fMRI of developmental stuttering: A pilot study

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Abstract

The purpose of this investigation was to explore the feasibility of fMRI in the study of developmental stuttering. Speech contrasts (loud versus silent reading) and language contrasts (reading of semantically meaningful text versus nonsense words) of six developmental stutterers and six nonstutterers were compared using a commercial 1 Tesla MR-Scanner (Siemens Expert). Results indicate that mapping cortical function in persons who stutter is indeed feasible, even with a 1TMR-system. Compared to normals the stutterers seemed to employ different and particularly less differentiated auditory and motor feedback strategies in speech. They apparently rely on auditory processing and on cerebellar contribution as much during silent reading as during reading aloud. Moreover, they showed a greater involvement of the right hemisphere in language processing, activating not only the typical language areas on the left but also and with equal magnitude the right side homologues of these areas. In spite of the promising results, at present several practical problems such as possible movement artifacts and possible masking through scanner noise still hamper a more straightforward use of fMRI in the study of developmental stuttering.

Keywords: Developmental stuttering; Dysfluency; Brain imaging; fMRI

1. Introduction

Developmental stuttering is a disorder of speech in which an individual knows precisely what he wishes to say, but at the time is unable to say it because of an involuntary repetition, prolongation or cessation of a sound (World Health Organization, 1977). Stuttering has an estimated prevalence of 1% worldwide and occurs three to four times more frequent in males than in females (Bloodstein, 1995). Onset of the disorder is usually between 2 and 5 years of age (Silverman, 1992).

One of the puzzling things about developmental stuttering is that its etiology is still unknown. In the course of the years numerous theories relative to etiology have been formulated. One line of thinking has been that stuttering is of neurogenic origin. The first formal theory of this kind was the ‘cerebral dominance theory,’ proposed by Orton (1927) and Travis (1931). They hypothesized that in stutterers there is a lack of cerebral dominance for speech creating mistiming of the motor impulses to the bilateral innervated speech muscles. However, failure to clearly demonstrate a lack of cerebral dominance, along with the failure of therapies aimed at installing hemispheric dominance in stutterers, caused the theory to lose its initial popularity. For some decades environmental theories of stuttering prevailed. The basis of the cerebral dominance theory, however, was not refuted. Moreover, the theory of Orton and Travis regained interest again when Jones (1966) suggested bilateral speech representation in four stutterers, using the Wada technique. The ensuing years several studies of the cerebral dominance of stutterers were reported. A whole variety of neuropsychological approaches were used including dichotic listening, auditory tracking, tachistoscopic investigation, verbal manual time-sharing and electroencephalography (see Bloodstein, 1995, for a review). The results of these studies range from equivocal to the conclusion that
there is in stutterers a bilateral language representation, an inverse cerebral dominance, less outspoken left cerebral dominance, right hemisphere dominance, interference of the right hemisphere with left hemisphere activities, or more right hemispheric speech production but no difference for speech perception.

In recent years, PET has opened new avenues in the search for the neurogenic basis of stuttering. Although interpretation of the PET findings in stuttering is not straightforward and most if not all studies can be criticized as to the subjects used and the methodology employed (Logan, 1999), the results yet largely confirm that stutterers show differences in cerebral dominance when compared to normal controls (Braun et al., 1997; Fox et al., 1996; Ingham, Fox, & Ingham, 1994; Ingham et al., 1996; Kroll, De Nil, Kapur, & Houle, 1997; Wu et al., 1995, 1997). Areas found to be of particular interest are the cerebellum, Broca’s and Wernicke’s area, the supplementary motor area and limbic structures.

The purpose of the present investigation was to examine the feasibility of fMRI in the study of stuttering. Compared to PET, fMRI has the undeniable advantage of being noninvasive. Furthermore, spatial and temporal resolution and endogenous contrast are far better in fMRI than in PET and it might be hoped for that fMRI helps to determine with greater precision which brain areas are involved in stuttering (Cherry & Phelps, 1996; Cohen, 1996). There are, however, also potential problems in the use of fMRI in the study of stuttering. One issue to be considered is that some stutterers show speech related dyskinesias which may result in movement artifacts. Also, it is well known that in stutterers a masking noise during speech may lead to a temporary speech improvement. Perhaps scanner noise could have the same effect. Another obstacle is that the occurrence of fluency failures in a given patient may vary considerably from time to time. Moreover the population of people who stutter is by no means a homogenous one. Yet, the strengths of fMRI in comparison with more invasive methods are considerable and provided the impetus for the present investigation.

2. Materials and methods

2.1. Subjects

The subjects for this study were six stuttering and six nonstuttering male individuals ranging in age from 19:10 to 37:5 years. The stutterers were recruited with the help of ‘VZW Best,’ a Flemish self-help organization for stutterers, addressing mainly adult chronic stutterers. The nonstutterers were recruited among undergraduate students and their acquaintances. All participants were native speakers of Dutch and were reportedly right-handed for everyday activities such as writing, combing one’s hair, using scissors, et cetera. None of the nonstuttering subjects had any history of speech language problems. In all of the stuttering subjects the dysfluency was of developmental origin and had its onset in childhood. All stuttering individuals were clinically screened to be stutterers without severe synkinesias so that stutter episodes inside the magnet would not create significant artifacts. They had all followed one or more episodes of therapy of variable duration for their fluency problem but none of them was still enrolled in speech therapy at the moment of testing. However, they did attend meetings and encounter-weekends of the self-help organization from time to time. Although the self-help organization does promote the use of prolonged speech and speaking in a sing-song manner, none of the participants of the present study made use of these fluency techniques for controlling their speech behavior.

2.2. Functional magnetic resonance imaging (fMRI)

All imaging was performed on a commercial 1 Tesla MR-scanner (Siemens Expert). The fMRI session consisted of two parts. First, anatomical imaging of the brain was carried out using a 3D-MPRAGE T1-weighted sequence: TR = 9.7 ms, TE = 4 ms, flip-angle = 8°, slices = 178, slice thickness = .9 mm, matrix = 230 × 256, FOV = 250 mm, NEX = 1. For fMRI, subsequent whole-head imaging was performed with an optimized echo-planar sequence (TR = 1.8 ms, TE = 70 ms, flip-angle = 90°, slices = 32, slice thickness = 4 mm, matrix = 64 × 64, FOV = 256 mm, NEX = 1) with a total repetition time of 5 s per volume (Achten et al. HBM99, abstract 1088, Duesseldorf, June 1999). A total of 480 volumes was acquired in each of the subjects.

Because abnormalities in brain activation in subjects with developmental stuttering have been reported in the PET literature to involve several pathways (Logan, 1999), and because it has been suggested that both motor and linguistic processes may underlie stuttering (De Nil, 1999), a dynamical paradigm with both motor-speech and language components was selected. Four levels of performance included reading normal semantically meaningful text both aloud and silent, and reading nonsense text aloud and silent.

The meaningful texts were selected paragraphs from an entertaining booklet on habits and vices of Belgian people (Mason, 1995). The nonsense words contained monosyllabic as well as polysyllabic words of various phonological composition all of them being theoretically permissible word shapes in Dutch. Although no attempt was made to exactly match the nonsense texts with the meaningful texts as to phonological build-up, it was taken care of that in each nonsense text a whole range of different phonological shapes was covered. It is well known that stutterers may show an adaptation effect in
reading, i.e. the number of dysfluencies may drop on consecutive readings of the same text (Bloodstein, 1995). Therefore a total of 48 different texts was prepared (a series of 12 texts for each of the four levels of performance) corresponding to the total number of scanning instances.

All the texts were manually presented to the subjects on panels and sequentially changed every 50 s (10 volumes). The order of presentation of the 48 panels and the order of reading aloud or silent was identical for all subjects. Clear instructions were given to all participants about how to read aloud or silently: normal reading speed, with good articulation if overt and with a normal volume. Instructions were given to maintain the same reading speed for overt and covert. This was exercised and tested before the subjects were placed inside the magnet. Issues concerning noise, movement, breathing and swallowing were addressed prior to scanning and all subjects were debriefed about their performance and impressions after finishing the fMRI procedure. Foam earplugs were used to protect against the excessive noise produced by the scanner during fMRI with the additional advantage that even in the very noisy scanner environment it was easy to hear one’s own voice, due to reliance on bone conduction rather than on air conduction.

2.3. Data analysis

All images were transferred to a workstation where they were combined to 480 sequential volumes readable for SPM99b (Welcome Department of Neuroimaging, London, UK: http://www.fil.ion.ucl.ac.uk/spm/). Preparation of the data before statistical analysis consisted of SPM99b’s realignment using sinc interpolation, normalization with an EPI template (3 x 3 x 3 mm³, 12 parameters affine and nonlinear 4 x 5 x 4, MNI bounding box, trilinear interpolation) and smoothing with a 9 mm square kernel. Statistical parametric maps (SPM{t})’s were generated with SPM99b using the ‘delayed boxcar’ model, no temporal derivative, no covariates of no interest, a high pass filter set to 200 s and a temporal smoothing flag. For inference, a corrected height threshold of p < .05 was used for the SPM{t}’s.

A total of 6 ‘contrasts’ or ‘brain activation states’ were studied in each group. There were 3 ‘motor-speech’ contrasts: (1) the activation difference of the brain between reading loud and silent with semantically meaningful text (indicated as LSM), (2) the activation difference of the brain between reading loud and silent with nonsense words (LSN), and (3) the overall activation difference of the brain between reading loud and silent (LSMN). There were 3 ‘language’ contrasts: (1) the activation difference of the brain between reading meaningful text and nonsense words while reading silently (MNS), (2) the activation difference of the brain between reading meaningful text and nonsense words while reading aloud (MNL), and (3) the overall activation difference of the brain between reading meaningful text and nonsense words (MNSL). Areas with significant activation were identified in Talairach coordinate space and linked with corresponding Brodmann areas (Talairach & Tournoux, 1988). The amount of activation over threshold was categorized into four classes depending on the amount of pixels activated above threshold in a certain area and the highest T value (Table 1). The amount of pixels was estimated from visual inspection and categorized into four classes depending on the amount of pixels activated above threshold in a certain area.

Table 1

<table>
<thead>
<tr>
<th>Score</th>
<th>Cluster size</th>
<th>Value of T-statistic</th>
<th>Notation in Table 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>No activation</td>
<td>None</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Minimal activation</td>
<td>Small</td>
<td>4.84 &lt; T &lt; 6</td>
<td>+</td>
</tr>
<tr>
<td>Clear activation</td>
<td>Medium</td>
<td>T &gt; 6</td>
<td>++</td>
</tr>
<tr>
<td>Strong activation</td>
<td>Large</td>
<td>T &gt; 6</td>
<td>+++</td>
</tr>
</tbody>
</table>

*The size of clusters was estimated from visual inspection and categorized as indicated in the table.

**The value of the T-statistic indicated here is the maximum value found in the clusters on the SPM{t}’s.

3. Results

The realignment plots from SPM99b in all subjects predicted acceptable head movement for all subjects despite the minimal head fixation and the long paradigm testing. All subjects reported that during reading aloud they heard their own voice clearly in the noisy scanner environment and that reading the nonsense words was more difficult in respect to attention and articulation than the semantically meaningful texts. Debriefing of all subjects also showed that while reading the 50 s periods, the end of the text was never reached on the individual panels and that transition form one panel to the next prompted an easy paradigm shift. The importance of this being that the boxcar model for BOLD (see below) was valid in all cases. All stutterers reported some
dysfluencies but at this stage no attempt has been made to quantify these.

Table 2 lists the activation areas of importance for the group of normal subjects (N-group) and for the group of stutterers (S-group).

3.1. Motor-speech contrasts (Fig. 1)

Although the activation in the primary motor areas for speech (BA4, left and right lateral M1 regions) was equal in magnitude and number of pixels in both groups, the activation in the auditory cortex regions in the bilateral superior temporal gyrus (BA41/42/22) seen in the N-group was nearly absent in the S-group (see Fig. 1). These regions became only apparent in the S-group when nonsense words had to be read (Fig. 2). The N-group did not show this grading effect. Activation was strong in the cerebellum and the anterior temporal pole regions (BA38) in the N-group but weak to absent in the SPM's of the S-group.

3.2. Language contrasts (Fig. 3)

Broca's area (left BA44/45) was seen in both groups with equal amplitude, but secondary motor areas related to speech (BA8) showed unilateral left-sided activation in the N-group and weak bilateral activation in the S-group (contrast 'MNLS'). A right-sided tertiary motor area (BA10) was activated in all contrasts with the S-group and not with the N-group.
Areas typically linked with semantic processing (BA21/22/38) were entirely left-sided in the N-group and clearly bilateral in the S-group. The contrast in the visual areas (BA17/18) was somewhat less in the S-group than in the N-group. While the left-sided angular gyrus region (BA39) involved in visual and auditory sensory integration was clearly activated in the N-group, it did not show up in any of the language contrast for the S-group. In both groups, cerebellar activation was prominent, but with distinct different location. In the N-group the activation was definitely more posterior.

4. Discussion

Although fMRI has the potential to study individual results, the primary purpose of the present pilot study was to examine the feasibility of fMRI in the study of
stuttering and indicate possible generic activation differences in the heterogeneous population of stutterers. Therefore a group difference analysis is presented. The results of this investigation are promising. They indicate that mapping cortical function in persons who stutter is indeed feasible, even with a 1TMR-system. Moreover, the results obtained are in line with some of the findings of previous PET studies.

When considering the motor-speech contrasts (loud versus silent reading), this study shows large differences in the activation in primary and secondary auditory cortex for persons who stutter as compared to normals. Whereas in normals the auditory cortices were clearly activated bilaterally, whether reading meaningful text, nonsense words or combined, no activation, left nor right, was present above threshold in the S-group. Only when contrasting loud versus silent reading of nonsense words (a task reportedly more difficult), did the auditory cortex show bilateral activation above threshold. The researcher who presented the texts to the subject reported that each individual, with or without developmental stuttering produced audible speech during overt reading while inside the magnet. Some performance differences in loudness and speed of speech were noted in both groups, but these were not quantified. It is altogether not probable that the large differences in the motor-speech contrasts between the N- and the S-group can be explained on the basis of a large inter-group difference in the loudness or speed of overt performance. Therefore, this finding probably reflects different auditory processing in stutterers compared to normals. The absence of activation in stutterers when contrasting loud versus silent reading of meaningful text suggests that in this task stutterers rely on auditory processing as much during silent reading as during reading aloud. It is only in the more demanding task like reading nonsense words that there is more auditory processing during reading aloud. Similarly, also the difference that was seen for the anterior temporal region (BA38) suggests different auditory processing in stutterers. In the N-group this activation was strong, in the S-group activation was weak. Again, it would seem that the stutterers, as opposed to the non-stutterers, rely on cerebellar contribution almost as much during silent reading as during reading aloud. From these findings one is tempted to conclude that stutterers employ different and particularly less differentiated auditory and motor feedback strategies than

Table 2
Comparing activation between Normals (N) and subjects with stuttering (S)

<table>
<thead>
<tr>
<th>Contrast: speech activated</th>
<th>LSM</th>
<th>LSN</th>
<th>LSMN</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BA</strong></td>
<td>Function</td>
<td>N</td>
<td>S</td>
</tr>
<tr>
<td>4L/R</td>
<td>M1 speech muscles</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>41/42/22 L</td>
<td>Auditory: primary and secondary</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>41/42/22 R</td>
<td>Auditory: primary and secondary</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>38 L</td>
<td>Semantics</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>38 R</td>
<td>Semantics</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>19L/7R</td>
<td>Secondary vision</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>46 L/R</td>
<td>Tertiary motor</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>40 L</td>
<td>Tertiary sensory</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>40 R</td>
<td>Tertiary sensory</td>
<td>0</td>
<td>+</td>
</tr>
</tbody>
</table>

— Deep cerebellar nuclei (L & R) | +++ | + | +++ | + | +++ | + |

<table>
<thead>
<tr>
<th>Contrast: language activated</th>
<th>MNS</th>
<th>MNL</th>
<th>MNSL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BA</strong></td>
<td>Function</td>
<td>N</td>
<td>S</td>
</tr>
<tr>
<td>44/45 L</td>
<td>Broca</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>44/45 R</td>
<td>Right side homologue of Broca</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>6 L</td>
<td>Premotor</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>8 L</td>
<td>Secondary motor (prefrontal)</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>8 R</td>
<td>Secondary motor (prefrontal)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>22/21 L</td>
<td>Lexical written word</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>22/21 R</td>
<td>Right-sided homologue of 21/22 L</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>38 L</td>
<td>Semantics</td>
<td>++</td>
<td>0</td>
</tr>
<tr>
<td>38 R</td>
<td>Semantics</td>
<td>0</td>
<td>++</td>
</tr>
<tr>
<td>39 L</td>
<td>Visual and auditory sensory integration</td>
<td>++</td>
<td>0</td>
</tr>
</tbody>
</table>

Language contrast (meaningful text > nonsense words) were calculated for reading silently (MNS), reading aloud (MNL) and for the combination of the two (MNSL). Similarly, motor-speech contrasts (loud > silent) were calculated for semantically meaningful text (LSM) nonsense words (LSN) and for the combination (LSMN). The functions attributed in the table for the BA were derived from knowledge about these regions and common sense in relation to the paradigm. BA, Brodmann area.
normals. Such an interpretation fits in well with the well-known observations that a change in feedback such as a delay, a frequency shift or masking can lead to a temporary improvement of speech (Bloodstein, 1995; Ingham, 1984; Stuart, Kalinowski, Armson, Stenstrom, & Jones, 1996).

On the language part of this study (meaningful text versus nonsense words), typical language areas were only activated on the left side in normal subjects (Fig. 3): the angular gyrus (BA39), Wernicke’s area (posterior BA22), the middle temporal gyrus (BA22), the anterior temporal pole (BA38), Broca’s area (BA44/45) and a part of the premotor area (BA6) are activated well above threshold. It was surprising to find such strong activation in BA38, but since this study was performed at IT, we believe that the lesser susceptibility problems were for once an advantage rather than a disadvantage. The S-group activated the same regions on the left side except BA39, but also, and with equal magnitude, the right side homologue of Wernicke, part of the right middle temporal gyrus and the right temporal pole. These findings could be interpreted as a confirmation of the cerebral dominance theory formulated by Orton and Travis who suspected that a lack of cerebral dominance is at the origin of developmental stuttering. They are moreover in line with some of the PET studies who also found more bilateral language processing in stutterers (Ingham, Fox, & Ingham, 1997; Kroll et al., 1997).

As opposed to silent reading, reading aloud shifted the activation along the left middle temporal gyrus (BA22) more to the anterior temporal pole (BA38), and somewhat less activation was apparent in Broca’s area (BA44/45) and other lateral prefrontal areas. The same findings were evident from the contrast of the S-group, but more so on the left side. The right-sided homologue for Wernicke’s remained visible. The reason for this shift and the meaning of a more outspoken left-sided shift in the stutterers is unclear. Another interesting finding was the strong activation of cerebellar regions in the language contrasts in both the N-group and the S-group. It has been suggested that certain cerebellar regions are linked to semantics (Leiner, Leiner, & Dow, 1993) but the exact nature of the cerebellar contribution in language and cognition is still open to debate (Ackermann, Wildgruber, Daum, & Grodd, 1998). Surprisingly though, upon close inspection, the precise location of the activated cerebellar region’s were different in the two groups, namely more posterior in the normals (Fig. 4). The reason for this difference is unclear. It is also unclear why a more important activation was seen in areas of the primary and secondary visual cortex (BA18/19) in normals than in persons who stutter.

The paradigm used in the present study does not allow for a closer comparison with the available results of PET studies of stuttering. The PET studies themselves did moreover use a variety of paradigms, some comparing stutterers to normals at rest, others comparing stutterers to normals during different verbal tasks, and still others comparing brain activation in stutterers while stuttering with activation during fluency enhancing conditions, et cetera. At any rate, it is encouraging to find that our results too point in the direction of implication of right hemisphere in developmental stuttering and that differences at the level of the auditory cortices and the cerebellum were found. As a noninvasive technique fMRI allows for repeated experiments in subjects. This must make it possible in the future to further unravel the neural circuitry that underlies developmental stuttering.

These promising results do not mean, however, that the use of fMRI in the study of stuttering is straightforward. One problem is that of movement artifacts. Persons who stutter often show speech-related synkinesias. The stuttering subjects in this study where carefully selected for the absence of gross synkinesias and this may have introduced some bias, which should be taken into account when considering generalization of our findings. Some stimulus correlated head movement was detected on each of the individual realignment plots. From previous unpublished data, we known that such head motion can introduce errors in interpretation of the results. None of the realignment plots showed any high frequency motion and there was no visible difference between the two groups, nor was stimulus correlated motion bigger than half a voxel size, e.g., 2 mm. Therefore we feel that it is safe to state that this small amount of stimulus correlated motion did not influence our findings.

Acoustic noise of the MR-system is another of the main problems of MRI and fMRI in particular in neuroimaging studies of brain activation for speech and language. Scanner noise can induce brain activity in the primary auditory cortex and possibly the motor cortex as well (Kent, 1998). Moreover, in stutterers the acoustic scanner noise could have a fluency enhancing effect. With the earplugs and the head stabilizers, all subjects of the present study could hear their own reading well despite the presence of acoustic noise. To what extent the scanner noise effected their fluency levels remains to be determined. If fMRI is to become a powerful research instrument in the study of stuttering, future studies will certainly have to address the question how to record the subjects’ verbal output during imaging at a level that is sophisticated enough to allow quantification of the dysfluencies.

In conclusion, it seems warranted to say that fMRI is a potentially viable technique for the study of developmental stuttering. However, several problems and obstacles need to be considered.

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References


Ingham, R. J., Fox, P. T., & Ingham, J. C. (1994). Brain image investigation of the speech of stutters and nonstutters. ASHA, 36, 188.


