuropsychologia*, *28*, 471–485.

Delis, D.C., Kramer, J.H., Kaplan, E., & Ober, B.A. (1994). *Manual for the California Verbal Learning Test–Children's Version*. San Antonio, TX: The Psychological Corporation.

Eliassen, J.C., Baynes, K., & Gazzaniga, M.S. (1999). Direction information coordinated via the posterior third of the corpus callosum during bimanual movements. *Experimental Brain Research*, *128*, 573–577.

Eliassen, J.C., Baynes, K., & Gazzaniga, M.S. (2000). Anterior and posterior callosal contributions to simultaneous bimanual movements of the hands and fingers. *Brain*, *123*, 2501–2511.

Fagard, J., Morioka, M., & Wolff, P.H. (1985). Early stages in the acquisition of a bimanual motor skill. *Neuropsychologia*, *23*, 535–543.

Ferriss, G.S. & Dorsen, M.M. (1975). Agenesis of the corpus callosum. 1. Neuropsychological studies. *Cortex*, *11*, 95–122.

Fischer, M., Ryan, S.B., & Dobyns, W.B. (1992). Mechanisms of interhemispheric transfer and patterns of cognitive function in acallosal patients of normal intelligence. *Archives of Neurology*, *49*, 271–277.

Geffen, G., Nilsson, J., Quinn, K., & Teng, E.L. (1985). The effect of lesions of the corpus callosum on finger localization. *Neuropsychologia*, *23*, 497–514.

Geffen, G.M., Forrester, G.M., Jones, D.L., & Simpson, D.A. (1994a). Auditory verbal learning and memory in cases of callosal agenesis. In M. Lassonde & M.A. Jeeves (Eds.), *Callosal agenesis: A natural split brain? Advances in Behavioral Biology* (pp. 247–260). New York: Plenum Press.

Geffen, G.M., Jones, D.L., & Geffen, L.B. (1994b). Interhemispheric control of manual motor activity. *Behavioural Brain Research*, *64*, 131–140.

Gerloff, C. & Andres, F.G. (2002). Bimanual coordination and interhemispheric interaction. *Acta Psycholica*, *110*, 161–186.

Giedd, J.N., Castellanos, F.X., Casey, B.J., Kozuch, P., King, A.C., Hamburger, S.D., & Rapoport, J.L. (1994). Quantitative morphology of the corpus callosum in attention deficit hyperactivity disorder. *American Journal of Psychiatry*, *151*, 665–669.

Gladstone, M., Best, C.T., & Davidson, R.J. (1989). Anomalous bimanual coordination among dyslexic boys. *Developmental Psychology*, *25*, 236–246.

Gott, P.S. & Saul, R.E. (1978). Agenesis of the corpus callosum: Limits of functional compensation. *Neurology*, *28*, 1272–1279.

Heaton, R.K., Chelune, G.J., Talley, J.L., Kay, G.G., & Curtiss, G. (1993). *Wisconsin Card Sorting Test manual*. Odessa, FL: Psychological Assessment Resources, Inc.

Hines, R.J., Paul, L.K., & Brown, W.S. (2002). Spatial attention in agenesis of the corpus callosum: shifting attention between visual fields. *Neuropsychologia*, *40*, 1804–1814.

Hynd, G.W., Hall, J., Novey, E.S., Eliopulos, D., Black, K., Gonzalez, J.J., Edmonds, J.E., Riccio, C., & Cohen, M. (1995). Dyslexia and corpus callosum morphology. *Archives of Neurology*, *52*, 32–38.

Hynd, G.W., Semrud-Clikeman, M., Lorys, A.R., Novey, E.S., & Eliopulos, D. (1990). Brain morphology in developmental dyslexia and attention deficit disorder/hyperactivity. *Archives of Neurology*, *47*, 919–926.

Hynd, G.W., Semrud-Clikeman, M., Lorys, A.R., Novey, E.S., Eliopulos, D., & Lyytinen, H. (1991). Corpus callosum morphology in attention deficit-hyperactivity disorder: Morphometric analysis of MRI. *Journal of Learning Disabilities*, *24*, 141–146.

Janzen, L.A., Nanson, J.L., & Block, G.W. (1995). Neuropsychological evaluation of preschoolers with fetal alcohol syndrome. *Neurotoxicology and Teratology*, *17*, 273–279.

Jeeves, M.A., Silver, P.H., & Jacobson, I. (1988a). Bimanual coordination in callosal agenesis and partial commissurotomy. *Neuropsychologia*, *26*, 833–850.

Jeeves, M.A., Silver, P.H., & Milne, A.B. (1988b). Role of the corpus callosum in the development of a bimanual motor skill. *Developmental Neuropsychology*, *4*, 305–323.

Jeret, J.S. & Serur, D. (1991). Fetal alcohol syndrome in adolescents and adults [Letter to the editor]. *Journal of the American Medical Association*, *266*, 1077.

Johnson, V.P., Swayze, V.W., II, Sato, Y., & Andreasen, N.C. (1996). Fetal alcohol syndrome: craniofacial and central nervous system manifestations. *American Journal of Medical Genetics*, *61*, 329–339.

Jones, K.L. & Smith, D.W. (1973). Recognition of the fetal alcohol syndrome in early infancy. *Lancet, 2*, 999–1001.

Jones, K.L., Smith, D.W., Ulleland, C.N., & Streissguth, A.P. (1973). Pattern of malformation in offspring of chronic alcoholic mothers. *Lancet, 1*, 1267–1271.

Kinney, H., Faix, R., & Brazy, J. (1980). The fetal alcohol syndrome and neuroblastoma. *Pediatrics, 66*, 130–132.

Landesman-Dwyer, S., Ragozin, A.S., & Little, R.E. (1981). Behavioral correlates of prenatal alcohol exposure: A four-year follow-up study. *Neurobehavioral Toxicology and Teratology, 3*, 187–193.

Larson, E.B., Burnison, D.S., & Brown, W.S. (2002). Callosal function in multiple sclerosis: bimanual motor coordination. *Cortex, 38*, 201–214.

Lemoine, P., Harousseau, H., Borteryu, J.P., & Menuet, J.C. (1968). Les enfants des parents alcooliques: Anomalies observeés. À propos de 127 cas [Children of alcoholic parents: Abnormalities observed in 127 cases]. *Ouest Medical, 21,* 476–482.

Marion, S.D., Kilian, S.C., Naramor, T.L., & Brown, W.S. (2003). Normal development of bimanual coordination: Visuomotor and interhemispheric contributions. *Developmental Neuropsychology, 23*, 399–421.

Mattson, S.N., Goodman, A.M., Caine, C., Delis, D.C., & Riley, E.P. (1999). Executive functioning in children with heavy prenatal alcohol exposure. *Alcoholism: Clinical and Experimental Research, 23*, 1808–1815.

Mattson, S.N., Gramling, L., Delis, D.C., Jones, K.L., & Riley, E.P. (1996a). Global-local processing in children prenatally exposed to alcohol. *Child Neuropsychology, 2*, 165–175.

Mattson, S.N. & Riley, E.P. (1996). Brain anomalies in fetal alcohol syndrome. In E.L. Abel (Ed.), *Fetal alcohol syndrome: From mechanism to prevention* (pp. 51–68). New York: CRC Press.

Mattson, S.N. & Riley, E.P. (1998). A review of the neurobehavioral deficits in children with fetal alcohol syndrome or prenatal exposure to alcohol. *Alcoholism: Clinical and Experimental Research, 22*, 279–294.

Mattson, S.N. & Riley, E.P. (1999). Implicit and explicit memory functioning in children with heavy prenatal alcohol exposure. *Journal of the International Neuropsychological Society, 5*, 462–471.

Mattson, S.N. & Riley, E.P. (2000). Parent ratings of behavior in children with heavy prenatal alcohol exposure and IQ-matched controls. *Alcoholism: Clinical and Experimental Research, 24*, 226–231.

Mattson, S.N., Riley, E.P., Delis, D.C., Stern, C., & Jones, K.L. (1996b). Verbal learning and memory in children with fetal alcohol syndrome. *Alcoholism: Clinical and Experimental Research, 20*, 810–816.

Mattson, S.N., Riley, E.P., Gramling, L., Delis, D.C., & Jones, K.L. (1997). Heavy prenatal alcohol exposure with or without physical features of fetal alcohol syndrome leads to IQ deficits. *Journal of Pediatrics, 131*, 718–721.

Mattson, S.N., Riley, E.P., Gramling, L., Delis, D.C., & Jones, K.L. (1998). Neuropsychological comparison of alcohol-exposed children with or without physical features of fetal alcohol syndrome. *Neuropsychology, 12*, 146–153.

Mattson, S.N., Riley, E.P., Jernigan, T.L., Ehlers, C.L., Delis, D.C., Jones, K.L., Stern, C., Johnson, K.A., Hesselink, J.R., & Bellugi, U. (1992). Fetal alcohol syndrome: A case report of neuropsychological, MRI, and EEG assessment of two children. *Alcoholism: Clinical and Experimental Research, 16*, 1001–1003.

Mattson, S.N., Riley, E.P., Jernigan, T.L., Garcia, A., Kaneko, W.M., Ehlers, C.L., & Jones, K.L. (1994). A decrease in the size of the basal ganglia following prenatal alcohol exposure: A preliminary report. *Neurotoxicology and Teratology, 16*, 283–289.

Mattson, S.N., Riley, E.P., Sowell, E.R., Jernigan, T.L., Sobel, D.F., & Jones, K.L. (1996c). A decrease in the size of the basal ganglia in children with fetal alcohol syndrome. *Alcoholism: Clinical and Experimental Research, 20*, 1088–1093.

Mattson, S.N. & Roebuck, T.M. (2002). Acquisition and retention of verbal and nonverbal information in children with heavy prenatal alcohol exposure. *Alcoholism: Clinical and Experimental Research, 26*, 875–882.

Moore, L.H., Brown, W.S., Markee, T.E., Theberge, D.C., & Zvi, J.C. (1995). Bimanual coordination in dyslexic adults. *Neuropsychologia, 33*, 781–793.

Moore, L.H., Brown, W.S., Markee, T.E., Theberge, D.C., & Zvi, J.C. (1996). Callosal transfer of finger localization information in phonologically dyslexic adults. *Cortex, 32*, 311–322.

Njiokiktjien, C., de Sonneville, L., & Vaal, J. (1994). Callosal size in children with learning disabilities. *Behavioural Brain Research, 64*, 213–218.

O'Brien, G. (1994). The behavioral and developmental consequences of corpus callosal agenesis and Aicardi Syndrome. In M. Lassonde & M.A. Jeeves (Eds.), *Callosal agenesis: A natural split brain? Advances in behavioral biology* (pp. 235–246). New York: Plenum Press.

O'Malley, K.D. & Nanson, J. (2002). Clinical implications of a link between fetal alcohol spectrum disorder and attention-deficit hyperactivity disorder. *Canadian Journal of Psychiatry, 47*, 349–354.

Oakes, K.L., Marion, S.D., Killian, S.C., Thrasher, E.D., McBurney-Rebol, K., & Brown, W.S. (2002). Gender, hormones, and bimanual coordination. *Journal of the International Neuropsychological Society, 8*, 280.

Paul, L.K., Schieffer, B., & Brown, W.S. (2004). Social processing deficits in agenesis of the corpus callosum: Narratives from the Thematic Apperception Test. *Archives of Clinical Neuropsychology, 19*, 215–225.

Paul, L.K., Van Lancker-Sidtis, D., Schieffer, B., Dietrich, R., & Brown, W.S. (2003). Communicative deficits in agenesis of the corpus callosum: Nonliteral language and affective prosody. *Brain and Language, 85*, 313–324.

Peiffer, J., Majewski, F., Fischbach, H., Bierich, J.R., & Volk, B. (1979). Alcohol embryo- and fetopathy: Neuropathology of 3 children and 3 fetuses. *Journal of the Neurological Sciences, 41*, 125–137.

Preilowski, B. (1972). Possible contributions of the anterior forebrain commissures to bilateral motor coordination. *Neuropsychologia, 10*, 267–277.

Preilowski, B. (1975). Bilateral motor interaction: Perceptual and motor performance of partial and complete "split brain" patients. In G.C. Galbraith (Ed.), *Cerebral localization* (pp. 115–132). Berlin: Springer.

Riley, E.P., Mattson, S.N., Sowell, E.R., Jernigan, T.L., Sobel, D.F., & Jones, K.L. (1995). Abnormalities of the corpus callosum in children prenatally exposed to alcohol. *Alcoholism: Clinical and Experimental Research, 19*, 1198–1202.

Roebuck, T.M., Mattson, S.N., & Riley, E.P. (1998). A review of the neuroanatomical findings in children with fetal alcohol syndrome or prenatal exposure to alcohol. *Alcoholism: Clinical and Experimental Research, 22*, 339–344.

Roebuck, T.M., Mattson, S.N., & Riley, E.P. (1999). Behavioral and psychosocial profiles of alcohol-exposed children. *Alcoholism: Clinical and Experimental Research*, *23*, 1070–1076.

Roebuck, T.M., Mattson, S.N., & Riley, E.P. (2002). Interhemispheric transfer in children with heavy prenatal alcohol exposure. *Alcoholism: Clinical and Experimental Research*, *26*, 1863–1871.

Roeltgen, M.G. & Roeltgen, D.P. (1989). Development of attention in normal children: A possible corpus callosum effect. *Developmental Neuropsychology*, *5*, 127–139.

Sauerwein, H.C. & Lassonde, M. (1994). Cognitive and sensorimotor functioning in the absence of the corpus callosum: neuropsychological studies in callosal agenesis and callosotomized patients. *Behavioural Brain Research*, *64*, 229–240.

Schieffer, B., Paul, L., & Brown, W. (2000). Deficits in complex concept formation in agenesis of the corpus callosum. *Journal of the International Neuropsychological Society*, *6*, 164.

Silver, P.H. & Jeeves, M.A. (1994). Motor coordination in callosal agenesis. In M. Lassonde & M.A. Jeeves (Eds.), *Callosal agenesis: A natural split brain? Advances in Behavioral Biology* (pp. 207–219). New York: Plenum Press.

Solursh, L.P., Margulies, A.I., Ashem, B., & Stasiak, E.A. (1965). The relationships of agenesis of the corpus callosum to perception and learning. *Journal of Nervous and Mental Disease*, *141*, 180–189.

Sowell, E.R., Jernigan, T.L., Mattson, S.N., Riley, E.P., Sobel, D.F., & Jones, K.L. (1996). Abnormal development of the cerebellar vermis in children prenatally exposed to alcohol: Size reduction in lobules I–V. *Alcoholism: Clinical and Experimental Research, 20*, 31–34.

Sowell, E.R., Mattson, S.N., Thompson, P.M., Jernigan, T.L., Riley, E.P., & Toga, A.W. (2001a). Mapping callosal morphology and cognitive correlates: Effects of heavy prenatal alcohol exposure. *Neurology*, *57*, 1–15.

Sowell, E.R., Thompson, P.M., Mattson, S.N., Tessner, K.D., Jernigan, T.L., Riley, E.P., & Toga, A.W. (2001b). Voxel-based morphometric analyses of the brain in children and adolescents prenatally exposed to alcohol. *NeuroReport*, *12*, 515–523.

Spreen, O. & Strauss, E. (1998). *A compendium of neuropsychological tests: Administration, norms, and commentary* (2nd ed.). New York: Oxford University Press.

Steese-Seda, D., Brown, W.S., & Caetano, C. (1995). Development of visuomotor coordination in school-age children: The Bimanual Coordination Test. *Developmental Neuropsychology*, *11*, 181–199.

Stratton, K., Howe, C., & Battaglia, F. (1996). *Fetal alcohol syndrome: Diagnosis, epidemiology, prevention, and treatment*. Washington, DC: National Academy Press.

Streissguth, A.P., Barr, H.M., Kogan, J., & Bookstein, F.L. (1996). *Final report: Understanding the occurrence of secondary disabilities in clients with fetal alcohol syndrome (FAS) and fetal alcohol effects (FAE)*. Seattle, WA: University of Washington Publication Services.

Streissguth, A.P., Bookstein, F.L., Sampson, P.D., & Barr, H.M. (1989). Neurobehavioral effects of prenatal alcohol: Part III. PLS analyses of neuropsychologic tests. *Neurotoxicology and Teratology*, *11*, 493–507.

Streissguth, A.P. & O'Malley, K. (2000). Neuropsychiatric implications and long-term consequences of fetal alcohol spectrum disorders. *Seminars in Clinical Neuropsychiatry*, *5*, 177–190.

Swayze, V.W., 2nd, Johnson, V.P., Hanson, J.W., Piven, J., Sato, Y., Giedd, J.N., Mosnik, D., & Andreasen, N.C. (1997). Magnetic resonance imaging of brain anomalies in fetal alcohol syndrome. *Pediatrics*, *99*, 232–240.

Wechsler, D. (1991). *Manual for the Wechsler Intelligence Scale for Children–Third Edition*. San Antonio, TX: The Psychological Corporation.

Wisniewski, K., Dambska, M., Sher, J.H., & Qazi, Q. (1983). A clinical neuropathological study of the fetal alcohol syndrome. *Neuropediatrics*, *14*, 197–201.

Zaidel, D. & Sperry, R.W. (1974). Memory impairment after commissurotomy in man. *Brain*, *97*, 263–272.