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Research Report

Functional MRI evidence for fine motor praxis dysfunction in children with persistent speech disorders ☆

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Abstract: Children with persistent speech disorders (PSD) often present with overt or subtle motor deficits; the possibility that speech disorders and motor deficits could arise from a shared neurological base is currently unknown. Functional MRI (fMRI) was used to examine the brain networks supporting fine motor praxis in children with PSD and without clinically identified fine motor deficits.

Methods: This case-control study included 12 children with PSD (mean age 7.42 years, four female) and 12 controls (mean age 7.44 years, four female). Children completed behavioral evaluations using standardized motor assessments and parent reported functional measures. During fMRI scanning, participants completed a cued finger tapping task contrasted passive listening. A general linear model approach identified brain regions associated with finger tapping in each group and regions that differed between groups. The relationship between regional fMRI activation and fine motor skill was assessed using a regression analysis.

Results: Children with PSD had significantly poorer results for rapid speech production and fine motor praxis skills, but did not differ on classroom functional skills. Functional MRI results showed that children with PSD had significantly more activation in the cerebellum during finger tapping. Positive correlations between performance on a fine motor praxis test and activation multiple cortical regions were noted for children with PSD but not for controls.

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Conclusions: Over-activation in the cerebellum during a motor task may reflect a subtle abnormality in the non-speech motor neural circuitry in children with PSD.

1. Introduction

Speech disorders, characterized by errors in speech production, are common in children up to five years of age with prevalence estimates ranging from 14% to 25% (Jessup, Ward, Cahill, & Keating, 2008; McLeod & Harrison, 2009). As children enter the elementary school years many of these disorders resolve as the prevalence rates drop to 3.8%–9% (National-Institue-on-Deafness-and-Other-Communication-Disorders, 2010; Shriberg, Tomblin, & McSweeny, 1999). Children who present with speech disorders beyond the preschool years may have a Persistent Speech Disorder (PSD) (Shriberg et al., 2010). The lack of resolution of PSD may be a clinically sensitive sign of a more generalized delay in neurological development.

An emerging body of research supports the idea that the motor skills and speech and language follow similar developmental trajectories. Typically developing infants demonstrate a correlation between the longitudinal changes in their articulatory movements and early communication development (Nip, Green, & Marx, 2011). Children with speech disorders (persistent or resolving) also demonstrate a similar, but delayed, trajectory. Gross and fine motor differences are noted in children with speech disorders (Cermak, Ward, & Ward, 1986) as well as in children with co-occurring speech and language disorders (Owen & McKinlay, 1997; Sommers, 1988; Visscher et al., 2010; Visscher, Houwen, Scherder, Moolenaar, & Hartman, 2007; Webster et al., 2006; Webster, Majnemer, Platt, & Shevell, 2005). Deficits in oral-motor praxis have been specifically linked to both an existing language deficit (Alcock, 2006) and long term written language outcomes (Lewis et al., 2011). These findings suggest that speech and motor delays may be associated with a common developmental deficit of fine motor function.

Children with speech disorders also demonstrate subtle motor deficits outside of the realm of speech (Locke, 1983; Newmeyer, Grether, & Grasha, 2007; Peter & Stoel-Gammon, 2008). These children are slower when asked to complete rapid repetition of speech sounds, but also demonstrate differences in oral motor control compared to typically developing children (Lewis et al., 2011). Children with speech disorders also demonstrated deficits in paced repetitive finger tapping and clapped rhythm activities compared to typical controls (Peter & Stoel-Gammon, 2008), as well as lower levels of performance for grasping, object manipulation, and visual motor skills (Newmeyer et al., 2007). These studies support the perspective of a general deficit in planning and programming motor movements that affects speech production, as well as, fine motor limb and finger movements rather than a speech-specific motor impairment; and in fact that speech may be a sensitive marker of overall motor programming or execution differences (Lewis et al., 2011). The underlying mechanism is not known, but these findings support the need for studies of sensorimotor processes in children with speech disorders of unknown origin (Shriberg, Gruber, & Kwiatkowski, 1994).

Neuroimaging may be a useful tool for understanding the developmental differences in the neural structures and pathways present in children with speech disorders, including PSD. Although behavioral data are only measured through the observed endophenotype, neuroimaging may provide a unique insight into the differences in neurological processing and programming that support the execution of observable behaviors. To date, there have been relatively few imaging studies investigating the anatomical and functional markers of developmental speech disorders. In one recent study of children with speech production errors, greater activation during receptive language was noted in multiple regions including the cerebellum, insula, and cingulate cortex (Preston et al., 2012). Differences were found in the neural substrates for phonological memory necessary to complete a speech repetition task as well (Tkach et al., 2011). During this speech production activity, children with speech disorders demonstrated both regions of hypoactivation and hyperactivation when compared to typically developing peers. Specifically, stronger activation was noted in the cerebellum and in the pre- and supplementary motor cortex in participants with speech disorder than in controls (Tkach et al., 2011). The cerebellum, pre-, and supplementary motor cortex regions were also implicated in a positron emission tomography (PET) activation study of the widely studied KE family (Belton, Salmond, Watkins, Vargha-Khadem, & Gadian, 2003; Vargha-Khadem et al., 1998; Watkins et al., 2002) a group of related individuals with a high prevalence of speech disorders. Compared with non-affected KE family members, members presenting with speech disorders had gray matter volume differences in Broca's area, the pre-supplementary motor area (SMA), the caudate nucleus, and the lentiform nucleus (Belton et al., 2003; Vargha-Khadem et al., 1998; Watkins et al., 2002). Findings from these studies show differences in various regions of the brain not limited to speech and language production, supporting the hypothesis that children with speech errors may have a more generalized underlying neurological difference. The specific location of neural differences in relation to motor deficits in children with a PSD and how it may present both behaviorally and functionally is not currently known. Improved understanding of the underlying neural differences in praxis may provide insight in improving current therapeutic interventions or developing novel approaches.

Functional MRI can also be used to elicit the underlying neural activation patterns for motor patterns, and specifically fine motor praxis. Finger tapping tasks are a common method of investigating the motor system when completing fMRI. In multiple studies finger tapping tasks have been shown to activate

primary motor and sensory cortex, superior frontal regions (supplementary motor), subcortical regions including basal ganglia, and the cerebellum (Witt, Laird, & Meyerand, 2008). In children, one recent study (De Guio, Jacobson, Molteno, Jacobson, & Meintjes, 2012) demonstrated that children, compared to adults, had increased activation in a number of regions of this motor network, including the cerebellum.

In the present study, we sought to investigate the associations between motor praxis and the behavioral presentation of these possible associations in children with PSD, as well as how these associations compare to children with typical speech production. To determine this, functional MRI was used to elucidate the neural correlates of fine motor praxis during a cued fingertapping task. The neural correlates obtained during the cued fingertapping task were then compared to behavioral tests of fine motor praxis to determine if fine motor proficiency had a relationship with the neural activation patterns in children with PSD. Behavioral test results for children with PSD were also compared to the results obtained from the children with typical speech production. Based on findings from previous behavioral and imaging studies, we hypothesized that participants with PSD would have lower accuracy on motor skills tasks compared to age-matched controls, and that performance differences would be associated with differential activation of neural networks in regions regulating motor output as detected by fMRI.

2. Results

Speech, Language, Cognitive, and Motor Assessments

Results of all the general speech and language assessments are presented in Table 1. Children with PSD had significantly lower scores on speech (Goldman-Fristoe Test of Articulation-2, GFTA-2 (Goldman & Fristoe, 2000)), language (Clinical Evaluation of Language Fundementals-4, CELF-4 (Semel, Wiig, & Secord, 2003)), and full-scale IQ assessments (Wechsler Abbreviated Scale of Intelligence, WASI (Weschler, 1999)), although the mean language and IQ scores were within normal limits for both groups. Table 2 presents the results of motor testing. On the School Function Assessment (SFA, (Coster, Deeney, Haltiwanger, & Haley, 1998)) groups did not significantly differ in their total participation in the school environment (Total Score, $p=.09$) nor did they significantly differ on several sub-tests presented in Table 2 including Using Materials, Clothing Management, and Computer and Equipment Use (all $p>.05$). A significant difference was found for the Written-Work sub-test ($t(19)=2.15$, $p=0.045$). Diadochokinesia (DDK) rates are also presented in Table 2. Children with PSD were significantly slower for only two of the 5 DDK syllable measures: the two syllable combination ($t(21)=-2.43$, $p=.02$) and the three syllable combination ($t(21)=-2.63$, $p=.02$). All single syllable measures did not differ significantly between the two groups. The Purdue Pegboard test (Tiffin, 1948) did reveal significant differences for the left hand ($t(21)=2.35$,

Table 1 – Assessment summary of speech, language, cognitive testing standard scores for PSD and Control groups (mean=100, SD±15).

	Domain	Psychometric information	PSD (SD)	Controls (SD)	T	P value
GFTA-2[1]	Single word speech production	Norm-referenced; Reliability[4]-internal consistency .94-.96, test-retest .98; Validity-samples 23 of 25 English consonants in all word positions	78.55 (17.13)	105.75 (3.31)	5.40	<0.0001**
CELF-4[2]	Expressive and receptive language	Norm-referenced; Reliability- Test re-test reliability .88-.92[5], internal consistency.87-.95; Sensitivity .87–1.0; Specificity .82-.96	89.55 (18.71)	112.36 (18.71)	3.27	0.004**
WASI[3] verbal IQ	Word knowledge	Norm-referenced; Reliability- internal consistency .93, test-retest .92	102.14 (9.81)	110.11 (14.85)	1.22	0.24
WASI performance IQ	Visual stimuli	Norm-referenced; Reliability- internal consistency .94, test-retest .88	94.86 (14.42)	107.78 (11.85)	1.97	0.07
WASI full scale IQ	General cognitive	Norm-referenced; Reliability- internal consistency .96, test-retest .93 Validity- acceptable correlations with other measures of intelligence	98.38 (10.23)	110.22 (11.34)	2.25	0.02*

* $p<.05$.
** $p<.01$.
[1] Goldman-Fristoe Test of Articulation-2 (Goldman & Fristoe, 2000).
[2] Clinical Evaluation of Language Fundamentals-4 (Semel, Wiig, & Secord, 2003).
[3] Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999).
[4] Ranges are due to different norms for males and females.
[5] Ranges across various subtests.

Table 2 – Summary of motor skill assessments; scores presented as means (standard deviation).

	Domain	Psychometrics	Subtests	PSD	Controls	t -value	p - value
SFA[1,2]	Gross and fine motor	Criterion-referenced;	Total score (range 0–36)	35.1 (1.58)	36 (0.0)	1.82	0.09
		Reliability- internal consistency .92-.98; test-retest .80-.99;	Using materials (range 0–100)	96.4 (5.99)	95.1 (11.67)	0.32	0.75
		Validity- comprehensive, tested in multiple populations including in children with learning disabilities, cerebral palsy	Clothing management (range 0–68)	64.91 (5.22)	66.6 (3.27)	0.88	0.39
			Computer and equipment use (range 0–48)	31.00 (6.86)	34.4 (7.41)	1.09	0.29
			Written work (range 0–48)	41.64 (7.02)	46.6 (2.12)	2.15	0.045*
DDK[3,4] **(measured in seconds)**	Rapid speech production	Norm-referenced;	3-syllable (putuku)	6.88 (1.43)	5.68 (.66)	2.63	0.02*
		Reliability- test/retest accuracy test/ retest accuracy ±.03-.35 s for DDK;	2-syllable (putu)	6.70 (2.73)	4.59 (1.20)	2.43	0.02*
			1-syllable (pu)	4.96 (3.67)	4.01 (0.75)	0.88	0.39
		Validity- valid across developmental processed and when compared to neurological populations	1-syllable (tu)	5.68 (4.52)	4.21 (0.89)	1.1	0.28
			1-syllable (ku)	4.94 (3.08)	4.09 (3.08)	0.92	0.37
Purdue Pegboard[5] **(raw number of pegs)**	Fine motor	Norm-referenced;	Left hand	8.36 (1.69)	10.0 (1.65)	2.35	0.029*
		Reliability- single run test-retest ranges .68-.73;	Right hand	8.82 (1.25)	11.67 (1.56)	4.80	<.001**
		Validity- normed and validated in children (Gardner and Broman (1979))	Both hands	6.91 (1.51)	8.42 (1.73)	2.22	0.038*

* $p<.05$.
** $p<.01$.
[1] School function assessment (Coster, Deeney, Haltiwanger, & Haley, 1998).
[2] Maximum scores for each individual test indicated with title.
[3] Diadochkinesia rates from OSMSE-3 (Louis & Ruscello, 2000).
[4] lower score indicates better performance.
[5] Purdue Pegboard (Lafayette-Insturment-Company, 1985; Tiffin, 1948).

$p=.029$), right hand ($t(21)=4.80$, $p<.001$), and the simultaneous right and left measure ($t(21)=2.22$, $p=.038$) (Table 2).

fMRI Results

2.1. Group composites and comparisons

Activation patterns were similar across both groups during the cued finger-tapping fine motor praxis task. In each group, significant regions of activation included bilateral cerebellum, bilateral middle and inferior occipital regions, fusiform gyrus bilaterally. Other significant regions of activation were in sensorimotor regions of the precentral and postcentral gyrus extending into supramarginal gyrus bilaterally, and the supplementary motor region in bilateral superior frontal gyri (Fig. 1A and 1B). Controls showed decreased activation for cued finger-tapping relative to the cue listening baseline in the parahippocampal gyrus, posterior cingulate cortex and cuneus/precuneus (components of the "default-mode" network, Fig. 1B). In a group comparison, significant differences were noted in the posterior cerebellum, bilaterally, with the PSD group demonstrating greater activation than controls (Fig. 2). MNI coordinates of all clusters of activation are included in Table 3.

2.2. Correlation analysis

Significant correlations between regional activation and Purdue Pegboard scores were noted for the PSD group but not for the controls. Activation in the left striatum, left middle frontal gyrus, right precentral gyrus, and superior frontal gyrus bilaterally (including supplementary motor regions) was positively correlated with the left-hand pegboard score (Fig. 3A). The strength of these correlations (Cohen, 1988) was small to moderate in the striatum and right precentral gyrus (>.10, <.30,), moderate to large (>.30, <.50,) in the left supplementary motor cortex, right superior frontal gyrus, right supplementary motor cortex, and right precentral gyrus) and large (>.50) in the left middle frontal gyrus. Activation in the left striatum, left supramarginal gyrus, left insula and precentral superior frontal gyri bilaterally (including supplementary motor regions) was positively correlated with

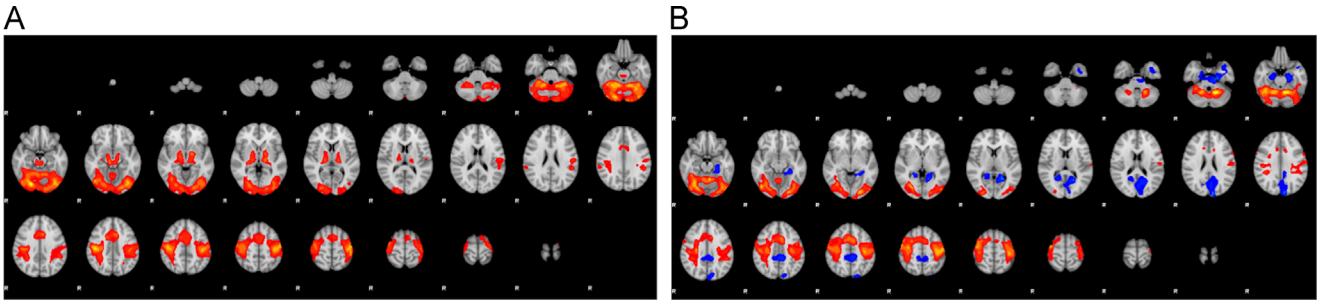

Fig. 1 – Group composite activation maps for (A) children with PSD and (B) controls while performing a cued fingertapping task; Tap > listen [z > 2.3, p < 0.05 as determined by cluster-based inference]. Images are in radiologic orientation.

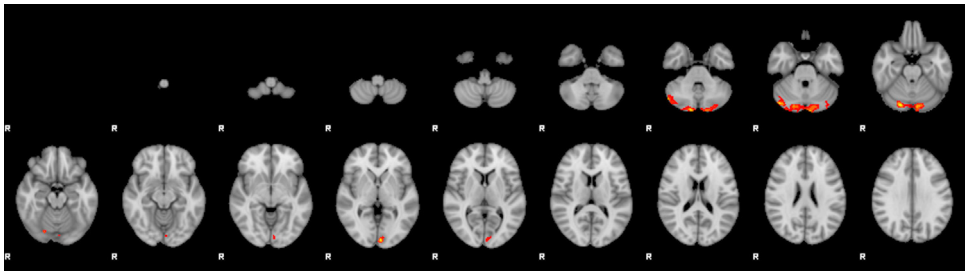

Fig. 2 – Comparison map demonstrating regions of increased activation in children with PSD compared to controls; PSD > controls; [z > 2.3, p < 0.05 as determined by cluster-based inference]. Image is in radiologic orientation.

Table 3 – MNI coordinates for regions of activation during the cued finger tapping task in children with PSD and healthy controls, and regions of activation that differed between groups.

Region	x (mm)	y (mm)	z (mm)	Extent in Voxels
Regions active for finger tapping > Cue listening in children with PSD				
L Supramarginal gyrus	−49.8	−29	33.9	243
L Precentral/Postcentral	−37.5	−20.5	56	328
L Fusiform gyrus	−35.6	−77.2	−12	264
L Cerebellum V-VI	−17.7	−57.4	−25.2	377
L Lingual gyrus	−4.31	−89.7	−13	397
R/L Supplementary motor cortex	2.17	5.67	49.1	297
R Lateral occiptal/Fusiform gyrus	23.1	−91.3	3.94	101
R Cerebellum VI	30.5	−52.6	−25.9	256
R Fusiform gyrus	32.1	−74.5	−15.7	268
R Precentral/Postcentral	40.1	−25.6	47.6	587
Regions active for finger tapping > Cue listening in healthy control children				
L Precentral/Postcentral	−39.7	−18.7	49.3	509
L Lateral occipital cortex	−33	−82.1	−8.93	224
R Cerebellum I-IV	1.65	−53.1	−24.9	411
R/L Anterior cingulate, Supplementary motor cortex	2.49	12	43.3	259
R Fusiform gyrus	21.6	−85.7	−4.75	145
R Pallidum/Putamen	23.5	−3.66	−1.85	277
R Precentral/Postcentral	38	−17.5	49.4	480
R Fusiform gyrus/Lateral occipital cortex	38.4	−67.5	−12.2	188
Regions active for cue listening > Finger tapping in healthy control children (task-negative regions)				
L Lateral occipital cortex	−43.7	−67.8	21.9	100
L Parahippocampal gyrus	−22.5	−27.2	−20.3	79
L Precuneus	−12.9	−58.2	10.2	121
L Cuneus	−10	−83.6	28.4	98
R/L Posterior cingulate	−0.231	−35.8	45.5	95
Regions more active in children with PSD > Healthy control children				
L Intracalcarine cortex	−4.92	−89.8	−0.57	15
L Cerebellum crus II	−1.28	−85.4	−31.2	72
R Cerebellum crus I/II	7.01	−80.5	−24	28
R Cerebellum crus II	43.9	−73.2	−33.1	20

the pegboard score for the simultaneous left and right condition (Fig. 3B). Correlations in the left striatum and left insula were moderate while correlations in the left supramarginal gyrus and bilateral precentral superior frontal gyri were large. MNI coordinates of all clusters with significant positive correlation are included in Table 4.

3. Discussion

Children with speech sound disorders are, by definition, classified as having speech production deficits, as often have related language and literacy deficits (Lewis et al., 2011). However, the literature has also consistently reported associated motor deficits (Newmeyer et al., 2007; Peter & Stoel-Gammon, 2008; Visscher et al., 2010; Visscher et al., 2007; Webster et al., 2005) suggesting a more general neurodevelopmental difference. The aim of this study was to assess fine and oral motor skills in a clinically-recruited sample of children with PSD and to use fMRI to investigate neural substrates supporting fine motor functioning during a cued fine motor task. The participants with PSD in this study were comparable to age-gender matched controls on most functional measures of fine motor skills in their school environment (i.e. cutting, computer use) as measured by the SFA. However, findings from the PSD group for more challenging timed tests of motor praxis, including both fine motor and oral-motor measures, indicated significantly lower scores compared to controls.

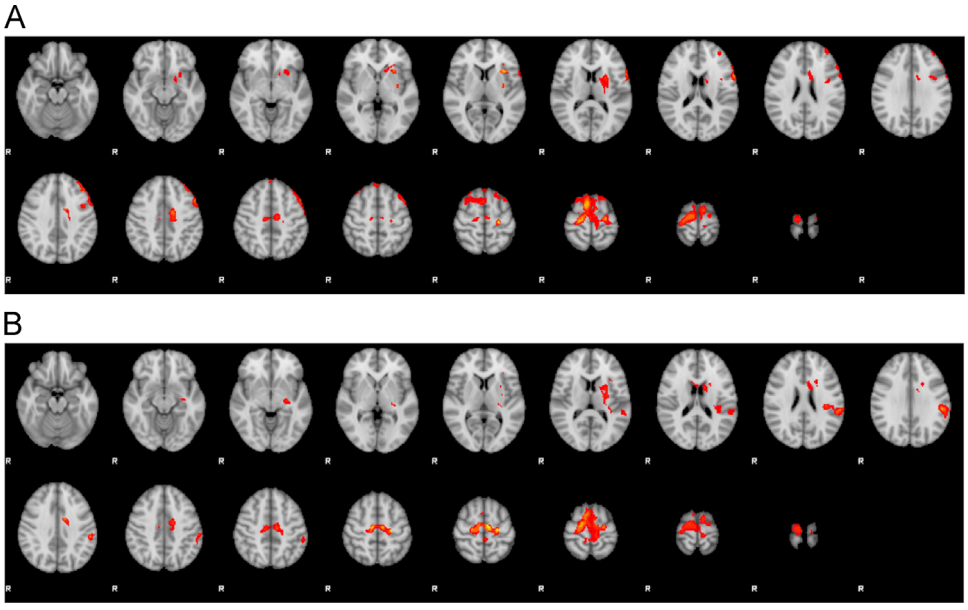

Fig. 3 – Regions where activation is positively correlated with the Purdue Pegboard scores for (A) the left hand and (B) both hands in children with PSD. [$z > 1.64$ $p < 0.05$ as determined by cluster-based inference]. Image is in radiologic orientation.

Table 4 – MNI coordinates for regions of activation positively correlated with Left Hand and Both Hands Purdue Pegboard Score in Children with PSD.

Region	x (mm)	y (mm)	z (mm)	Extent in voxels	Correlation coefficient
Regions positively correlated with left hand Purdue Pegboard score in children with PSD					
L Middle frontal gyrus	−49.3	13.9	45.5	12	0.58
L Frontal pole/Middle frontal gyrus	−38	42.6	31.5	25	0.51
L Putamen	−28.6	9.95	6.25	19	0.16
L Supplementary motor cortex	−13.9	−9.61	42	23	0.32
R Precentral	0.246	−16	64.6	89	0.29
R Superior frontal gyrus	7.06	17.8	62.4	82	0.42
R Supplementary motor cortex	11.8	−5.9	68.4	40	0.38
R Precentral	16.8	−15.6	69.2	19	0.40
Regions positively correlated with both hands Purdue Pegboard score in children with PSD					
L Supramarginal	−56.2	−33.5	28.5	75	0.59
L Insula	−30.6	−22.6	10.2	39	0.43
L Caudate	−17	6.35	19.3	52	0.38
L Precentral/Supplementary motor cortex	−6.69	−16	49.1	64	0.55
R Precentral/Supplementary motor cortex	2.19	−16.4	61	53	0.64

Imaging findings suggest that during a fine motor praxis task, children with PSD activate brain networks similar to controls, and results were consistent with other studies employing similar tasks (Witt et al., 2008). Unlike controls, children with PSD did not show deactivation in the "default mode" or task-negative network (although this difference in deactivation did not reach significance in the direct comparison between groups at the threshold used). This suggests they may be less effective at suppressing this network; reduced task-negative deactivation has also been observed in children with ADHD (Peterson et al., 2009) and neuropsychiatric conditions (Whitfield-Gabrieli & Ford, 2012). However, children with PSD showed increased activation in the cerebellum, a region known to contribute to fine motor skill execution, timing mechanisms, and motor learning (Manto et al., 2012). An fMRI study comparing activation during finger tapping in children and adults (De Guio et al., 2012) found that 10–13 year-old children had increased cerebellar activation relative to adults; they suggested that children need more resources within the motor system in order to perform a fingertapping task. A similar need for increased resources may be present in children with PSD; their motor system may also be less mature than in healthy controls. The cerebellum was also identified as an area of increased activation during speech production in children with speech disorders by Tkach (Tkach et al., 2011). Given the consistent findings of hyper-activation in the cerebellum, children with PSD may require additional engagement of the cerebellum to execute the rapid, precise movements necessary for both fine motor praxis and speech production.

Results of the correlational analyses between fMRI activation during the fine motor task and the Purdue Pegboard Scores in children with PSD demonstrated a positive relationship between activation in regions of interest and measures of fine motor skill collected outside of the scanner for the left hand and bilaterally (Figs. 3A & 3B). Specifically, participants in the PSD group who scored higher on the more challenging subtests of the Purdue Pegboard test (non-dominant hand and both hands) showed increased activation in the left striatum and bilateral superior frontal gyri (including supplementary motor regions) during the fMRI fine motor task. This suggests that children with PSD and better fine motor skills had increased activation and were recruiting more resources during the motor task; the children with PSD with poorer motor skills may have been under activating the regions needed for task completion. Children who had a higher both-hand Purdue Pegboard score had greater activation in the left insula and supramarginal gyrus. We speculate that these regions may be involved in bimanual coordination or increased attention associated with executing the bimanual movement (Aramaki, Honda, Okada, & Sadato, 2006; Serrien, Ivry, & Swinnen, 2006; Wenderoth, Debaere, Sunaert, & Swinnen, 2005).

As a whole, the control group was significantly better than the PSD group on the Purdue Pegboard task and there was less variability, which may have contributed to a lack of statistical correlation between activation and performance.

The behavioral fine motor and oral-motor findings from this study are consistent with findings and conclusions from previous studies of children with active and persistent (i.e., PSD) speech sound disorders (Lewis et al., 2011; Newmeyer et al., 2007; Owen & McKinlay, 1997; Peter & Stoel-Gammon, 2008; Sommers, 1988). For example, similar to children in another study of children with PSD (Newmeyer et al., 2007), significant deficits were not found in functional fine motor skills, but they were found in tasks assessing more challenging motor behaviors. Although fine motor deficits in children with PSD may not be severe enough to cause functional differences as assessed by parents and teachers, they may be sufficient to require compensatory strategies to successfully complete some types of challenging motor tasks. These compensatory strategies, however, may be so subtle and sufficiently effective that parents and teachers are not aware of the child's use of them. Interestingly, only one child in the PSD group ever received occupational therapy for an identified fine motor deficit; he was subsequently discharged when he reached age-appropriate performance. Given the known relationships of fine motor and oral-motor skills with later developing language and learning deficits, oral-motor and fine motor skills may constitute an additional functional domain to consider when determining treatment targets and long-term prognoses for children with PSD.

Our finding that children with PSD have increased activation levels than controls during a fine motor task suggests between-group differences in the development and organization of motor networks. In addition to behavioral differences, children with PSD may have differences in the neural circuitry network underlying fine motor praxis. As above, such differences may underlie deficits in motor skills in multiple domains. Given the behavioral and neurological evidence supporting a relationship between speech and language and motor development, these findings may support perspectives that posit a centralized precision or timing deficit that is causal to the onset and/or persistence of at least some types of speech sound disorders (Peter & Stoel-Gammon, 2008). The timing deficit may manifest most severely in speech production, a domain requiring exquisite temporal coordination. Again, this perspective aligns with previously cited studies that have reported behavioral non-speech timing deficits in children with active and persistent speech sound disorders. Alternatively, these findings may suggest that both fine motor skills and oral-motor skills are highly sensitive manifestations of more generalized neurodevelopmental differences, not just related to timing, that underlie speech deficits (Lewis et al., 2011).

One limitation of this study is the small sample size, which did not allow us to examine possible subgroups of children with PSD. The children with PSD in this study were chosen from an available clinical sample and most had been enrolled in speech therapy for at least three years. Although they represent a group of children unlikely to spontaneously recover, the extent to which the underlying networks may have changed over time with therapy remains unknown. At the time of participation, children were relatively moderate in severity of their speech disorders, and the extent to which these results are generalizable to more severe children is unknown. Another potential limitation is the single out-of-scanner measure of precise fine motor skills, the Purdue Pegboard Assessment. More detailed assessments of fine motor skills may have allowed for more nuanced analyses of associations among speech production, fine motor skills

and activation levels. Finally, while in-scanner performance of the finger-tapping task was monitored on-line and later reviewed through video for appropriate execution and compliance, the precise timing and sequencing of finger movements is not visible due to the placement of the child in the scanner. It is, therefore, possible that the observed differences in cerebellar activation are attributable to extra or excessive movements by the PSD group rather than increased resources necessary to perform the task.

3.1. Conclusion

Through the use of fMRI, the study investigated differences in the neurological mechanisms supporting fine motor praxis in children with PSD when compared to children with typical speech development as well as the behavioral correlates of these neural mechanisms. The findings of this study suggest that children with PSD are less proficient at completing fine motor tasks than their typical peers and have neurological differences. These differences include neurological differences in the activation of the cerebellum when completing fine motor tasks when compared to children with typical speech development, as well as correlational relationships between activation and performance in known motor regions not present in children with PSD. Additionally, these differences are behaviorally reflected by performance on more challenging fine motor tasks but do not appear to functionally impact children in their school setting. The results of this study provide some support for the hypothesis that persistent speech errors may be a manifestation of a more generalized developmental difference. Children presenting with PSD should be thoroughly assessed for fine motor differences by more sensitive testing than parent or teacher reported measures. Understanding the link between general fine motor praxis and persistent speech sound errors in children may ultimately assist in determining the prognosis and identifying the appropriate types of interventions for these children.

4. Experimental Procedures

4.1. Participants

Children with PSD were recruited through local speech-language pathologists (SLPs). These SLPs identified children with a clinical diagnosis of a speech disorder over the age of five and currently receiving speech therapy for unresolved speech production errors. Twelve children currently receiving speech therapy due to a PSD were recruited. These children were enrolled in therapy for an average of 35 months (range 18–60 months). Twelve age-approximate (within 12 months) and gender-matched controls with typical development were recruited through various sources including word of mouth and a research database maintained by Cincinnati Children's Hospital Medical Center that includes families who have indicated they are interested in participating as controls in research studies. Both groups included four females. The mean age was 7.42 (SD±1.25) for children with PSD and 7.44 (SD±1.25) for controls. Age and gender matching was done to minimize the potential confounding effects of development and gender. All children (PSD and controls) were self-reported to be right-handed, had normal pure-tone hearing, and had no known co-occurring neurological, genetic, or chronic conditions. ADHD is common in children with speech disorders (Lewis et al., 2012) was not considered exclusionary for this study. Both the PSD and the control group had one child diagnosed with ADHD. Informed consent from a parent/guardian and child assent were obtained for all participants, using consent/assent procedures approved by Cincinnati Children's Hospital Medical Center Institutional Review Board.

4.2. Speech, language, and cognitive assessments

All participants completed several standardized assessments including a single-word speech evaluation (Goldman-Fristoe Test of Articulation-2, GFTA-2 (Goldman & Fristoe, 2000)), a comprehensive language assessment (Clinical Evaluation of Language Fundementals-4, CELF-4 (Semel, Wiig, & Secord, 2003)), and an intelligence assessment (Wechsler Abbreviated Scale of Intelligence, WASI (Weschler, 1999)) to obtain additional information regarding the nature of the PSD and to ensure intelligence was within normal limits. These are all norm-referenced tests with standardized scoring. The results of the GFTA-2 confirmed the clinical diagnosis of PSD. Combined this testing was completed in approximately 1.5–2 h.

None of the participants were receiving occupational therapy at the time of the exam; one participant had received occupational therapy but was discharged as he was performing at age-level. For most children this testing took place on the same day although some were tested within two weeks of the fMRI testing. Testing was generally completed in a soundproof booth located within the hospital; the CELF-4 and Oral Speech Mechanism Screening Evaluation-3 (OSMSE-3) were occasionally given outside the booth. All speech and language testing was completed by a certified speech-language pathologist.

4.3. Motor skill assessment

4.3.1. Fine motor skill

The Purdue Pegboard Test (Tiffin, 1948) was administered to all participants after completing the fMRI portion of the study. This test measures fine movements of hands and fingers, as well as fingertip dexterity, through timed tasks. Participants were presented with multiple small, thin pegs and given directions on how to place the pegs into the pegboard as rapidly as possible. Per the testing guidelines the children were given 30 s to place as many pins as possible in individual holes. The child completed the right hand first, then the left had, followed by using both hands to place pegs bilaterally at the same time. Raw scores for the number of pegs appropriately placed in 30 s were recorded. The total time to complete this test is approximately 5 min.

4.3.2. Oral structures and oral-motor skills

All participants completed OSMSE-3 (Louis & Ruscello, 2000) to evaluate the integrity of the articulators (e.g. teeth present, velopharyngreal movement), the function of the articulators (e.g. lip pucker, sequencing lip movements), and the speed and rhythmicity of rapid syllable productions through diadochokinesia (DDK). DDK requires the child to produce simple syllables repetitively and increases in difficulty from

repeating the same syllable (e.g. pu-pu-pu) to alternating the syllables (pu-tu-ku). The DDK rate is timed to determine how long it takes a child to produce a set number of repetitions. The OSMSE-3 is a norm referenced test for children at or above five years of age. The structure and function subtests used pre-determined cutoff scores provided by the publisher to determine if the child passed these areas. Raw scores for the length of time (measured in seconds) to produce the syllables were included in the analyses for this study. This evaluation is generally completed in 5–10 min.

4.3.3. *General motor functioning*

A parent of each participant completed the School Function Assessment (SFA(Coster, Deeney, Haltiwanger, & Haley, 1998)). The SFA is a criterion-referenced survey that identifies the child's proficiency in completing functional tasks related to their academic environment and related social activities such as buttoning clothing, holding a pen, cutting with scissors, and using a computer. This survey has been validated in a sample of typically developing children and those identified with special needs (Coster et al., 1998). Scoring is criterion based and the range is determined by the individual subtest; these criterion scores were used for this study. The parent typically completed this evaluation while the child was completing the fMRI and behavioral portion of the assessment. Some parents chose to complete this at home and mail the survey when it was completed.

4.3.4. *Data analysis*

Raw and standard scores were calculated for all participants and entered into SAS for further analysis. Descriptive statistics were calculated and group mean differences were compared using a two-tailed independent samples t-test.

Functional MRI Testing

4.3.5. *Fine-motor praxis task*

This novel task of fine motor planning and praxis was developed for this study. During the active condition, the participants heard a sequence of 1–4 tones (100 ms duration, 100 ms between tones, 100 Hz). In response to this auditory cue, the participants were instructed to tap fingers bilaterally and sequentially starting with the finger closest to the thumb (index) and moving away from the thumb towards the little finger, matching the number of finger taps in the sequence with the number of tones presented. For example, if a participant heard one tone, only the index finger of each hand would be engaged; if four tones were presented, all four fingers of each hand would be engaged. This active condition was contrasted with a control condition in which participants heard the same sequences of 1–4 tones but did not tap their fingers; this contrast was intended to isolate the patterns of neural activity associated with fine motor planning and praxis from the auditory stimuli. The presumed increase in difficulty sequencing one set of tapping to four sets of tapping was designed to parallel increasing production difficulty children with PSD demonstrate as syllable length increases.

All of the participants were trained on how to perform the task prior to scanning. All participants demonstrated understanding and the ability to correctly execute these sequences prior to entering the scanner. The participants were then monitored visually and their compliance with the task was recorded through video. When the child was not properly executing the paradigm during imaging the scanner was stopped and the child was re-instructed in the task to ensure the task was being completed appropriately. Appropriate execution of the task was independently confirmed through video. For the fMRI experiment, the task paradigm was implemented as a block design, consisting of five cycles of active and control conditions.

4.3.6. *Functional MRI methods*

Participants were scanned on a 3 T Philips Achieva MRI Scanner. Functional volumes were acquired using a single shot gradient-echo echo planar imaging (EPI) sequence. Each volume consisted of 32 contiguous 5mm T2*-weighted axial slices covering the entire brain (TR/TE=2000/38 ms, FOV 25.6×25.6 cm, matrix 64×64;voxel size of $4 \times 4 \times 5$ mm). High-resolution T1-weighted anatomical images were also obtained using the following parameters: TR/TE=8.0/3.7 ms, FOV $25.6 \times 25.6 \times 19.2$ cm, matrix 256×256, voxel size 1 mm isotropic. fMRI data analysis was performed using FSL, FMRIB Software Library v5.0, (Jenkinson, Beckmann, Behrens, Woolrich, & Smith, 2012; Smith et al., 2004; Woolrich et al., 2009). To correct for motion, each volume of the EPI data set was registered to a single reference volume within the image. After spatial normalization into MNI space, a general linear model with participant motion as a regressor was implemented to identify voxels activated by the task for each participant. Group activations and group comparisons for PSD and controls were thresholded with an initial $z > 2.3$ and corrected for multiple comparisons using FSL's cluster based inference to $p < 0.05$.

4.3.7. *Correlation analysis*

In order to more clearly understand the relationship between motor skill and activation during fingertapping, levels of activation (fingertapping > listening) for each participant were correlated on a voxel-wise basis with previously described Purdue Pegboard scores using a Pearson correlation. Resulting correlation maps were thresholded with an initial $z > 1.64$, and corrected for multiple comparisons using FSL's cluster based inference to $p < 0.05$.

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