


Learning to Read without a Left Occipital Lobe: Right-Hemispheric Shift of Visual Word Form Area

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Using anatomical and functional magnetic resonance imaging, we studied the pattern of brain lateralization during spoken and written language tasks, in an 11-year-old girl who underwent a left occipitotemporal resection for a Sturge–Weber angioma at the age of 4 years, that is, after the development of speech but before the acquisition of reading. We observed a selective and successful shift to the right hemisphere of the visual component of reading, particularly the Visual Word Form Area, whereas the verbal components remained strongly left-lateralized. This emphasizes the potential utility of a precise functional and developmental cartography of language for the surgical treatment of focal brain lesions in children.

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Left-hemispheric lesions occurring during early childhood are often compatible with a satisfactory language development,1 even after complete hemispherectomy,2,3 illustrating the right hemisphere’s potential to sustain most aspects of language, provided that compensation occurs early enough.3,4 Nevertheless, in children with focal left-hemispheric lesions, language lateralization is almost unpredictable,5 because of the intricate mutual links that constrain the development and lateralization of the distributed set of language-related brain modules.

Reading may constitute a simple and informative case on the dissociable lateralization of language mod-
ules. Reading may be broken down into two components that are distinct from functional, anatomical, and developmental points of view. First, during the acquisition of reading, the visual system develops an ability to recognize letter strings in a fast and parallel fashion, invariant for changes in case, font, size, or position.6 This ability involves the Visual Word Form Area (VWFA), in the midportion of the left occipitotemporal sulcus,6 which encodes, in adult readers, the abstract identity of strings of visual letters. This system reaches its adult properties by the age of 10 years,7,8 although it is already left-lateralized by the age of 7 years.9 In adults, destruction10 or deafferentation11 of the VWFA results in pure alexia. Second, children learn how to translate letter strings into phonological and lexical representations subtended by left perisylvian language areas. Left-hemispheric predominance for speech processing is discernible during the first months of life12 and is a major factor of functional organization by the age of 8 to 10 years.13,14 The observation of deep dyslexia after left-hemispherectomy at the age of 15 years15 suggests that once their lateralization is established, the phonological components of reading cannot be compensated by right-hemispheric structures.

Using anatomical and functional magnetic resonance imaging (MRI), we studied the pattern of lateralization during spoken and written language tasks in an 11-year-old girl who underwent left occipitotemporal resection at the age of 4 years, that is, after the development of oral speech but before the acquisition of reading.

Case Report

Medical History and Lesion Topography
The patient was an 11-year-old left-handed girl (Edinburgh score: −80%) with a history of Sturge–Weber disease, a condition responsible for unilateral occipital leptomeningeal angioma and secondary cortical dysfunction.16 Focal seizures appeared at the age of 8 months. The patient received clobazam and carbamazepine and remained seizure-free until the age of 4 years. Language and other cognitive abilities developed normally. At the age of 5 years, because of the recurrence of seizures, the patient underwent surgical resection of most of her left occipital lobe, extending into the temporal white matter. She was again seizure-free until the age of 10 years, allowing her to receive successful schooling, including the acquisition of proficient reading. After the relapse of seizures, a complementary superior occipital resection then was performed. However, seizures persisted and the imaging procedure reported here was performed to help further therapeutic decisions.

Spoken and written language production and comprehension were normal on clinical assessment. The patient had complete right hemianopia. She took 50 seconds to read aloud flawlessly a text of approximately 100 words, a performance within the lower range of normal adults. She was asked to read aloud rapidly a list of 165 familiar words, 3 to 9 letters in length.10 She made 2 of 165 minor errors. She had a mean correct latency of 720 milliseconds, with an average increase of 17 milliseconds per letter. Both the mean latency and the slope of the word length effect were 2.3 standard deviations above the mean of 9 normal adults with a full visual field.10

T1-weighted MRI showed that the resected volume included the occipital lobe, the posterior segment of the inferior and middle temporal gyri, and the white matter of the fusiform and parahippocampal gyri to about TC Z = −40 anteriorly (Fig 1). A patch of
disconnected ventral temporal cortex remained beneath the white matter resection, including the normal location of the VWFA.\textsuperscript{10}

**Functional Imaging**

**METHODS.** The lateralization of oral language was studied using two functional MRI protocols.\textsuperscript{3} First, the patient was presented auditorily with concrete nouns, one every 5 seconds and was instructed to covertly generate a simple subject-verb-object sentence, using the target word as the object. As a control condition, the patient was asked to rest, while the word “rest” was presented every 5 seconds. Second, the patient was asked to listen to sentences, one every 5 seconds, each about 2.5 seconds long. She was asked to rest, with no stimulus presentation, as a control condition. For each protocol, the patient received two sequences, each comprising an alternation of four blocks of stimulation with four blocks of rest. Each block comprised five trials, yielding a total duration of 215 seconds for each sequence. The echo planar imaging acquisition was modified by grouping the slice acquisition on a 1.5-second period within each TR, leaving a silent interval of 3.5 seconds allowing for the presentation of auditory stimuli.

Word reading was studied using a protocol adapted from Cohen and colleagues.\textsuperscript{10} The patient was presented visually with blocks of words, checkerboards, or a fixation point. Stimuli were presented centrally for 1,000 milliseconds, followed by a 1,400-millisecond blank screen. The patient was instructed to pay equal attention to all types of stimuli and to covertly read the words. She received three sequences, each comprising an alternation of four blocks of words, two blocks of checkerboards, and two blocks of fixation. Each block comprised 10 trials, yielding a total duration of 192 seconds for each sequence.

On each trial, one functional volume sensitive to blood oxygen level dependent contrast was acquired with a T2-weighted gradient echo, echo planar imaging sequence on a 1.5T Signa Imager (resolution=$5 \times 3.75 \times 3.75\text{mm}^3$). Four volumes were acquired at the beginning of each sequence to reach signal equilibrium and were discarded from the analyses.

Using the SPM99 software, functional images were realigned, normalized, and smoothed (5mm). Temporal filters were applied (high-pass at 240 seconds, low-pass Gaussian width 4 seconds). Activation on each type of trial was modeled by the Statistical Parametric Mapping hemodynamic function. Variables of noninterest modeled constant differences across sequences. We used a voxelwise threshold of $p$ value less than 0.001 and a cluster-level threshold of $p$ value less than 0.05 corrected.

**Results**

We first studied activations related to speech processing (Table; Fig 2). The subtraction of sentence perception minus baseline showed activation only in the left superior temporal gyrus (STG)/superior temporal sulcus (STS). The subtraction of sentence generation minus baseline showed left-sided activation in the dorsal and ventral Broca’s area, precentral cortex, supplementary motor area/cingulate, and STG/STS.

<table>
<thead>
<tr>
<th>Area</th>
<th>Voxel Z-Score</th>
<th>TC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sentence perception $&gt;$ baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left superior temporal</td>
<td>7.10</td>
<td>$-72$</td>
</tr>
<tr>
<td>Sentence generation $&gt;$ baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left superior temporal</td>
<td>5.23</td>
<td>$-72$</td>
</tr>
<tr>
<td>Broca’s area ventral</td>
<td>5.54</td>
<td>$-56$</td>
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<tr>
<td>Dorsal</td>
<td>6.31</td>
<td>$-48$</td>
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<tr>
<td>Left precentral</td>
<td>5.79</td>
<td>$-60$</td>
</tr>
<tr>
<td>Left SMA/cingulate</td>
<td>4.29</td>
<td>$-36$</td>
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<tr>
<td>Right ventral occipitotemporal</td>
<td>5.44</td>
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<tr>
<td>Reading words $&gt;$ checkerboards</td>
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<td></td>
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<tr>
<td>Broca’s area ventral</td>
<td>6.23</td>
<td>30</td>
</tr>
<tr>
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<td>Right precentral</td>
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<td>Left SMA/cingulate</td>
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<td>Left inferior parietal lobule</td>
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<td>Left SMA/cingulate</td>
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</tr>
</tbody>
</table>

TC = Talairach coordinates; SMA = supplementary motor area.
To identify activations related to visual word processing, we contrasted word reading minus checkerboards, masking by the contrast of words minus fixation \((p < 0.001)\). We observed activation in the left IPL, the left supplementary motor area/cingulate, ventral and dorsal Broca’s area, bilateral precentral cortex, and the right ventral occipitotemporal cortex. The latter region extended anteriorly in the fusiform gyrus to about \(TC \, Z = -40\), including peaks almost exactly symmetrical to the classical location of the VWFA (normal subjects TC \(-42 \pm 57 \pm 6, \pm 5\) mm; present patient: TC \(36 \pm 66 \pm 12\)). No activation appeared in the residual left ventral temporal cortex, even at lower statistical thresholds, or when contrasting words minus fixation.

**Discussion**

We report the case of a child who underwent a left occipitotemporal resection at the age of 4 years but nonetheless developed normal reading abilities. The VWFA, which normally provides the input to subsequent stages of word reading, was not removed entirely but was deprived of visual input because of the underlying white matter resection. Beyond anatomical evidence (see Fig 1), the lack of activation during reading tasks demonstrated that this residual patch of cortex was not functional (see Fig 2). The symmetrical right-hemispheric region (R-VWFA) showed strong activation to words versus fixation, suggesting that it supported the function normally devoted to the VWFA. Moreover, the R-VWFA was activated more strongly by words than by checkerboards, a pattern that is restricted to the VWFA in most normal readers, whereas the R-VWFA is activated to a comparable level by both types of stimuli. The patient’s R-VWFA thus was the necessary input pathway to her reading system, whereas in normal subjects, although activated, it is not required for normal reading, as demonstrated by the absence of alexia after right inferotemporal lesions. In contrast, all other language-related activations were strongly left-lateralized: Broca’s area during covert speech generation, the superior temporal cortex during tasks involving speech perception, and the inferior parietal lobule during reading.

In sum, because the lesion occurred before the acquisition of literacy, there was a selective and successful shift to the right hemisphere of the visual component of reading, whereas verbal transcoding and output remained in the left hemisphere. This adaptation may have taken advantage of direct transcallosal projections from the right occipitotemporal cortex to the language areas. Note that a similar interhemispheric shift may operate in adults who develop letter-by-letter reading as a compensation strategy in pure alexia. Finally, the demonstration with functional MRI of the absence of activation in the residual left ventral temporal cortex contributed to the decision to perform a further occipitotemporal resection. This led to a complete cessation of seizures, allowing the patient to resume normal schooling (11-year-old in sixth grade). This emphasizes the utility of a precise functional and developmental cartography of oral and written language for the surgical treatment of focal brain lesions in children.
References

In Vivo Detection of Microglial Activation in Frontotemporal Dementia
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Using positron emission tomography and \([11C](R)-PK11195\), a marker of “peripheral benzodiazepine sites” that is upregulated on activated microglia during progressive tissue pathology, we show increased binding of \([11C](R)-PK11195\) in frontotemporal lobar degeneration in the typically affected frontotemporal brain regions. This implies the presence of an active glial response reflecting progressive neuronal degeneration. It also suggests that increased \([11C](R)-PK11195\) binding, previously demonstrated for Alzheimer’s disease, may occur independently from increased amyloid plaque formation, given that it is not a characteristic feature of frontotemporal lobar degeneration.

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Frontotemporal lobar degeneration (FTLD) is characterized by focal atrophy of the temporal and frontal lobes. 1 Three main histopathological features are found: nonspecific changes of neuronal loss, microvacuolation, and gliosis; \(\tau\) deposition including Pick bodies; and ubiquitin-positive, \(\tau\)-negative inclusions. 2,3 Glial changes including activated microglia are common, but, unlike Alzheimer’s disease (AD), increased amyloid plaque formation is usually not seen. 4,5 The isoquinoline PK11195 is a ligand for the “peripheral benzodiazepine binding site” that is particularly abundant in cells of mononuclear-phagocyte lineage. High-resolution, single-cell, \([3H](R)-PK11195\) autoradiography combined with immunocytochemical...