Functional brain activation differences in stuttering identified with a rapid fMRI sequence

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ABSTRACT

The purpose of this study was to investigate whether brain activity related to the presence of stuttering can be identified with rapid functional MRI (fMRI) sequences that involved overt and covert speech processing tasks. The long-term goal is to develop sensitive fMRI approaches with developmentally appropriate tasks to identify deviant speech motor and auditory brain activity in children who stutter closer to the age at which recovery from stuttering is documented. Rapid sequences may be preferred for individuals or populations who do not tolerate long scanning sessions. In this report, we document the application of a picture naming and phoneme monitoring task in 3 min fMRI sequences with adults who stutter (AWS). If relevant brain differences are found in AWS with these approaches that conform to previous reports, then these approaches can be extended to younger populations. Pairwise contrasts of brain BOLD activity between AWS and normally fluent adults indicated the AWS showed higher BOLD activity in the right inferior frontal gyrus (IFG), right temporal lobe and sensorimotor cortices during picture naming and higher activity in the right IFG during phoneme monitoring. The right lateralized pattern of BOLD activity together with higher activity in sensorimotor cortices is consistent with previous reports, which indicates rapid fMRI sequences can be considered for investigating stuttering in younger participants.

Educational objectives: The reader will learn about and be able to describe the: (1) use of functional MRI to study persistent developmental stuttering; (2) differences in brain activation between persons who stutter and normally fluent speakers; and (3) potential benefit of time efficient fMRI sequences combined with a range of speech processing tasks for investigating stuttering in younger populations.

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Developmental stuttering impairs speech production and negatively impacts quality of life in more than three million Americans (Craig, Blumgart, & Tran, 2009; Yaruss, 2010). The underlying nature of the disorder appears to involve a genetic predisposition that is expressed neurologically in altered brain structure and function (Ambrose, Cox, & Yairi, 1997; De Nil, Kroll, Kapur, & Houle, 2000; Sommer, Koch, Paulus, Weiller, & Büchel, 2002). In this study, we discuss the initial results of a neuroimaging project aimed at developing rapid optimized imaging protocols to study persistent developmental stuttering

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in children and adults. A rapid functional sequence that reliably identifies speech production activity in the speech system has multiple applications including imaging individuals who do not tolerate long scans and permits more time during an MRI session for a battery of imaging protocols.

Varied functional imaging investigations have documented an atypical speech production system in AWS that comprises both aberrant increases in brain activity and relative deactivations in speech relevant brain regions. Certain differences in functional activity appear to reflect a general state of the speech production system in AWS, because they have been observed across studies and during fluent speech production or silent verbal processing (De Nil et al., 2000). AWS have shown higher brain activity in left and right cortical motor areas, and the right inferior frontal gyrus during speech tasks relative to normally fluent adults or NFA (Brown, Ingham, Ingham, Laird, & Fox, 2005). In contrast, a relative reduction or suppression of cortical activity has been detected in the bilateral temporoparietal cortex of AWS (auditory association areas) and left inferior frontal gyrus during overt speech (Braun et al., 1997; Fox et al., 1996; Neumann et al., 2005) in many of the same studies showing over-activity in other areas. The distribution of cortical activity in AWS also appears more bilaterally symmetrical across the two hemispheres or is right hemisphere lateralized in contrast with the left predominant activity of NFA (Fox et al., 1996; Neumann et al., 2005). These functional anomalies in brain activity during speech are increasingly being linked to atypical neuroanatomical development in the same cortical regions or adjacent white matter connections (Chang, Erickson, Ambrose, Hasegawa-Johnson, & Ludlow, 2008; Sommer et al., 2002).

Despite progress in identifying an aberrant cerebral system for speech production in adults, it is uncertain whether these functional differences are causal or an adaptation to stuttering. This vexing issue undermines attempts to determine the cause and mechanisms of recovery. Moreover, functional imaging results of a single task on its own may not be suited for identifying causal mechanisms unless supplemented with other methods, including structural scans or a battery of functional tasks. Another need is to study brain activity in younger groups such as children closer to the point of documented recovery from stuttering or documented persistency. Numerous challenges, however, confront neuroimaging studies of younger participants as they will more frequently be reluctant to enter the scanner or will only tolerate short imaging protocols. Yet, in pediatric populations, fMRI sequences have been successfully employed to identify cortical language areas (O'Shaughnessy, Berl, Moore, & Gaillard, 2008).

To address some of these challenges, we developed a 3 min fMRI sequence that employs either an oral picture naming task or a phoneme monitoring task to test whether potential neural correlates of stuttering can be identified in AWS with a time-optimized sequence. The naming task is predicted to elicit higher activity in the bilateral oral motor cortex, and right inferior frontal gyrus and relatively decreased responses in auditory processing areas in AWS relative to NFA. The auditory monitoring task is used as a non-motor contrast for the auditory processing prediction. The tasks were selected because young children have performed similar tasks in fMRI experiments and the tasks are sensitive to developmental changes in brain activity (Wilke et al., 2006).

1. Methods

1.1. Participants

Eleven AWS (10 males, 1 female; mean age = 25.9 years, sd = 4.4) and ten normally fluent adults (9 males, 1 female; mean age = 25.2 years, sd = 3.8) participated in the study. Each subject was right-handed and a monolingual English speaker. None of the participants had a history of psychological, psychiatric, neurological or communicative disorders other than a diagnosis of persistent developmental stuttering in the experimental group. All methods were approved by the Institutional Review Board of the University of Illinois at Urbana/Champaign.

1.2. Tasks and analyses

The two tasks were oral picture-naming and silent auditory-phoneme monitoring. A block design was used to detect blood-oxygen-level-dependent (BOLD) activity during both tasks. A 10 s ON/OFF period was utilized which minimizes movement artifacts during speech tasks (Birn, Cox, & Bandettini, 2002). During each 10 s task block, either 5 pictures were named by the participant or 5 words were presented acoustically and the participant listened for the /s/ sound (Run duration = 3 min). The active tasks were contrasted with silent rest blocks. All images were acquired with a 3T Siemens Allegra Headscanner: 32 axial slices, TR = 2000 ms, TE = 30 ms, flip angle = 90, FOV = 240 mm. Separate pairwise contrasts were used to compare BOLD activity between the stuttering and control groups during oral naming and phoneme monitoring. The whole brain contrasts were corrected for multiple comparisons and reported at a corrected alpha level of $p < 0.05$.

2. Results

Participants in both groups showed robust and distinct activity in speech-relevant brain areas during the 3 min scanning period for each task. The hemodynamic responses in Fig. 1A from a healthy control indicate clear task related responses were present in the primary oral motor cortex for the oral naming task and in the superior temporal gyrus for the auditory monitoring task. In Fig. 1B and C, whole brain activity for each group is shown separately for both tasks. During oral naming,
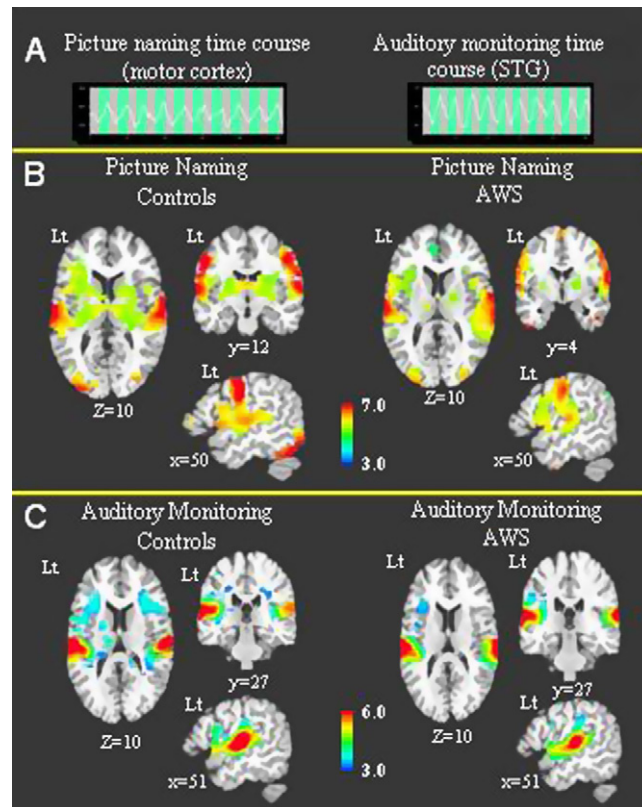
Fig. 1. (A) BOLD signal time courses from single voxels are shown for a control participant. The first time course is from the oral motor cortex during the picture naming task and the second is from the superior temporal gyrus during the auditory monitoring task. (B) The average BOLD activity during the picture naming task is shown for each group. (C) The average BOLD activity during the auditory monitoring task is shown for each group.

both groups showed bilateral cortical activity in the precentral gyrus, superior temporal gyrus (STG), inferior frontal gyrus, insula and supplementary motor area (SMA) along with bilateral subcortical activity in the thalamus and basal ganglia (Fig. 1B). During auditory monitoring, the predominant BOLD activity for both groups was detected bilaterally in the STG encompassing the primary auditory cortex and planum temporale (Fig. 1C). Less intense BOLD activity was noted in inferior frontal areas and insula bilaterally (Fig. 1C). Overall, the BOLD activity for both groups was characterized by a high degree of similarity in both tasks.

The results of the group contrast for oral naming indicated that AWS show significantly higher BOLD activity across both hemispheres ($p < .05$ corrected). On the left side, AWS had higher BOLD activity than controls in the precentral gyrus (BA 4, 6) and the superior temporal sulcus (STS) (Fig. 2). The group differences were more prominent in the right hemisphere as AWS showed higher activity in the inferior frontal gyrus (IFG), insula, superior temporal sulcus (STS) and middle temporal gyrus (MTG). AWS further showed higher BOLD activity in the subthalamic nucleus bilaterally. The group contrast for auditory monitoring indicated AWS had higher BOLD activity in the right inferior frontal gyrus ($p < .05$ corrected). NFA did not show higher activity than AWS in either task contrast.

3. Discussion

The purpose of this study was to evaluate whether a rapid fMRI scan would be sensitive to relevant differences in brain activity between AWS and NFA that conform to previous functional imaging reports. The AWS showed prominently higher BOLD activity in the right IFG, including Brodmann areas (BA) 44, 45 and 46, and the insula. An increase in right IFG activity in AWS is a recurring finding in neuroimaging studies (Neumann et al., 2005). The shift shown by AWS away from Broca's area to the right hemisphere homologue could hinder rapid temporal sequencing required for fluent speech. The right shift in IFG activity may also be related to the increased white matter volume found this cortical region in AWS (Jancke, Hanggi, & Steinmetz, 2004). Although, the contribution of right IFG activity to stuttering is debated, the consistency with which it is observed (Brown et al., 2005) point to the IFG as a candidate region for explaining part of the deviant speech production representation in stuttering.

AWS exhibited higher BOLD activity in the bilateral primary sensory and motor cortices during oral naming. Most reports have documented increased sensorimotor activity during speech in AWS (Chang, Kenney, Loucks, & Ludlow, 2009; Fox et al.,
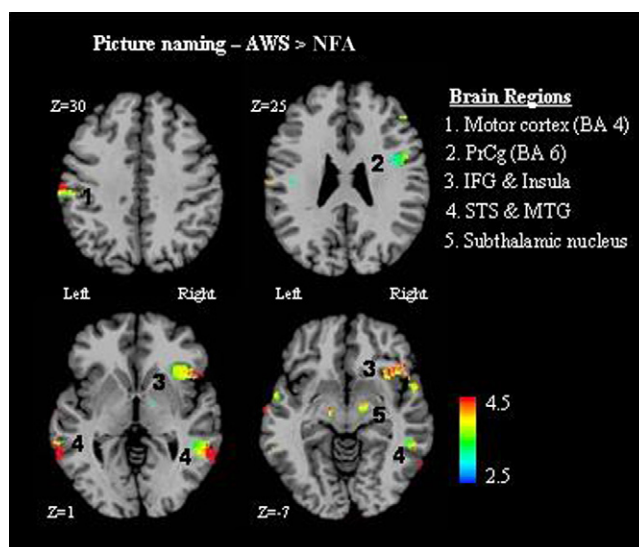
Fig. 2. The results of the group contrast between AWS and NFA for the picture naming task are presented. Clusters of significant voxels that indicate higher BOLD activity for the AWS are labeled numerically.

1996; De Nil et al., 2000). This cortical motor activity difference in the stuttering group was accompanied by higher activity in the subthalamic nucleus bilaterally. Possible explanations for increased sensorimotor activity are that stuttering results from instabilities in the generation of feedforward motor commands or that AWS are more dependent on sensorimotor feedback to maintain fluency. Higher motor activity is even present during non-speech oral tasks in AWS (Chang, Kenney, Loucks, Poletto, & Ludlow, 2009) suggesting it might be related to the underlying disorder; although it may represent a strategy adopted in childhood.

The right hemisphere activity detected in the STS and MTG of the AWS is important given this was a picture naming task. Research in normal subjects indicate these regions are associated with word storage and retrieval, but much more so for the left hemisphere (Vandenberge, Price, Wise, Josephs, & Frackowiak, 1996). Activation of the right hemisphere homologues in AWS further confirms their language system has a right hemisphere bias.

Decreased auditory activity in the Planum temporale was not evident in the group contrast. However, robust activity in this region was found bilaterally for both groups during oral naming. This certainly does not eliminate the possibility that reduced auditory activity is a functional marker of stuttering, but may reflect the variability of stuttering and emphasizes the highly task dependent nature of functional imaging results.

During auditory monitoring, the predominant BOLD activity for both groups was predictably within the STG encompassing both the primary auditory cortex and planum temporale. Less intense BOLD activity was noted in inferior frontal areas and insula that tended to be left lateralized. The left frontal activity may be related to an automatic engagement of articulatory planning areas even though the task is nonverbal (Chang, Kenney, Loucks, et al., 2009). The group contrast indicated that AWS exhibited increased BOLD activity in the right homologue of Broca's area (BA 44) during phoneme monitoring relative to the controls. Activity in this area is of interest because it suggest some phonological processing in AWS may be mediated in the right hemisphere. Recently, Weber-Fox, Spruill, Spencer, and Smith (2008) reported that children who stutter show some preference for processing rhyming effects in the right hemisphere. Again this points to a right hemisphere bias in AWS that is even present during covert processing.

The right hemisphere presentation is consistent with numerous reports of brain function in AWS (Fox et al., 1996; Moore, 1993). It is consistent with the long-standing suggestion that right hemisphere functional lateralization may be a compensatory mechanism (Braun et al., 1997) that prompts a neuroplastic reorganization of language activity. Other researchers have proposed that right hemisphere involvement interferes with speech fluency pathways and may be a cause of stuttering (Andrews, Quin, & Sorby, 1972; Webster, 1990). "In the adult system it may be difficult to distinguish between mechanisms responsible for stuttering and those developed to compensate" (Ludlow, 2000). Whether the right hemisphere activity is predominately an attribute of AWS is a central research question that studies of children who stutter can address.

The picture naming and phoneme-monitoring tasks are designed to test a range of ages from 5 years and up. This study was successful in showing that an efficient 3 min scan with distinct but straightforward tasks can identify neural correlates of stuttering. The results did not find a decrease in auditory activity or increased cerebellar activity, which have been previously linked to stuttering (Brown et al., 2005). Other tasks or structural scans may be necessary to supplement the protocol used here, but can be implemented with this time efficient approach.

Acknowledgements

CONTINUING EDUCATION

Functional brain activation differences in stuttering identified with a rapid fMRI sequence

QUESTIONS

1. Previous research using functional neuroimaging to investigate neural activation in stuttering and non-stuttering speakers:
   a. Has discovered a neurological cause of stuttering
   b. Has discovered there no differences in motor-related areas and auditory areas between stuttering and non-stuttering speakers
   c. Has not differentiated between causal and compensatory brain activity patterns in persistent stuttering
   d. Differences between stuttering and non-stuttering adults are limited to the cerebellum
2. Using functional imaging techniques such as functional MRI, researchers can:
   a. Investigate structural abnormalities in the brains of persons who stutter
   b. Identify changes in brain areas associated with the performance of various speech tasks
   c. Isolate changes in neuronal electrical activity resulting from local synaptic changes
   d. None of the above
3. Rapid functional MRI sequences will be important for studying children because:
   a. Short sequences are more sensitive to group differences.
   b. Children may be reluctant to enter the MRI scanner
   c. Short sequences reduce the probability of head movements
   d. Long sequences cannot identify lateralization differences
   e. Both b and c
4. The current study comparing adults who stutter and normally fluent speakers showed that:
   a. Adults who stutter had relatively higher brain activity in the bilateral sensorimotor cortices in the oral naming task
   b. Cortical and cerebellar activity was higher in adults who stutter during the oral naming task
   c. Adults who stutter showed a right hemisphere bias in brain activity in the oral naming task
   d. Both a and c
5. The results from this investigation show that:
   a. Rapid fMRI pulse sequences with straightforward speech and language tasks can identify functional brain activity differences in adults who stutter
   b. Compensatory brain activity in adults who stutter is limited to the right hemisphere
   c. Neural activation in the bilateral superior temporal gyrus is always decreased in adults who stutter
   d. Increased sensorimotor activity is the most reliable biomarker of persistent stuttering
   e. None of the above

References

Ambrose, N., Cox, N., & Yairi, E. (1997). The genetic basis of persistent and recovered stuttering. *Journal of Speech, Language, and Hearing Research*, *40*, 567–580.
Andrews, G., Quin, P. T., & Sorby, W. (1972). Stuttering: An investigation into cerebral dominance for speech. *Journal of Neurology, Neurosurgery and Psychiatry*, *35*, 414–418.
Birn, R. M., Cox, R. W., & Bandettini, P. A. (2002). Experimental designs and processing strategies for fMRI studies of overt verbal responses. *Neuroimage*, *23*(3), 1046–1058.
Braun, A. R., Varga, M., Stager, S., Schulz, G., Selbie, S., Maisog, J. M., et al. (1997). Altered patterns of cerebral activity during speech and language production in developmental stuttering. An H$_2$^{15}O positron emission tomography study. *Brain*, *120*, 761–784.
Brown, S., Ingham, R. J., Ingham, J. C., & Fox, P. T. (2005). Stuttered and fluent speech production: An ALE meta-analysis of functional neuroimaging studies. *Human Brain Mapping*, *25*, 105–117.
Chang, S. E., Erickson, K. I., Ambrose, N. G., Hasegawa-Johnson, M. A., & Ludlow, C. L. (2008). Brain anatomy differences in childhood stuttering. *Neuroimage*, *39*, 1333–1344.
Chang, S., Kenney, M. K., Loucks, T. M., & Ludlow, C. L. (2009). Brain activation abnormalities during speech and non-speech in stuttering speakers. *Neuroimage*, *46*(1), 201–212.
Chang, S., Kenney, M., Loucks, T. M., Poletto, C., & Ludlow, C. (2009). Common neural substrates support speech and nonspeech vocal tract gestures. *Neuroimage*, *47*(1), 314–325.
Craig, A., Blumgart, E., & Tran, Y. (2009). The impact of stuttering on the quality of life in adults who stutter. *Journal of Fluency Disorders*, *34*(2), 61–71.
De Nil, L. F., Kroll, R. M., Kapur, S., & Houle, S. (2000). A Positron Emission Tomography study of silent and oral single word reading in stuttering and nonstuttering adults. *Journal of Speech, Language and Hearing Research*, *43*, 1038–1053.
Fox, P. T., Ingham, R. J., Ingham, J. C., Hirsch, T. B., Hunter Downs, J., Martin, C., et al. (1996). A PET study of the neural systems of stuttering. *Nature*, *382*, 158–162.

Jancke, L., Hanggi, J., & Steinmetz, H. (2004). Morphological brain differences between adult stutterers and non-stutterers. *BioMedCentral Neurology*, *4*(23), 1–8.

Ludlow, C. L. (2000). Stuttering: Dysfunction in a complex and dynamic system. *Brain*, *123*(10), 1983–1984.

Moore, W. H. (1993). Hemisphere processing research. In E. Boberg (Ed.), *Neuropsychology of stuttering* (pp. 39–72). Edmonton (AB): University of Alberta Press.

Neumann, K., Preibisch, C., Euler, H. A., Gudenberg, A., Lanfermann, H., Gall, V., et al. (2005). Cortical plasticity associated with stuttering therapy. *Journal of Fluency Disorders*, *30*(1), 23–39.

O'Shaughnessy, E. S., Berl, M. M., Moore, E. N., & Gaillard, W. D. (2008). Pediatric functional magnetic resonance imaging (fMRI): Issues and applications. *Journal of Child Neurology*, *23*(7), 791–801.

Sommer, M., Koch, M., Paulus, W., Weiller, C., & Büchel, C. (2002). Disconnection of speech-relevant brain areas in persistent developmental stuttering. *The Lancet*, *360*, 380–383.

Vandenberge, R., Price, C., Wise, R., Josephs, O., & Frackowiak, R. (1996). Functional anatomy of a common semantic system for words and pictures. *Nature*, *383*(6597), 254–256.

Weber-Fox, C., Spruill, J. E., III, Spencer, R., & Smith, A. (2008). Atypical neural functions underlying phonological processing and silent rehearsal in children who stutter. *Developmental Science*, *11*(2), 321–327.

Webster, W. G. (1990). Motor performance of stutterers: A search for mechanisms. *Journal of Motor Behavior*, *22*, 553–571.

Wilke, M., Lidzba, K., Staudt, M., Buchenau, K., Grodd, W., & Krageloh-Mann, I. (2006). An fMRI task battery for assessing hemispheric language dominance in children. *Neuroimage*, *32*(1), 400–410.

Yaruss, J. S. (2010). Assessing quality of life in stuttering treatment outcomes research. *Journal of Fluency Disorders*, *35*(3), 190–202.

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