Crossed Nonaphasia in a Dextral With Left Hemispheric Lesions

A Functional Magnetic Resonance Imaging Study of Mirrored Brain Organization

Margret Hund-Georgiadis, MD; Stefan Zysset, PhD; Kathrin Weih; Thomas Guthke, PhD; D. Yves von Cramon, MD, PhD

Background—General conclusions concerning mechanisms of cerebral lateralization may be learned from the investigation of functional brain organization in patients with anomalous lateralization.

Case Description—The functional organization of language, attention, and motor performance was investigated in a 42-year-old patient with crossed nonaphasia by means of functional MRI. The strongly right-handed man experienced a left middle cerebral artery infarction documented by MRI without exhibition of aphasia. However, the left hemispheric stroke was accompanied by visuospatial impairment, right-sided slight sensory and motor paresis, and right homonymous hemianopia. No history of familial sinistrality or prior neurological illness was present. Functional MR language mapping revealed strong right hemispheric activation in inferior frontal and superior temporal cortices. Finger tapping with the right hand recruited ipsilateral premotor and motor areas as well as supplementary motor cortex. A Stroop task, usually strongly associated with left-sided inferior frontal activation in dextrals, resulted in strong right hemispheric frontal activation.

Conclusions—From our data there is clear evidence that different modalities, such as language perception and production, attention, and motor performance, are processed exclusively by 1 hemisphere when atypical cerebral dominance is present. (Stroke. 2001;32:2703-2707.)

Key Words: cognitive disorders ■ language ■ laterality ■ magnetic resonance imaging ■ motor activity

A typical lateralization of cognitive functions is observed in a small percentage of right-handed patients with unilateral brain damage. It becomes evident as crossed aphasia when right hemispheric brain lesions are associated with language dysfunction. The precise incidence of this type of anomalous language lateralization is unknown for numerous methodological reasons. Claims range from 1% to 13% of all aphasias.1 “Crossed nonaphasia” is declared when left brain damage occurs without aphasia but with visuospatial and other deficits typical of right brain damage. The number of reported cases with crossed nonaphasia is a small fraction of those with crossed aphasia, certainly <1%.

Thus far, behavioral research did not offer a comprehensive theory of these rare anomalous cases.1 Visuospatial functions have been claimed to normally lateralize to the right brain.2 However, shifted laterality of language or handedness can account for a lateralization of visuospatial functions to the left brain.3 This is particularly the case in right-handed persons with unexpected absence of aphasia after left brain damage. A specific and comprehensive profile of visuospatial deficits due to right brain damage in typical right-handed persons has not yet been established. It is definitely hampered by the unequivocal bilateral representation of certain visuospatial functions.4 However, a comprehensive profile could reveal, in behavioral terms, the fundamental association between handedness, language, praxis, and visuospatial function. Developmental and genetic factors have been claimed to account for the relationship between handedness and cerebral laterality in typical cases and in most special cases of mirrored brain organization.5 A number of theories have been proposed as to the neuropsychological and/or neurobiological mechanisms that might be responsible for anomalous brain organization, but there is still disagreement about its possible significance.

Functional brain mapping of language and attention may help to clarify the underlying phenomenology. This study presents comprehensive functional and structural MRI data of a patient with crossed nonaphasia. There may be general conclusions concerning mechanisms of cerebral lateralization to be learned from the investigation of functional brain organization in patients with anomalous lateralization.

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The long-term memory subtest of the Wechsler Memory Scale–Revised (WMS-R) and the German version of the California Verbal Learning Test (CVLT) were applied to examine whether verbal and nonverbal materials were processed equally. The CVLT estimates the patient’s verbal and nonverbal learning strategies on the basis of a list learning test.

Functional MRI

Language Tasks
A comprehensive language mapping protocol was applied to reveal perceptual and productive aspects of language processing. A semantic word classification task was used, which has been established in previous research within our laboratory. Moreover, a silent sentence completion task was believed to reveal different levels of word and sentence processing. During the sentence completion task, the patient was instructed to rapidly complete a simple German sentence after visual presentation of a sentence fragment consisting randomly of a subject, predicate, or object. A training test determined the patient’s ability to solve the task in the MR scanner.

Motor Mapping
A finger-tapping task was performed in response to a visual stimulus on the screen, with the use of a blocked design. The right and left hands were recorded separately.

Attentional Task
A color/word-matching Stroop task, previously developed and studied in our laboratory, was applied to test the hemispheric distribution during a selective and divided attention task. The patient had to decide during this interference task whether the color of the letters in the top row corresponded to the color of a word in the bottom row.

Equipment
The experiments were performed on a 3-T scanner (Medspec 300/100, Bruker). Sixteen axial slices (field of view, 19.2 cm; matrix, 64×64; slice thickness, 5 mm; spacing, 2 mm) parallel to the anterior commissure–posterior commissure plane and covering the whole brain were acquired with the use of a single-shot, gradient-recalled echo-planar image sequence (echo time [TE], 30 ms; repetition time [TR], 2 seconds; 90° flip angle). Before the functional runs, 16 anatomic T1-weighted MDEFT images (data matrix, 256×256; TR, 1.3 seconds; TE, 10 ms) and 16 T1-weighted echo-planar images with the same parameters as the fMRI data were recorded. Perfusion images were obtained by dynamic first-pass bolus tracking of Gd-DTPA (Magnevist, Schering) with a gradient-echo echo-planar imaging sequence (TR, 1000 ms; TE, 30 ms). The contrast agent bolus (0.1 ml/kg) was administered by a power injector (Spectris MR Injector) at a rate of 5 ml/s. The concentration-time curves were processed on a pixel-by-pixel basis to determine maximum peak and time-to-peak maps.

The Lipsia Software package was used for functional data analysis. Preprocessing included 2-dimensional movement correction and baseline correction, ie, functional data were filtered in the temporal domain by a low-pass filter. Functional images were created by generating statistical z maps with z values >4 on a single pixel level. The individual data were transformed into the Talairach coordinate system for better comparison.

Results

Neuropsychological Testing
According to the Edinburgh Handedness Inventory, the patient was 100% right-handed. No aphasia was present on the basis of AAT results. The AAT revealed unimpaired spontaneous speech on the basis of six 6-point rating scales (6 points for each subtest). The percentage scores of the 5 AAT subtests showed normal language processing: Token Test (100%), Repetition (99%), Written Language (100%), Confrontation Naming (100%), and Comprehension (98%).

Subjects and Methods

Case Report

A 48-year-old right-handed patient suffered from a right-hand sensory and motor deficit due to a left hemispheric stroke event. Language processing was reported to be intact. Two months later the patient experienced right homonymous hemianopia and a complete paresis of the right arm and hand. Again, fully intact language comprehension and production without any hints of aphasic symptoms were assessed. However, the patient complained of problems in the visuospatial domain, such as orientation in the hospital environment. T1-weighted MRI revealed a hypointense lesion in the prefrontal, parietal, and temporo-occipital territory of the left middle cerebral artery (Figure 1). The anterior and middle portions of the temporal lobe appeared structurally intact. The stroke lesion involved the left posterior cerebral artery as well, in particular the territory of the arteria calcarina and the posterior temporal artery. The maximum peak (maximum peak/local relative maximum of contrast agent concentration) and time-to-peak maps (time to peak/time in seconds to reach the maximum peak concentration) gained through perfusion imaging were coregistered with the anatomic image and visualized on the axial plane. L indicates left; R, right.

Laterality Testing and Neuropsychological Examination

Right-handedness was assessed on the basis of the Edinburgh Handedness Inventory (range, ±100%). The presence of aphasia was assessed by means of the Aachen Aphasia Test (AAT).
A dissociation in the processing of verbal and nonverbal materials was the main neuropsychological finding. Although the WMS-R delivered normal test results, when verbal material was presented, percent range \((PR)\) was 70\%, memorization of nonverbal abstract material was significantly impaired \((PR = 13\%)\). In the CVLT, verbal learning was found to be intact \((PR = 99\%)\), while nonverbal learning showed an impaired ability to recall abstract drawings \((PR = 10\%)\). In summary, all tests were normal whenever verbal stimuli were applied. Testing of nonverbal material regularly showed prolonged latencies and higher amounts of errors.

**Functional MRI**

Figure 2 displays the functional data of the fMRI tasks overlaid on the 2-dimensional anatomic image of the patient.

**Language Tasks**

Both word classification and silent sentence production elicited strong right hemispheric activations of language-associated cortices in our patient, whereas they were previously associated with strong left hemispheric activation in healthy dextrals.\(^9,10\) In our patient the word classification task recruited right middle and inferior frontal cortices (pars triangularis and pars orbitalis). Moreover, a task-related blood oxygenation level–dependent (BOLD) MR signal change was present in the superior temporal gyrus of the right hemisphere. Covert sentence production resulted in similar activation patterns with respect to the right inferior frontal and temporal cortices. However, additional activation was found in the right hemisphere along the inferior frontal sulcus, supplementary motor cortex, and right thalamus. The Talairach coordinates\(^14\) of the main activations, maximum \(z\) values, and volumes are summarized in the Table. The performance data (mean latencies, number of errors, and reaction times required to complete sentences) assessed during the language tasks did not differ significantly from control results acquired earlier.

**Motor Task**

Random tapping of the right-hand fingers showed unusual distribution patterns of activation (Table). It was associated with strongly ipsilateral, ie, right hemispheric activation of the primary motor cortex, premotor cortex, and supplementary motor area. On the cerebellar level, clearly right hemispheric, ie, ipsilateral activation was present. In contrast, left-hand finger tapping showed normal functional distribution patterns,\(^11\) ie, contralateral involvement of primary and secondary motor cortices and ipsilateral cerebellar involvement.

**Stroop Task**

This interference task elicited activations in the pars triangularis of the right inferior frontal sulcus, along the right inferior frontal sulcus, in the intraparietal sulcus, and in the premotor area. In contrast to the normal control study,\(^12\) the distribution of task-related activation again showed a reverse lateralization toward the right hemisphere. Behavioral data during the interference task did not differ significantly from those obtained from healthy elderly control subjects.

**Perfusion Study**

Comparison of the perfusion profiles of both hemispheres showed corresponding maximum peak maps and time-to-peak maps in structurally intact gray and white matter compartments. Even in brain regions adjacent to the ischemic necrosis, no perfusion deficits were evident, ie, in the middle portion of the temporal lobe the following data were acquired from the maximum peak and the time-to-peak maps: maximum peak, right versus left: 0.42 versus 0.46; time to peak, right versus left: 30.5 versus 31 seconds (Figure 1).

**Discussion**

To the best of our knowledge, this is the first fMRI study of a patient with crossed nonaphasia. The coincidence of an extended left hemispheric lesion without exhibition of aphasia in a strongly right-handed patient pointed toward this syndrome. Thus far, the underlying functional organization of language had remained unclear in these rare cases.

The most intriguing finding of our study is that the right hemisphere was almost exclusively involved, regardless of the examined domain (language processing, motor performance, or attention). Perceptive and expressive language processing elicited activations in inferior frontal and superior temporal cortices of the right hemisphere. Even structurally intact and normally perfused left hemisphere language cortices were not significantly involved during the language tasks. Since the patient never exhibited aphasia, the “functional shift to the right” is unlikely to be due to reorganizational changes. Moreover, the absence of task-related BOLD MR signal changes in the left hemisphere was not caused by impaired cerebral hemodynamics. Brain perfusion was demonstrated to be normal in structurally intact brain regions. In accordance
with our findings, a previous fMRI study in a neurologically intact dextral demonstrated that a mirrored organization of language can exist without obvious penalty to language function.\textsuperscript{15}

Moreover, our patient performed a Stroop task, which in young adults is associated with left inferior frontal activation, with exclusively right hemispheric activations. Interesting functional distribution patterns were obtained as well from the motor mapping study: while finger tapping of the left hand delivered normal activation patterns involving the contralateral primary and premotor cortex as well as the ipsilateral cerebellum, motor mapping with the right hand showed extensive recruitment of ipsilateral premotor, motor, and cerebellar cortices. This "shift to ipsilateral homologous motor cortices" is known as a compensatory strategy in patients with central lesions.\textsuperscript{16} Note that our patient had fully recovered from his motor paresis at the time of the functional mapping session. Nevertheless, reorganizational changes cannot be fully excluded in the motor domain.

In summary, our case provides evidence for a mirrored right hemispheric dominance associated with crossed non-aphasia. However, the anomalous organization is not restricted to language functions but includes attentional and motor processing as well. Moreover, our case suggests that the completely reversed functional anatomy existed from a very young age without penalizing any brain function.

**References**


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**Talairach Coordinates, Maximum z Values, and Volumes of Main Activations During Language, Attention, and Motor Mapping**

<table>
<thead>
<tr>
<th>Area</th>
<th>Talairach Coordinates</th>
<th>Volumes (Maximum z)</th>
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<tbody>
<tr>
<td></td>
<td>Left</td>
<td>Right</td>
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<tr>
<td>Word classification task</td>
<td></td>
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<tr>
<td>IFG (BA44)</td>
<td>−41</td>
<td>−3</td>
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<td>STG</td>
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<td>Silent sentence production task</td>
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<td>IFG (BA44)</td>
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<td>Stroop task</td>
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<td>IPS</td>
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<tr>
<td>Motor task: tapping right hand</td>
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<td>MC (BA4)</td>
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<td>PMC (BA6)</td>
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<td>Motor task: tapping left hand</td>
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<td>SMA</td>
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IFG indicates inferior frontal gyrus; STG, superior temporal gyrus; IFS, inferior frontal sulcus; IPS, intraparietal sulcus; SMA, supplementary motor area; MC, primary motor cortex; and PMC, premotor cortex.


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