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Sensory-Motor Deficits in Children with Fetal Alcohol Spectrum Disorder Assessed Using a Robotic Virtual Reality Platform

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Background: Fetal alcohol spectrum disorder (FASD) is associated with a large number of cognitive and sensory-motor deficits. In particular, the accurate assessment of sensory-motor deficits in children with FASD is not always simple and relies on clinical assessment tools that may be coarse and subjective. Here we present a new approach: using robotic technology to accurately and objectively assess motor deficits of children with FASD in a center-out reaching task.

Methods: A total of 152 typically developing children and 31 children with FASD, all aged between 5 and 18 were assessed using a robotic exoskeleton device coupled with a virtual reality projection system. Children made reaching movements to 8 peripheral targets in a random order. Reach trajectories were subsequently analyzed to extract 12 parameters that had been previously determined to be good descriptors of a reaching movement, and these parameters were compared for each child with FASD to a normative model derived from the performance of the typically developing population.

Results: Compared with typically developing children, the children with FASD were found to be significantly impaired on most of the parameters measured, with the greatest deficits found in initial movement direction error. Also, children with FASD tended to fail more parameters than typically developing children: 95% of typically developing children failed fewer than 3 parameters compared with 69% of children with FASD. These results were particularly pronounced for younger children.

Conclusions: The current study has shown that robotic technology is a sensitive and powerful tool that provides increased specificity regarding the type of motor problems exhibited by children with FASD. The high frequency of motor deficits in children with FASD suggests that interventions aimed at stimulating and/or improving motor development should routinely be considered for this population.

Key Words: Fetal Alcohol, Sensory-Motor Function, Children.

ALCOHOL CONSUMPTION DURING pregnancy is harmful to the developing embryo/fetus, and can have adverse effects on child development, growth, and central nervous system (CNS) function (Chudley et al., 2005). Fetal alcohol spectrum disorder (FASD) is an umbrella term introduced to capture the continuum of the teratogenic effects of ethanol in the human (physical, behavioral, and/or neurocognitive), ranging from full-blown fetal alcohol syndrome (FAS) to alcohol-related neurodevelopmental disorder (ARND; Chudley et al., 2005).

There are many documented cognitive (for review, see Koren et al., 2003) and motor problems (for review, see Mattson and Riley, 1998) in children with FASD, necessarily affecting various daily activities and skills. Cognitive impairments have been associated with a wide range of neurobehavioral difficulties, including deficits in speed and efficiency of information processing (Burden et al., 2005); poorer performance on complex tasks, compared with typically developing children (Aragon et al., 2008); and problems with visual-perceptual skills and sensory processing impairments such as in tactile, movement, visual/auditory, and taste/smell sensitivity (Franklin et al., 2008). Further neurobehavioral difficulties include neurological signs, such as kinetic tremors, weak grasp, seizures, and hypotonia (Spohr et al., 1993), while studies of motor development and motor skills have described motor incoordination (Roebuck-Spencer et al., 2004), difficulty with eye–hand coordination (Adnams et al., 2001), and poor balance (Barr et al., 1990), as a result of prenatal alcohol exposure. Studies in infants and children exposed prenatally to alcohol have demonstrated motor performance deficits and impaired development of both fine and gross motor skills (for review,

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see Autti-Ramo and Granstrom, 1991; Kalberg et al., 2006; Osborn et al., 1993). However, the field lacks specificity regarding the type of motor problems that are characteristic of FASD and information relating to the underlying neurophysiological mechanisms.

Robots have been widely used in the study of motor control for several decades (e.g., Klassen et al., 2005; Shadmehr and Mussa-Ivaldi, 1994) and more recently have made their way into the clinical arena, most notably in the field of stroke rehabilitation (e.g., Burgar et al., 2000; Lum et al., 2002). However, the use of robots for the *assessment* of motor function and dysfunction has recently gained in popularity (see Scott and Dukelow, 2011; Volpe et al., 2009). Recently, robotic devices have been used to quantify impairments in upper-limb sensory and motor function of subjects with stroke (Bosecker et al., 2010; Coderre et al., 2010; Dukelow et al., 2010, 2012; Ellis et al., 2008; Trumbower et al., 2008) and traumatic brain injury (Debert et al., 2012).

The main goal of the study was to use robotic technology in conjunction with a visually guided reaching task to examine sensory-motor impairments in the upper limbs of children with FASD. Reaching tasks have become an important paradigm for studying how regions of the brain are involved in the planning and control of voluntary movement (Shadmehr and Wise, 2005) and for understanding how sensory information is processed and converted into coordinated motor behavior in both the typically developing population as well as in populations with neurological disorders (Coderre et al., 2010).

Present diagnostic and clinical assessments of multijoint motor skills rely predominantly on qualitative descriptions of movement and provide only a coarse, subjective measure of motor function, leading to the global hypothesis of the current research project that robotic technology will serve as an effective tool for identifying and measuring specific, neurologically based motor deficits in children with FASD. Furthermore, we hypothesized that children with FASD would exhibit atypical performance in a visually guided reaching task, compared with their typically developing counterparts.

MATERIALS AND METHODS

Participants

All experimental procedures were reviewed and approved by the Human Research Ethics Board of Queen's University. The study population consisted of a total of 183 children (152 typically developing children and 31 children diagnosed with FASD), all between the ages of 5 and 18 years. Typically developing children were recruited from the local community, and had no known neurological or psychiatric disorders. Children with FASD were recruited from communities in southeastern Ontario. The children in the FASD group were previously assessed at local diagnostic clinics and had a diagnosis within the FASD spectrum (FAS, partial FAS, ARND) according to the Canadian Guidelines (Chudley et al., 2005). Children were excluded from the study if they had an ongoing musculoskeletal compromise of the shoulder or elbow. Participants received refreshments during the testing session (juice/water and fruit, granola bar, cookies) and received a $10 gift card for their time and contribution to the research project.

Experimental Apparatus

Robotic assessment was performed using the bimanual KINARM robot (BKIN Technologies Ltd., Kingston, ON, Canada; see Scott, 1999); a schematic representation of the experimental setup is shown in Fig. 1*A*. Participants sat in the wheelchair base with each arm snugly fit within an exoskeleton, which was adjusted to the dimensions of the child's limb. The robot constrains limb movement to the horizontal plane and monitors hand, shoulder, and elbow motion. Children were allowed free head movement, but vision of their arms and hands was occluded. Hand position feedback was provided by a computerized representation (small white circle, 0.4 cm radius) of the tip of the child's index finger.

Experimental Task

The experimental task was similar to that described in Coderre and colleagues (2010), although adjusted slightly for children. Briefly, the goal of the task is to make unassisted reaching movements "quickly and accurately" from a central target to 1 of 8 peripheral targets (all 1 cm radius) distributed uniformly on the circumference of the circle (6 cm from the center to each peripheral target). The central target was selected to be near the center of the arm's workspace (90° of elbow flexion and 30° of shoulder extension; see Fig. 1*B*). Children began each trial by holding their index finger tip within the central target for 1,250 to 1,750 ms, after which a peripheral target was illuminated. Children were then given 3,000 ms to complete the reach. The 8 peripheral targets were presented once each in a block design and repeated 8 times for a total of 64 trials. After completion of all trials using 1 arm (selected randomly), the same protocol was repeated with the other arm.

Data Analysis

Movement onset and offset were identified using the algorithm described in Coderre and colleagues (2010); essentially, statistical thresholds based on hand speed during the central target hold time were calculated for each participant, and these were used to determine when the participant had left the central target and when they had ended their movement.

Reaching performance was quantified using 12 movement parameters calculated from each trial (see Coderre et al., 2010). These parameters were categorized into 5 attributes of sensorimotor control: (a) *postural control*, how well children were able to hold posture (*ps*, postural stability in m/s, the mean speed of the hand during the central target hold time); (b) *reaction time*, how quickly children were able to respond to the target presentation (*rt*, reaction

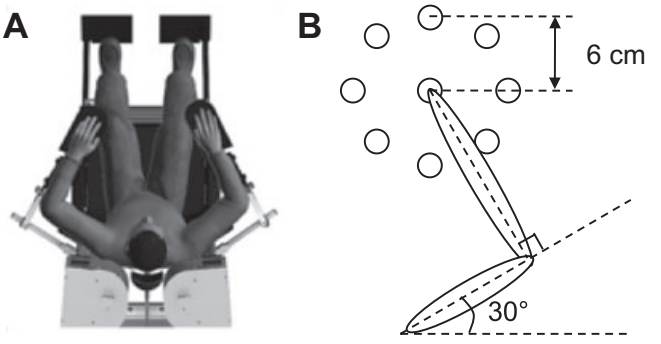

Fig. 1. KINARM robotic device. (**A**) Picture and schematic of device, showing a top–down view with a virtual subject sitting in the chair and resting their arms in the robotic exoskeleton. (**B**) Children moved from the central target, set at 30° of shoulder extension and 90° of elbow flexion, to 8 surrounding targets in a 6 cm radius.

time in seconds; *nmo*, number of trials with no reaction time, that is, no movement onset); (c) *initial movement*, measures of the initial part of the movement before any corrections (*ide*, initial movement direction error in degrees; *imr*, initial movement ratio, the proportion of the total movement that was the initial movement; *hsr*, initial hand speed ratio, the ratio of the first hand speed maximum to the mean speed); (d) *corrected movements*, measures of the subsequent corrected movements after the initial part (*nsp*, number of speed peaks; *dsm*, differences between speed maxima/minima in m/s; *nme*, number of trials for which no movement end detected); and (e) *total movement metrics*, general measures of the overall movement (*mt*, movement time in seconds; *plr*, hand path length ratio; *mhs*, maximum hand speed in m/s). The only changed parameter from Coderre and colleagues (2010) is the use of hand path length ratio rather than total hand path length. This parameter was deemed a better measure because it takes into account the total hand path length and normalizes it to the shortest distance from the central target to the hand end point.

Statistical analyses were performed in MATLAB (Mathworks, Natick, MA) and SPSS (IBM, Armonk, NY). We used linear regression to quantify age-related changes for each parameter. The data from the typically developing children were first checked for normality (Lilliefors test, $p < 0.05$). In the case of nonnormal data, a transformation was applied to the data and another test was performed. Transformations applied were logarithmic, square root, or exponential. Logarithmic transformations were applied to the following data: postural stability; initial direction error; number of speed peaks; differences between speed maxima/minima; movement time; and maximum hand speed. If no transformation produced normal data for the parameter (no transformation possible), the data were split up into 3 distinct age groups of 5 to 9, 10 to 13, and 14 to 18 years (number of trials with no reaction time; initial direction ratio; initial hand speed ratio; number of trials for which no movement end detected; path length ratio). Kolmogorov–Smirnoff tests were used to quantify effects of sex (males vs. females) and active arm (dominant vs. nondominant). If significantly different, data from each group were separated and used to compute normative statistics.

Performance of the typically developing children was used to identify a normative range that spanned 95% of the group and reflected the influence of age, sex, and handedness. The 95% range could be 2-sided (for initial movement ratio, hand speed ratio, and movement speed) or 1-sided (all other parameters). Values for each parameter were converted into a normalized score for visualization purposes by converting the 5th, median, and 95th percentiles to −1, 0, and 1, respectively.

RESULTS

A total of 183 children were tested during the performance of the reaching task and entered for statistical analyses. Both groups had similar mean ages (11.1 years for the typically developing group and 11.5 years for the FASD group). Participant demographic information for the group of typically developing children and the group of children with FASD entered in the final analysis is reported in Table 1, with extra specifics for the FASD population in Table 2. Ethnicity information for the control group was not routinely collected, although the great majority of children in this group were Caucasian as is reflected by the local population. Similarly, the FASD group in this study was predominantly Caucasian (30 children were Caucasian, 1 child was First Nations).

Table 1. Participant Demographics

	Typically developing	FASD	Significantly different?
n	152	31	N/A
Age range (years)	5–18	5–18	N/A
Mean age + SD (years)	11.16 ± 4.1	11.5 ± 3.3	No ($t_{181} = 0.50$, $p = 0.617$)
Sex (M:F)	48:52%	61:39%	No ($Z = 1.33$, $p = 0.184$)
Dominant hand (R:L)	89:11%	68:32%	Yes ($Z = 2.36$, $p = 0.018$)

FASD, fetal alcohol spectrum disorder.

Table 2. Specific Information on the Children with FASD

Characteristic	Total	Males	Females
Gross motor (upper) ability	6% p, 42% f, 52% g	5% p, 30% f, 65% g	9% p, 64% f, 27% g
Fine motor ability	38% p, 36% f, 26% g	45% p, 50% f, 5% g	27% p, 9% f, 64% g
Learning disability (Y:N)	87:13%	90:10%	82:18%
Comorbid ADHD (Y:N)	71:29%	85:15%	85:15%
Prescribed medication (Y:N)	77:23%	85:15%	63:37%
Adopted (Y:N)	97%:(1 missing)	95%:(1 missing)	100:0%

ADHD, attention-deficit hyperactivity disorder; FASD, fetal alcohol spectrum disorder.

Motor ability scores are as rated by parents: p = poor, f = fair, g = good. For the other scores, Y = yes and N = no; adopted includes living with grandparents.

Global Features

Illustrative reaching data for a typically developing child and a child with FASD are shown in Fig. 2. There was a pronounced age effect; unsurprisingly older children (Fig. 2*B*,*D*) tended to make straighter reaches than younger children (Fig. 2*A*,*C*). Furthermore, younger children with FASD (Fig. 2*C*) made generally less straight reaches than younger typically developing children (Fig. 2*A*), whereas this discrepancy diminished in the older children.

Group Effects

The group demographics were similar (all *p*s > 0.1) except for a significant difference in handedness between the 2 groups: typically developing children were significantly more likely to be right-handed than children with FASD (2-tailed Fisher's exact test, $p = 0.006$). However, there were no differences in performance between the groups due to hand dominance for any of the parameters. All group data including mean, standard deviation, *F*-tests, and effect sizes are shown in Table 3.

To test group effects for postural control, a 1-way analysis of variance was used with group as the independent variable and postural stability as the dependent variable. A significant effect was found, $F(1, 182) = 25.03$, $p < 0.001$, typically

developing children tended to have lower postural speed than children with FASD. To test group effects for the other sets of parameters (reaction time, initial movement, corrective movements, and total movement metrics), a multivariate analysis of variance was used with group as the independent variable and the parameters in the set (e.g., reaction time itself and the number of no movement onsets for reaction time) as the dependent variables, at an alpha level of 0.05. Initial movement, corrective movements, and total movement metrics all showed a significant effect of group, while reaction time did not, reaction time: $F(2, 180) = 2.36$, $p = 0.098$; initial movement: $F(3, 179) = 15.40$, $p < 0.001$; corrective movements: $F(3, 179) = 11.40$, $p < 0.001$; total movement metrics: $F(3, 179) = 12.94$, $p < 0.001$. Of the 12 individual variables tested, the majority (9/12) showed significant effects of group. Generally, typically developing children performed better on all of these metrics compared with children with FASD. Also, half of the variables tested had a large effect size (Cohen's $d > 0.8$). The variables that had the largest effect sizes and thus the largest difference between the control and FASD populations were initial direction error, path length ratio, differences in speed maxima and minima, postural speed, initial movement ratio, and the number of speed peaks. Thus, large differences were observed in elements of all aspects of reaching control except for reaction time in children with FASD compared with typically developing children.

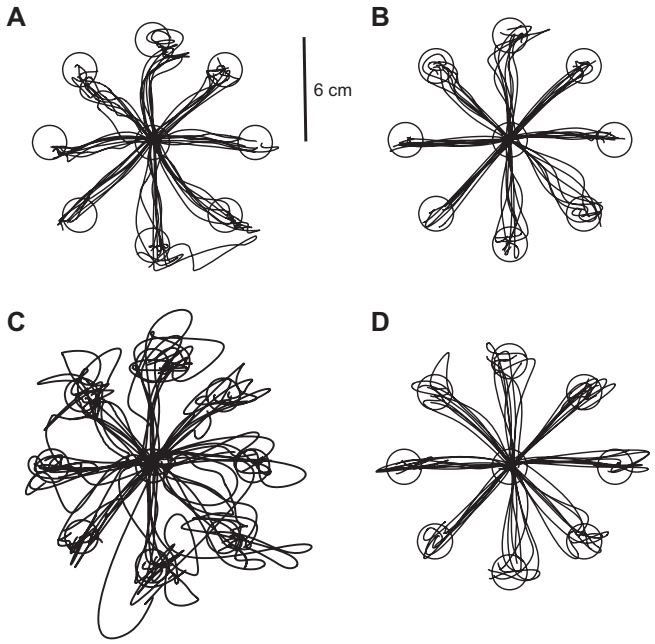

Fig. 2. Data from representative subjects; dominant (right) arm shown only. (**A**) Younger and (**B**) older typically developing children; (**C**) younger and (**D**) older children with fetal alcohol spectrum disorder (FASD). Younger children were aged between 5 and 6; older children were aged between 15 and 16. There appeared to be few differences between the older children, but a markedly worse performance in the younger children with FASD than in the younger typically developing children.

Group Effects Taking Age into Account

Normative models were created from the typically developing children's data for each of the 12 outcome measures; see the Materials and Methods section for information on the construction of these models. Postural speed and reaction time were broken down by handedness as there were differences in the normative models generated from the typically developing children. No normative models showed differences due to sex. Figure 3*A–C* shows these normative models for 3 of the outcome measures: postural hand speed; initial movement direction error; and path length ratio. The medians, quartiles, and 95% confidence intervals were plotted to show a normative range of performance for each parameter, depending on age (Fig. 3*A*: no correction necessary; Fig. 3*B*: exponential correction; Fig. 3*C*: no correction possible). Postural hand speed was influenced by hand dominance, so data are separated for dominant (black) and nondominant hands (gray). In each panel, data obtained from

Table 3. Summary of Means (and Standard Deviations) for Each Parameter, Comparing the Typically Developing and FASD Groups. *F*-test Values and Effect Sizes (Cohen's *d*) are also Shown

Attribute of control	Parameter name	Mean (SD)		*F*-value	Effect size *d*
		Typical	FASD		
Postural control	Postural stability (*ps*)	0.38 (0.13)	0.53 (0.22)	$F(1, 182) = 25.03$	0.99***
Reaction time	Reaction time (*rt*)	0.38 (0.09)	0.42 (0.11)	$F(1, 181) = 4.37$	0.41*
	No movement onsets (*nmo*)	0.48 (0.89)	0.62 (1.00)	$F(1, 181) = 0.66$	0.16
Initial movement	Initial direction error (*ide*)	4.43 (1.64)	6.47 (2.30)	$F(1, 181) = 34.29$	1.16***
	Initial movement ratio (*imr*)	0.77 (0.11)	0.67 (0.12)	$F(1, 181) = 21.24$	0.91***
	Hand speed ratio (*hsr*)	0.95 (0.04)	0.93 (0.04)	$F(1, 181) = 6.53$	0.51**
Corrective movements	Number of speed peaks (*nsp*)	2.44 (0.44)	2.82 (0.50)	$F(1, 181) = 3.55$	0.82***
	Differences between speed max/min (*dsm*)	1.59 (0.58)	2.23 (0.82)	$F(1, 181) = 10.71$	1.03***
	No movement end points (*nme*)	1.03 (1.89)	2.03 (2.79)	$F(1, 181) = 25.72$	0.49*
Total movement metrics	Movement time (*mt*)	1.07 (0.20)	1.11 (0.18)	$F(1, 181) = 1.27$	0.22*
	Path length ratio (*plr*)	1.22 (0.10)	1.33 (0.14)	$F(1, 181) = 31.25$	1.11***
	Max hand speed (*mhs*)	14.3 (3.43)	14.3 (3.06)	$F(1, 181) < 0.001$	<0.01

FASD, fetal alcohol spectrum disorder.
Asterisks show small (*), medium (**), and large (***) effect sizes.

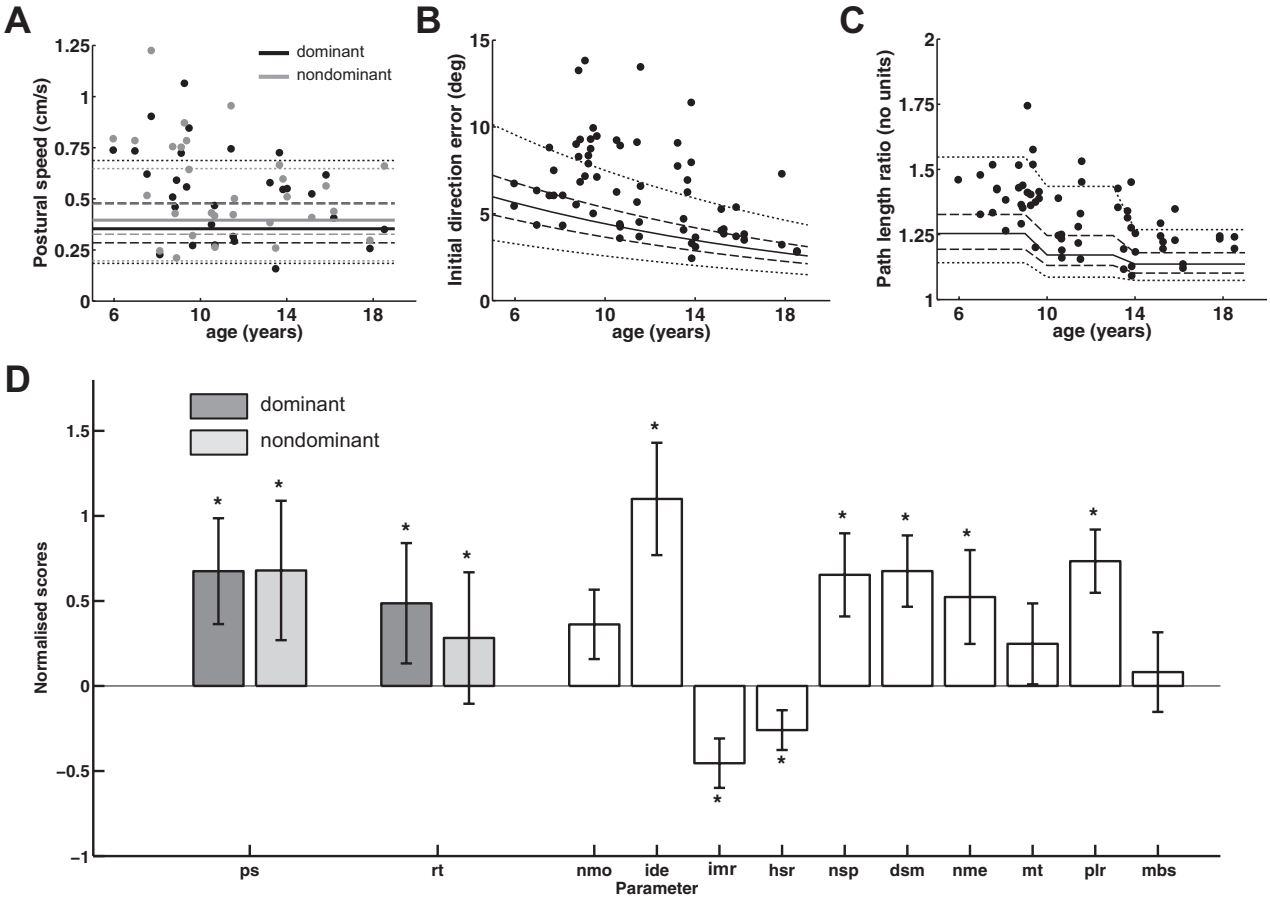

Fig. 3. Age-corrected reaching performance. (**A**) Postural hand speed. Circles denote performance of children with fetal alcohol spectrum disorder (FASD). Normative models constructed from data from the typically developing children (solid lines, 50th; dashed lines, 25th and 75th; dotted lines 5th, and 95th percentiles). Data for dominant (black lines/circles) and nondominant (gray lines/circles) hands were separated due to significant difference for this parameter. (**B**) Initial direction errors. Data for dominant and nondominant were combined as there was no significant difference for this parameter. (**C**) Path length ratio. Data format same as panel **B**. (**D**) Group differences in normalized scores for each parameter. Bars show means and standard errors of normalized scores for children with FASD, taking zero as the baseline set by the normative models from the typically developing children and ± 1 as the 95% confidence intervals. *Significantly different from control, $p < 0.05$.

the children with FASD are superimposed, and illustrate that the majority of the children with FASD are not randomly distributed around the median values of the normative range, but are instead strongly skewed to a higher range with a large fraction outside the 95% confidence intervals.

For each individual participant, normalized scores can be created for each parameter where a score of 0 indicates the median and ± 1 indicates the 95% confidence interval. Thus, individual participants with scores >1 or <−1 can be said to be outside the normal range. Figure 3*D* shows the group data for the children with FASD across all parameters as normalized, age-corrected scores. *t*-Tests, corrected for unequal variances where necessary, were used to test for significant differences in each parameter between children with FASD and typically developing children. Such differences were found for every parameter except number of no reaction times and the maximum hand speed; see Table 4 for details. Compared with typically developing children, children with FASD had higher postural hand speed, higher reaction times, a higher initial direction error, a lower initial direction ratio and hand speed ratio, higher values in all parameters of corrective movement, and higher total movement time and path length ratio. All of these results point to significantly impaired reaching control for the children with FASD compared with the typically developing children.

Individual Classification

As noted above, the normative models that were created from the typically developing children's data for selected outcome measures are shown in Fig. 3*A–C* with the data from children with FASD superimposed on them. It is evident from this analysis that a large proportion of children with FASD fall outside of the 95% confidence intervals of the normative models. In some cases, younger children are disproportionately outside this range (e.g., postural speed), whereas in other cases, children with FASD across all ages may fall outside this range (e.g., initial direction error).

To classify participants into typically developing or FASD, we looked at the percentage of children who had

Table 4. Summary of Group Differences for the Age-Corrected, Reaching Task Parameters Obtained from Typically Developing Children and Children with FASD

Attribute of control	Parameter	Mean (SD)			
		Typical	FASD	*t*-Value	*p*-Value
Postural control	*ps* (dom)	0.11 (0.49)	0.65 (0.82)	$t(34.4) = 3.59$	0.001*
	ps (nondom)	−0.07 (0.64)	0.65 (1.08)	$t(34.5) = 3.61$	0.001*
Reaction time	*rt* (dom)	0.03 (0.54)	0.49 (0.92)	$t(34.4) = 2.69$	0.011*
	rt (nondom)	−0.19 (0.63)	0.27 (1.01)	$t(35.0) = 2.48$	0.018*
	nmo	0.22 (0.37)	0.34 (0.54)	$t(36.1) = 1.12$	0.268
Initial movement	*ide*	0.07 (0.43)	1.03 (0.90)	$t(32.8) = 5.79$	<0.001*
	imr	−0.05 (0.35)	−0.46 (0.39)	$t(181) = -5.80$	<0.001*
	hsr	−0.08 (0.31)	−0.26 (0.32)	$t(181) = -3.03$	0.003*
Corrective movements	*nsp*	0.04 (0.46)	0.63 (0.64)	$t(36.5) = 4.83$	<0.001*
	dsm	0.09 (0.40)	0.64 (0.58)	$t(36.0) = 5.07$	<0.001*
	nme	0.16 (0.41)	0.50 (0.73)	$t(26.4) = 2.17$	0.039*
Total movement metrics	*mt*	0.04 (0.52)	0.26 (0.64)	$t(181) = 2.03$	0.043*
	plr	0.10 (0.40)	0.70 (0.52)	$t(37.5) = 6.00$	<0.001*
	mhs	0.06 (0.62)	0.05 (0.65)	$t(181) = -0.02$	0.981

FASD, fetal alcohol spectrum disorder; dom, dominant; nondom, nondominant.
*Significant differences. See Table 3 for definitions of parameter abbreviations.

failed (i.e., were outside the 95% confidence intervals for) a certain number of core parameters, that is, we calculated the number of parameters failed by typically developing children and children with FASD. Overall, children with FASD failed significantly more parameters than typically developing children (Fig. 4*A*, Kolmogorov–Smirnov, $p = 0.019$). Seventy-two percent of typically developing children failed on zero parameters, which drops to just 26% for the children with FASD. The graph shows that the typically developing children saturate quickly, with almost 100% of typically developing children failing no more than 3 parameters, whereas some children with FASD fail on up to 7 parameters.

Figure 4*B* illustrates the same process using the same data as Fig. 4*A* based not only on the number of fails but also split by age. Age classification was by threshold, and was divided into 3 bands, similar to those used in the normative models: "younger" (5 to 9 years), "middle" (10 to 13 years) and "older" (14 to 18 years). The figure shows that in the younger age range over 90% of children with FASD failed at least 1 parameter, compared with 55 to 65% of children in the middle and older ranges. Furthermore, for the older children, the percentage who failed 3 parameters or less increases to almost the same percentage as typically developing children, whereas both the middle- and younger-aged children take much longer to reach this stage. We found that "younger" and "middle" but not "older" aged children with FASD failed more parameters than similarly aged typically developing children (Kolmogorov–Smirnoff; younger, $p = 0.019$; middle, $p = 0.004$; older; $p = 0.603$). This is consistent with clinical findings that the symptoms of FASD tend to be less acute as children get older.

DISCUSSION

The current study sought to investigate the potential of robotic technology to identify and measure specific, neurologically based sensory-motor deficits in individuals with FASD. The robot can measure various deficits in sensory-motor control via a range of parameters that describe good reaching control. The observed pattern of problems in the reaching task in those with FASD include greater upper-limb instability, combined with errors in direction within the first movement of the reach, leading to more corrective movements, which were often inefficient in themselves, as evidenced by longer path length ratios.

Children with FASD showed considerable deficits in virtually all aspects of sensory-motor control. This finding is consistent with studies investigating fine motor performance in young children prenatally exposed to alcohol, which report increased errors and latency on fine motor tasks included in the Wisconsin Fine Motor Steadiness Battery (Barr et al., 1990) and deficits in motor speed and visual-motor integration tested using the Beery-Buktenica Developmental Test of Visual-Motor Integration and the Grooved Pegboard Test (Mattson et al., 1998). Group mean motor deficits have been documented in eye and hand coordination tasks, using the Griffiths Mental Development Scales (Adnams et al., 2001), and in complex bimanual coordination tasks (Roebuck-Spencer et al., 2004).

Impairment in Control During Execution of a Reach

A key feature of goal-directed reaching movements is that the hand follows a fairly straight path; however, the complex mechanics of multilimb movement complicate the generation of muscle activity required to make such a straight trajectory and thus the CNS must actively take the biomechanics of the limb into account (Vesia et al., 2005). The CNS has to predict the mechanical effects that arise from motion of the linked limb segments when preplanning arm muscle activity, particularly for the initial motion of the arm toward a target (Sainburg et al., 1999). One way this prediction may take place is through an internal model of the movement, which

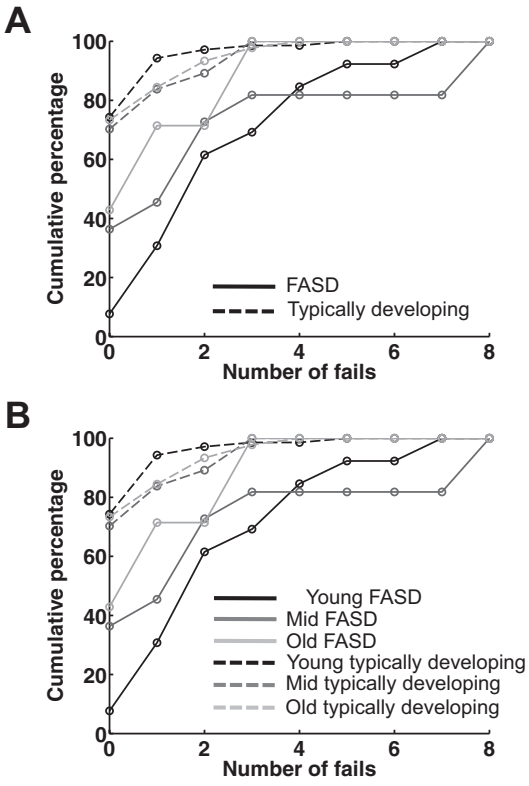

Fig. 4. Classification based on failure rate, that is, how many parameters children were scored outside the 95% confidence limits. The *y*-axis shows the cumulative percentage of children with equal to or more than a particular number of fails (shown on the *x*-axis). (**A**) Approximately 70% of children with fetal alcohol spectrum disorder (FASD) (solid lines) and 30% of typically developing children (dotted lines) were outside the 95% confidence limits for at least 1 parameter, dropping to around 12 and 1% for 5 parameters, respectively. (**B**) When divided by age, older children with FASD (light gray, solid lines) fell to the same failure rate as typically developing children (dotted lines) at 4 fails or more, whereas the failure rate of younger children with FASD (black and mid-gray solid lines) was consistently higher.

the CNS gradually develops during practice of novel tasks and then uses to control movements made under similar task conditions (Miall and Wolpert, 1996; Shadmehr and Mussa-Ivaldi, 1994; Thoroughman and Shadmehr, 1999). When interaction effects from muscle torques are not anticipated, errors in hand path occur, which can be seen in patients following nervous system injury (Flash and Henis, 1991). We found that children with FASD demonstrated impaired ability to execute straight hand movements to each target, exhibiting difficulty in integrating information about the arm and the target to effectively plan and execute smooth reaching movements.

As the controller must possess an internal representation of how the controlled system behaves to generate the appropriate outgoing motor commands (Vesia et al., 2005), in those with FASD in the current study, impairment in the predictive system may cause the observed deficits in the initial portion of the reach. But the CNS also makes use of both internal and external feedback during reaching movements—current theories such as optimal feedback control (Scott, 2004) hypothesize that rapid feedback responses are necessary for the smooth control of the limb, as the predictive controller is updated by feedback loops as the movement unfolds (Sainburg et al., 1999). The FASD group also showed deficits in feedback control during the execution of a reaching movement, demonstrated by their lack of ability to correct for errors made in the initial phase of movement.

Another possible mechanism underlying the poorer performance of children with FASD in the current study is that of inadequate sensory processing; for example, Piek and Dyck (2004) demonstrated a link between developmental disorders and sensory-motor deficits. The reaching task we used relies on visual and proprioceptive sensory information, and we know that children with FASD appear to have deficits in the encoding (Coles et al., 2002) and processing (Burden et al., 2005) of such information. In addition, sensory processing deficits in children with FASD have been shown to be 2 to 6 times greater than in typically developing children between the ages of 2 and 19 years (Carr et al., 2010). The current results point to several indicators of sensory processing difficulties: For example, the large deficits in initial movement angle may indicate that children with FASD are failing to integrate sensory information into planning and executing movements.

Finally, deficits in motor skills such as reaching may also reflect more general deficits in motor learning and cognitive processes that support skill acquisition. For example, children with FASD exhibit substantial and persistent deficits in eye-blink conditioning, a well-characterized form of motor learning (Jacobson et al., 2011a). Moreover, children with FASD are equally impaired in versions of the task that engage higher cortical structures to encode the learned response (Jacobson et al., 2011a,b). Thus, difficulties in reaching may reflect underlying impairments in a number of different sensory, motor, and/or cognitive processes. This result highlights the need to expand the range of behavioral tasks examined in children with FASD and in other neurological disorders, to tease apart the underlying impairments, allowing interventions to be focused on these underlying impairments.

Brain Regions Likely Implicated in Observed Performance Deficits

Past studies have implicated several brain regions as possible neural underpinnings of motor deficits in subjects with FASD, including the corpus callosum (CC), which plays a role in motor functioning and has been shown to be affected by exposure to alcohol in utero (Sowell et al., 2008a). Further support for the CC's role in this kind of motor task comes from a study that found that subjects with agenesis of the CC, on an arm movement task, performed slower and less accurately than typically developing subjects (Mueller et al., 2009). Disruption of fibers in the CC in those with

FASD is associated with impaired visuomotor integration (Sowell et al., 2008b) and may explain some of the observed deficits in the reaching task.

One brain region that is known to be involved in arm movements bilaterally is the dorsal premotor cortex (PMd). Cisek and colleagues (2003) showed that while the primary motor cortex (M1) is strongly activated during movements of the contralateral arm, the majority of cells in PMd were activated during the movement of either arm. Thus, the authors argue, PMd seems to represent movement in a more abstract or task-dependent and effector-independent way. From this perspective, PMd in both hemispheres participates in controlling movements of a given limb. Disruption of the CC would impact communication and interactions between the 2 PMds, leading to impairments in limb motor function.

Altered motor function is also consistent with damage to the cerebellum (Bookstein et al., 2006; Guerri et al., 2009), which has been shown to be vulnerable to alcohol's teratogenic effects. The cerebellum is known to be important for the representation of temporal information (Paquier and Marien, 2005), sensory processing (Restuccia et al., 2007), and the processing of spatial information (Nitschke et al., 2005). Individuals with cerebellar lesions have been shown to exhibit abnormal reaches, compared with controls (Bastian et al., 1996). In particular, sensory-motor function has been localized to the anterior portion of the cerebellum (Stoodley and Schmahmann, 2009), and indeed, the observed damage in cerebellum of those with FASD has been shown to be more pronounced in the anterior lobe (O'Hare et al., 2005). This observation might explain the impaired performance observed in those prenatally affected by alcohol in the sensory-motor task used in the current study.

Clinical Relevance

Knowledge of the distribution of kinematic parameters in those with FASD, compared to healthy subjects, is crucial for the evaluation of individuals who exhibit motor impairment due to prenatal alcohol exposure. In terms of clinical utility, assessment of children's motor abilities will help to identify specific areas of weakness. Knowledge and identification of impairment in motor development in individuals could improve prognosis as it may serve to increase services and support. The current findings suggest that some degree of motor dysfunction existed in almost all of the prenatally alcohol exposed individuals tested. Knowledge regarding how specifically their motor skills are impaired, through how they fare on various movement parameters compared with a normative model of typically developing children, may provide valuable information for families and professionals in developing new and appropriate (or ameliorating existing) programs for these children, targeting particular deficit areas, and thereby improving treatment.

Furthermore, we clearly demonstrate here that younger children with FASD tend to be significantly more impaired than their older cohorts. The ability to identify particular deficits that children with FASD have on this reaching task at various ages, compared with a typically developing population, is a key strength of our approach, and may provide a way to measure the improvement of motor skills as the child matures, and/or quantify the impact of intervention programs.

Future Directions

It is hypothesized that a continuum of interaction exists between neurological processing of sensory input and behavioral responses (Franklin et al., 2008); perhaps differing degrees of severity across the spectrum of fetal alcohol disorders would result in differing degrees of motor deficits. Exploring the different FASD diagnostic subgroups might expose some existing vulnerability of some subgroups, to sensory-motor deficits, compared with others.

The findings regarding motor deficits in the current study may not be specific to FASD—in fact, many of the children with FASD exhibited comorbidity with other neurological disorders such as attention-deficit/hyperactivity disorder (ADHD). Future evaluation of sensory-motor control in children with other developmental disorders, including ADHD, autism, developmental coordination disorder, and cerebral palsy will be important for determining whether our findings point to a particular pattern of motor deficit specific to those with FASD or is shared by other clinical populations, perhaps whose brain injury is overlapping or different. Further study of other neurodevelopmental disorders using robotic technology may help delineate motor profiles for each clinical disorder and allow us to address questions relating to overlapping versus distinct patterns of deficits in motor performance.

In summary, the current study has shown that robotic technology is a sensitive and powerful tool that provides increased specificity regarding the type of motor problems exhibited by children with FASD. The high frequency of motor deficits in children with FASD suggests that interventions aimed at stimulating and/or improving motor development should routinely be considered for this population.

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