A Functional Magnetic Resonance Imaging Study of Left Hemisphere Language Dominance in Children

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Background: Functional magnetic resonance imaging is a noninvasive method of assessing language dominance in a pediatric population.

Objective: To determine the pattern of receptive language lateralization in healthy children.

Design: We used functional magnetic resonance imaging to assess an auditory language task in 11 children (7 girls, 4 boys; mean age, 8.5 years). Participants alternately rested and listened to descriptors of nouns presented auditorily, naming the object described silently. Asymmetry indices ([left − right]/(left + right)) were calculated for a priori-determined regions of interest.

Results: The results showed strong activation bilaterally, with greater activation on the left in the superior and middle temporal gyri. Other areas of activation included the cuneus, the left inferior temporal gyrus, the prefrontal area, and the left fusiform and lingual gyri. Regions of interest analysis of individual scans showed additional activation in the left frontal lobe. Asymmetry indices showed strong left lateralization of the inferior frontal gyrus, middle frontal gyrus, and the Wernicke region.

Conclusions: Hemispheric lateralization was clearly demonstrated in 8 children. As in adults, left hemisphere lateralization of receptive language is present at age 8 years.

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IN MOST ADULTS, language function is primarily subserved by the left hemisphere, as indicated by various methods of assessment: lesions studies, the intracarotid sodium amobarbital procedure (IAP), electrocortical stimulation, and functional neuroimaging. However, the question remains as to whether left hemisphere specificity for language is innate or whether dominance develops as language is acquired.

Findings of anatomical asymmetries in the left planum temporale, or auditory association area, of neonates and infants, in addition to functional asymmetries in infants favoring the left hemisphere suggest that a left hemispheric specialization for language is present at birth. On the other hand, language has been found to develop to within the normal range on standardized measures in those with unilateral injury to the left hemisphere before the age of 6 months. These findings lend support to the equipotentiality hypothesis that proposes the equal capacity of either hemisphere to subserve language function. Moreover, infants and children do not suffer the same neurological consequences as do adults with analogous lesions of the left hemisphere, suggesting the developing brain’s functional plasticity. However, despite evidence of plasticity, other investigators have found language deficits after early left hemisphere insult.

In the absence of brain injury, there are 2 possible explanations for the development of left hemisphere language dominance: (1) Language is solely supported by the left hemisphere from birth; or (2) Language is supported by both hemispheres at an early age but becomes increasingly consolidated in the left hemisphere as language competency increases. The critical window of language development and neural plasticity has been debated to some extent, with some investigators proposing that it extends to puberty and others asserting a more conservative age of 5 or 6 years.

Functional magnetic resonance imaging (fMRI) has been shown to be an effective means of assessing laterality, with numerous advantages over the more invasive IAP procedure in terms of its safety, noninvasiveness, replicability, and ability to apply to a nonclinical population. Review of the adult imaging literature in the...
SUBJECTS AND METHODS

SUBJECTS

Participants were 11 children (7 female, 4 male). They ranged in age from 7.3 to 9.6 years (mean [SD], 8.5 [0.9] years). Participants were recruited from the community via posted advertisements. They were paid for their participation. All participants had normal neurologic examination results, normal structural MRI results, and were healthy. All were right-handed as assessed by a modified version of the Edinburgh Handedness Inventory, using 7 of the 10 original items most suitable for children. All children had a handedness score of 100, indicating strong preference for the right hand. If a participant had a diagnosis of learning or attentional difficulties, or English was not his or her first language, he or she was excluded from the study. Testing administered to 10 of the children subsequent to their scan indicated that, on average, these children performed in the high average-to-superior range on standardized measures of expressive naming, reading, and cognition. Children received a tour of the MRI facilities prior to scanning. This study received prior approval by the National Institutes of Neurological Disorders and Stroke institutional review board. Written parental consent and child assent were obtained.

PARADIGM

Stimuli for the Auditory Response Naming task consisted of auditorily presented several-word phrases.\(^2\) The participant silently named the object the phrase described. For example, the correct response to the phrase “long yellow fruit” was “banana.” Covert responses were used to minimize motion artifacts. Descriptions of age-appropriate items were generated from the Peabody Picture Vocabulary Test,\(^3\) the One-Word Expressive Picture Vocabulary Test,\(^4\) and the Boston Naming Test.\(^5\) Seven clues were presented in each 32-second epoch (interstimulus interval of 0.5 seconds). The individual had approximately 4 seconds to listen and to respond to the stimulus. Task difficulty was adjusted based on age so that participants would respond accurately approximately 85% of the time. The naming task alternated with a control task, in which the background noise of the scanner was present; the participant was instructed to rest during these periods. There were 6 cycles of the rest and task conditions for total task duration of 6 minutes 24 seconds. The same speaker delivered the stimuli binaurally over the scanner intercom into headphones worn by the participant. The headphones attenuated the noise of the scanner. A test run in which a sentence was read to the participant and the participant was asked to repeat it was conducted to ensure that the participant could adequately hear the stimuli.

IMAGING PARAMETERS

Images were collected with a 1.5-T General Electric Signa scanner (General Electric, Milwaukee, Wis.) equipped with a birdcage radio frequency coil. The participant’s head was stabilized with a forehead strap and foam padding. Functional images were acquired with a single-shot, blipped, gradient-echo-planar sequence (EPI) (echo time [TE] = 40 milliseconds, field of view [FOV] = 22 cm × 22 cm, acquisition matrix = 64 × 64). Subsequent to the collection of the functional images, anatomical images were acquired using a 3-dimensional fast spin-echo gradient sequence with an inversion impulse (TE = 3.5 milliseconds, repetition time [TR] = 10.1 seconds, TI = 600 milliseconds, flip angle = 20°, slice thickness = 5 mm, FOV = 24 cm × 24 cm, acquisition matrix = 256 × 256, voxel size = 3.4375 mm × 3.4375 mm × 5 mm). For both the functional and structural images, the whole brain was imaged with the collection of 20 contiguous axial images parallel to the anterior-posterior commissure plane. Total scanning time was 18 minutes.

DATA ANALYSIS

Group Data

The data were processed and analyzed using the general linear model\(^6\) with statistical parametric mapping 99 software (Wellcome Department of Cognitive Neurology, London, England). Prior to statistical analysis, all images were normalized to an EPI template conforming to the Talairach and Tournoux\(^7\) convention and then smoothed (full width at half maximum = 8 mm\(^3\)). To minimize false-positive and false-negative results, 2 different statistical analyses were performed: a fixed-effect design and a more stringent conjunction analysis.\(^8\) t Tests were used for all statistical contrasts of the rest condition to the experimental condition. The fixed analysis combined all scans of the same condition within a group. Individual voxels were significantly activated if they survived a height threshold of \(P<.001\) (corrected for multiple comparisons) and an extent threshold of 10 voxels. For the conjunction analysis, individual voxels were significantly activated only if each subject activated the identical voxel at or above a height threshold of \(P<.05\) (corrected). Thus, voxels not activated in every subject were effectively eliminated.

Individual Data

Analysis of data at the individual level can be a source of additional information. Analysis of individual participant data was conducted using a region of interest approach. A priori regions of interest (for each hemisphere) were drawn on raw EPI images: IFG, middle frontal gyrus (MFG), the Wernicke area, and MTG. Analyses of individual regions were conducted using semiautomated image-analyzing software that subtracted signal change between control and task conditions on a voxel-by-voxel basis. A voxel was significantly activated if it survived a threshold value of \(t>3.0\).\(^9\) The total number of activated voxels in each region was automatically calculated.

Lateralization of each region was determined with the calculation of an asymmetry index (AI). The AI for each region was calculated using the formula: \(AI=\frac{\text{left}−\text{right}}{\text{left}+\text{right}}\), with left and right representing the number of activated voxels in the respective hemisphere. A positive AI (\(>0.2\)) indicated left-hemisphere dominance and a negative AI (\(<−0.2\)) indicated right-hemisphere dominance. Any value falling between −0.2 and +0.2 was considered to be indicative of bilateral activation.\(^9\) Two other criteria were also met to consider an AI valid: (1) At least 4 voxels were activated in a particular region; and (2) There was at least a 3-voxel difference between homologous regions."
The conjunction analysis in Figure 2 showed strongly lateralized and highly significant activation in the left MTG and STG, which largely replicated the fixed-effect analysis. Smaller homologous regions in the right hemisphere were also activated (Table 2).

**Regions of Interest Results**

On a subject-by-subject basis, laterality based on regions of interest was most efficiently determined at a threshold of $t = 3$ (Table 3). Mean asymmetry indices per region revealed moderate left lateralization in each region and are presented in Figure 3. The MFG and Wernicke area were most strongly lateralized to the left, with
asymmetry indices of 0.43 and 0.41, respectively. Weaker lateralized activation was found in the MTG (mean, 0.20).

This fMRI study was designed to examine language laterality in children. Results of the study revealed highly lateralized activation in the left MTG and STG. These findings strongly indicate left hemisphere language dominance for auditory comprehension in children between the ages of 7 and 9 years. Group analysis showing bilateral activation of the STG, including the primary auditory cortex, is consistent with other studies of auditory stimuli. Activation was asymmetrical, favoring the left hemisphere, which reflects the lexical component of the stimuli.24,46 As anticipated, our results showed strong activation in the MTG. The MTG has been consistently associated with semantic processing30,33,47,48 although it has also been implicated in phonological processing.24,28,49,50

In addition to the hypothesized areas of activation, the fixed-effect analysis also revealed significant activation of the left cuneus, left ITG, and bilateral prefrontal
areas. Findings suggest that the cuneate region is used in creating a visual image.27,34,51,52 The paradigm used in our study may be conducive to this process since each stimulus describes a concrete noun of which one can easily generate a mental image. Activation of the ITG and prefrontal areas (BA10) are also consistent with previous studies that found these areas to be implicated in semantic processing, object recognition, and working memory, respectively.22,24,46,50,54,58

Examination of the mean asymmetry indices per region showed all regions to be lateralized to the left hemisphere, providing additional support for the presence of strong lateralization in children as young as 7 years. Standard deviations are large, indicating substantial subject variability in the amount of voxels activated in each region and in asymmetry indices. Because of the extent of anatomical variability in language cortices, the group-analysis method of analyzing data is insufficient and at times inaccurate.33 Analysis on a case-by-case basis can provide meaningful information. Overall, 8 of the 11 participants showed clear evidence of left hemisphere language dominance. Two of the remaining children expressed bilateral activation, and one child’s scan was nondiagnostic. With the use of additional scans and alternate language paradigms, more conclusive evidence of hemispheric dominance was provided for 2 participants.33,34

The group analyses did not produce any significant activation in the IFG as predicted; however, in the individual analyses, IFG and/or adjacent MFG activation was observed in most participants. There are several technical issues that pertain to the acquisition and analysis of child-specific data that may contribute to these conflicting findings.32 Many of these technical issues derive from anatomical differences between children and adults. For example, children’s brains are smaller,36 partly due to the process of myelination and synaptic pruning, which is not complete until adolescence.37 Myelination proceeds from posterior (occipital) to anterior (frontal) brain regions; thus, the frontal lobes may be particularly susceptible to distortion since they are less developed than the temporal lobes in the child brain.38 Furthermore, there is substantial individual variability in the location of language cortices.39 Distortion created when normalizing a child-size brain into a standard stereotactic space based on an adult-size brain, in conjunction with normal individual variability, may eliminate consistent areas of frontal lobe activation across individuals. Thus, an adult-based model may not be optimal (although will be used until a pediatric atlas becomes available). Finally, we speculate that variability in location of frontal lobe activation may reflect the use of different word-finding strategies among children.

Two fMRI studies of auditory comprehension in children have found predominantly bilateral activation.31,34 Consistent with these studies, analysis of our data at the

<table>
<thead>
<tr>
<th>Participant</th>
<th>Age, y</th>
<th>Frontal</th>
<th>IFG</th>
<th>MFG</th>
<th>Temporal</th>
<th>Wernicke</th>
<th>MTG</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.2</td>
<td>0.28/136</td>
<td>0.54/50</td>
<td>0.24/23</td>
<td>0.41/180</td>
<td>0.89/51</td>
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<td>0.22/58</td>
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<td>0.36/358</td>
<td>0.48/95</td>
<td>0.39/138</td>
</tr>
<tr>
<td>3</td>
<td>7.8</td>
<td>0.10/360</td>
<td>0.05/53</td>
<td>0.41/50</td>
<td>0.43/183</td>
<td>0.44/31</td>
<td>0.38/109</td>
</tr>
<tr>
<td>4</td>
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<td>0.09/6</td>
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</tr>
<tr>
<td>5</td>
<td>8.6</td>
<td>0.09/135</td>
<td>-0.29/12</td>
<td>0.37/61</td>
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<td>0.11/34</td>
<td>0.10/101</td>
</tr>
<tr>
<td>6</td>
<td>8.9</td>
<td>0.43/118</td>
<td>0.52/22</td>
<td>0.70/17</td>
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<td>8.9</td>
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<td>0.22/14</td>
<td>0.33/50</td>
<td>0.12/103</td>
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<tr>
<td>9</td>
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<td>0.83/11</td>
<td>0.56/7</td>
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<td>0.31/19</td>
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<td>-0.09/30</td>
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</tr>
</tbody>
</table>

*The first number is the asymmetry index; the second is the number of activated voxels. IFG indicates inferior frontal gyrus; MFG, middle frontal gyrus; and MTG, middle temporal gyrus.

Table 2. Conjunction Statistical Parametric Mapping Analysis*
individual level showed similar areas of activation in the temporal cortex, the IFG, and the prefrontal area. However, our study differed substantially in terms of lateralization. We found strong lateralization in the left hemisphere for the Auditory Responsive Naming paradigm. There may be a number of reasons for this difference. First, our sample size was larger than the other child studies and the age range more restricted. Second, our task differed from the others in that it was not overly difficult nor was it a passive task, as it required covert responses. Furthermore, each study used a different auditory language comprehension paradigm. Finally, Booth et al.34,35 and Ultrasound et al.33 used alternative methods from those used in our study to calculate laterality. Different analyses may affect outcome. For example, the earlier study by Booth et al.34 calculated correlations between percentage of voxels activated in each hemispheric region but when similar data were examined with an analysis of variance using percentage of activated voxels in hemispheres and regions as independent variables, left lateralization was found.33 The selection of the formula implemented in our study was based on its correspondence to Wada testing.19

In comparison with an analogous study conducted with 24 adults,36 there were no differences found between the number of activated voxels within regions or in asymmetry indices. In other words, on an identical listening comprehension task, children and adults show highly similar patterns in the extent of activation and degree of lateralization. In conclusion, there are several limitations of this study necessary to address. First, we used a small sample of children; therefore, broad conclusions are difficult to make. Second, language and cognitive testing indicated that these children performed in the high average to superior range; thus, it is possible that highly lateralized language in children of this age is partially a product of their substantial language and cognitive capacities. Finally, because we did not obtain behavioral data, we have no concrete evidence that the children were actually performing the task as instructed. However, the consistency of activation patterns across participants suggests task compliance.

This study used fMRI to demonstrate left hemispheric language dominance of auditory comprehension in normally developing 8-year-old children. At this age, children show a lateralized pattern highly similar to that of adults. Our data provide preliminary neuroimaging evidence in support of those anatomic, evoked response potential, and early unilateral injury findings that suggest early left hemisphere language lateralization.

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REFERENCES
