Effects of anomalous language representation on neuropsychological performance in temporal lobe epilepsy

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Article abstract—*Objective:* To examine the effects of anomalous language representation (i.e., mixed- and right-cerebral dominant) on neuropsychological performance. *Background:* Right cerebral language dominance resulting from early cerebral injury is associated with relatively preserved language function with decreased visuospatial ability. However, previous reports of this phenomenon have examined patients with relatively large cerebral injuries (e.g., infantile hemiplegia) or limited sample sizes. *Methods:* A total of 561 patients with complex partial seizures of left temporal lobe origin were studied. Patients were classified into left (n = 455), bilateral (n = 58), and right (n = 48) language dominant groups based on Wada testing. *Results:* Right language dominant patients performed more poorly on multiple tests of visuospatial function, including Performance IQ (PIQ), than did left language patients. No significant group differences were detected for measures of language or general verbal function. The effects of bilateral language on PIQ differed according to handedness. Lowered PIQ was present in the bilateral nondextral group but not for bilateral dextral patients, and this pattern was observed with other visuospatial measures. *Conclusions:* In patients with relatively small lesions restricted to the left mesial temporal lobe, a shift in language dominance to the right hemisphere is associated with decreased visuospatial functions but preserved verbal abilities. Nondextral patients with bilateral language representation also displayed decreased visuospatial performance, although dextral patients with bilateral language did not.

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Cerebral lesions that occur during brain maturation alter subsequent neural development. In patients who sustain early left hemisphere injury, a shift of language function to the uninjured right hemisphere may occur. Broca[1] discussed this phenomenon in 1865, describing a case with life-long seizures and congenital right-body hemiparesis without aphasia. Autopsy showed an absence of the third left frontal convolution, causing Broca to conclude, "the third right convolution had compensated for the absence of the left" (p. 1069). Although patients with right-body infantile hemiplegia may not necessarily have language developed to the same degree compared with patients without injury, they often display relatively normal language function despite the magnitude of left-hemisphere injury.[2,3]

The transfer of language dominance to the right hemisphere does not occur without an effect on normal right hemisphere functions; visuospatial skills are generally performed more poorly than verbal skills. Teuber[4] described this phenomenon as "crowding," and occurs when "one hemisphere tries to do more than it had originally been meant to do."

Although studies of patients with right-body infantile hemiplegia have documented language transfer to the right hemisphere, relatively poor performance on visuospatial tasks may simply reflect greater sensitivity of these measures to lesion effects. Neuropsychological tests that are sensitive to right hemisphere injury are also generally more sensitive to diffuse impairment than are language measures.[5] Additionally, language skills are relatively preserved in these patients but are not at normal levels. Thus, the effect on language may be related to the lesion size studied, may reflect mild but undetected impairment of the presumably intact right hemisphere, or result from the intrinsic inability of the right hemisphere to adequately mediate language function as well as the left hemisphere. Therefore, it cannot be determined whether poor

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Specific group performances for all neuropsychological tests included may be accessed at http://www.neuro.mcg.edu/boze/NPCrowd.html

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visuospatial function is the result of language transfer to the right hemisphere, which "crowds out" normal right hemisphere function, or whether it reflects the effect of large cerebral lesions.

Prior studies examining crowding in patients without extensive cerebral lesions have been limited by small sample size[6] because right cerebral language representation occurs rarely. Because transfer of language is typically associated with larger lesions extending outside of the temporal lobe,[7] it has been difficult to obtain a homogeneous sample with Wada-confirmed dominance.

We report the results from a multicenter collaborative study designed to investigate the relationship of atypical language representation on neuropsychological function. We hypothesized that patients with right hemisphere language would perform significantly more poorly on neuropsychological measures of visuospatial function than patients with typical left cerebral language dominance, with no group differences on measures of language function. Patients with bilateral cerebral language dominance were anticipated to perform in an intermediate position on visuospatial tasks between left and right language dominant groups. We also investigate the effect of handedness on this phenomenon as reflected by verbal and performance IQ measures.

Methods. *Subjects.* The Bozeman Epilepsy Consortium retrospective neuropsychology database served as the data pool for the current project. The Bozeman Epilepsy Consortium is a multicenter collaborative research group consisting of neuropsychologists from eight epilepsy surgery centers: Cleveland Clinic Foundation, EpiCare Center, Long Island Jewish Hospital, Mayo Clinic, Medical College of Georgia, New York University, University of British Columbia and University of Victoria, and Yale University. The group is named after Bozeman, MT, which was the site of the group's first formal meeting.

The database was searched for patients with complex partial seizures of left temporal lobe origin who underwent Wada testing as part of their preoperative evaluation for possible epilepsy surgery. We restricted our sample to patients with left temporal seizure onset to increase sample homogeneity because we were interested in the effect of language shift from the left to the right hemisphere. Patients with WAIS-R Full-Scale IQs lower than 65 were excluded. A total of 561 patients were identified (left language dominant = 455 [81%], bilateral language dominant = 58 [10%], right language dominant = 48 [9%]). Sample characteristics are presented in table 1.

Neuropsychological tests. All patients received a comprehensive neuropsychological evaluation for possible epilepsy surgery, although variations in neuropsychological test selection existed among institutions. The Wechsler Adult Intelligence Scale–Revised (WAIS-R) provided measures of verbal (verbal IQ [VIQ]) and nonverbal (performance IQ [PIQ]) cognitive function.[8] In addition to VIQ, verbal functions were measured with the Boston Naming Test,[9] FAS verbal fluency,[10] and individual Wechsler Adult Intelligence Scale–Revised (WAIS-R) verbal subtests (Information, Digit Span, Vocabulary, Arithmetic, Comprehension, Similarities). In addition to PIQ, nonverbal and visuospatial skill was assessed with the Rey-Osterrieth Complex Figure copy,[11] Judgment of Line Orientation,[12] Benton Facial Recognition Test,[12] and individual WAIS-R Performance subtests (Picture Completion, Picture Arrangement, Block Design, Digit Symbol). Recent memory and learning were tested using the Logical Memory and Visual Reproduction subtests from the Wechsler Memory Scale–Revised.[13] Additional test description of all the above tests can be found in Lezak[14] and in Spreen and Strauss.[15] Data on each measure were not available for all patients, and all patients did not receive all tests.

Table 1 Sample characteristics

Variable	Left dominant	Bilateral	Right dominant
Age, y, mean (SD)	30.7 (9.5)	30.4 (10.4)	30.4 (8.9)
Education, y, mean (SD)	12.5 (2.5)	12.2 (2.6)	12.3 (3.1)
Women/Men	239/216	33/25	29/19
Lesions (%)	127/455 (28)	17/58 (29)	20/48 (42)
Seizure onset, y, mean (SD)	11.3 (9.6)	8.6 (8.3)	9.5 (9.2)
Handedness (%)			
Dextral	405 (91)	40 (69)	24 (50)
Nondextral	40 (9)	18 (58)	24 (50)

A series of univariate analyses of variance (ANOVAs) was performed to analyze the effects of different cerebral language representation on performance on each. Significant group effects were further analyzed with pairwise Student's *t*-tests. This approach was adopted because missing data prevented multivariate analyses from being conducted.

Results. *Primary analyses.* Three primary dependent measures were identified a priori to exert some control over the experiment-wise Type I error rate: VIQ, PIQ, and Block Design. VIQ was selected to examine whether differences in general verbal cognition existed among the three language groups independently from nonverbal and visuospatial skills as reflected by PIQ or Block Design; both PIQ and Block Design were chosen to reflect nonverbal and visuospatial skills. Although PIQ is not completely independent of Block Design since Block Design is one of the subtests contributing to PIQ, we chose PIQ as a primary variable because the largest samples sizes in this database were present for WAIS-R IQ measures. Block Design was used because it is the single best measure from the WAIS-R of visuospatial function,[8] and we therefore expected it to be the most sensitive subtest to changes in functions subserved by the right hemisphere.

No VIQ difference was present among the three language groups (table 2). Conversely, a significant language effect was observed for both PIQ ($p < 0.0001$) and Block Design ($p < 0.005$). For each measure, the significant effect resulted from right cerebral language dominant patients performing significantly more poorly than either the left or bilateral language groups.

Secondary analyses. Analyses of the secondary dependent variables yielded a similar pattern. Cerebral lan-

Table 2 Neuropsychological test performance for IQ measures and neuropsychological measures reaching statistical significance

Variable	Left dominant	Bilateral	Right dominant	p Value
Verbal IQ	88.5 (12.1)	87.6 (10.4)	86.0 (10.9)	NS
Performance IQ	90.9 (13.2)	88.6 (14.4)	82.3 (10.0)	<0.0001*†
Block Design	8.8 (2.5)	8.9 (2.9)	7.0 (1.8)	<0.005*†
Digit Symbol	7.7 (2.5)	8.0 (2.8)	5.9 (1.4)	<0.003*‡
Line Orientation	22.7 (5.0)	22.1 (5.8)	20.1 (5.9)	<0.019§
Facial Recognition	44.7 (5.1)	42.2 (6.2)	42.1 (5.1)	<0.007‖¶
Complex Figure	25.1 (13.5)	26.1 (13.6)	18.2 (15.4)	<0.026§†

Values are mean (SD). Statistical significance levels are derived from one-way three-level analysis of variance. Pairwise comparisons are indicated in the footnotes.

*Left vs right ($p < 0.001$); †bilateral vs right ($p < 0.05$); ‡bilateral vs right ($p < 0.001$); §left vs right ($p < 0.01$); ‖left vs right ($p < 0.05$); ¶left vs bilateral ($p < 0.05$).

guage representation had no effect for any measure of verbal function. Conversely, relatively consistent significant group differences were observed for measures of visuospatial performance (i.e., Block Design, Digit Symbol, Line Orientation, Benton Facial Recognition, and Complex Figure Copy) (see table 2). With the exception of Benton Facial Recognition, performance of the bilateral language group did not differ from that of the left language group.

Effects of handedness. VIQ and PIQ also served as the principal dependent measures for analyses examining handedness effects. Handedness was investigated because it may produce effects of cerebral organization that is not fully reflected in language laterality.[16,17] No significant effects of handedness were present for VIQ. Conversely, nondextral patients with bilateral cerebral language (n = 18) displayed significantly lower PIQ than their right-handed counterparts (n = 14) ($p < 0.007$) (figure). No effect of handedness was present for patients with left or right cerebral language dominance.

We also examined handedness on the other measures with significant language differences in the bilateral language patients, realizing that these analyses were exploratory and limited due to sample size in which there were only 7 or 8 nondextral patients for each comparison. Despite the small sample size, there was a significant effect of handedness on Block Design, with nondextral patients with bilateral language performing more poorly than dextral patients with mixed language (7.0 [SD = 1.8] versus 9.4 [SD = 3.0], $p < 0.04$). A similar trend was present for Line Orientation (18.9 [SD = 4.3] versus 23.1 [SD = 5.9], $p < 0.09$), with no suggestion of group difference present for Digit Symbol, Benton Facial Recoguition, or the Complex Figure.

Age at seizure onset effects. We analyzed age at seizure onset (onset ≤5 years; onset >5 years) on VIQ and PIQ to determine whether the crowding pattern could be attributed to age of injury rather than a shift in language representation. The early onset patients (n = 191) had a mean VIQ of 86.2 (SD = 11.9), and the late onset patients (n = 311) had an average VIQ of 89.4 (SD = 11.4); the early onset patients had a mean PIQ of 86.4 (SD = 13.5), and the late onset group average PIQ was 91.3 (SD = 12.5). Although patients with earlier onset seizures performed more poorly, no statistical interaction was present, indicating that the negative effects of earlier seizure onset were similar for both VIQ and PIQ.

Discussion. When the right hemisphere assumes primary responsibility for language function in the setting of early left cerebral injury, there is a concomitant decrease in visuospatial ability for which the right hemisphere is typically dominant. This occurs even when the early injury is relatively restricted to the mesial temporal and away from primary perisylvian language zones. The shift to right hemisphere language dominance is not associated with a decline in language skill. On measures of visual confrontation naming, verbal generative fluency, and general verbal cognitive skills as reflected by the VIQ, no significant difference was present in patients with right cerebral language dominance when compared with their left dominant counterparts. This suggests that decreased linguistic ability in previous reports may reflect, in part, magnitude of lesion effects.

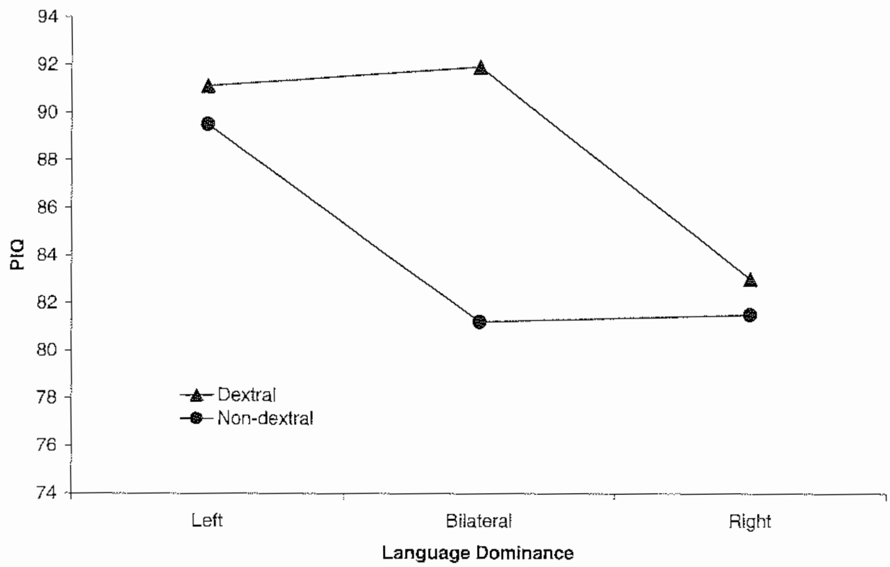

Figure. Mean performance IQ (PIQ) results for dextral and nondextral patients according to cerebral language dominance. A statistically significant PIQ difference is present as a function of handedness in the bilateral language group.

When the transfer of language is less complete and bilateral language is present, the effect on nonverbal skills is less straightforward. Of the six significant neuropsychological measures of visuospatial function, including PIQ, the bilateral language group performed more poorly than left language patients on only a single measure (Benton Facial Recognition). Decreased visuospatial performance in patients with bilateral language appears to be, at least in part, related to handedness. Although there was no effect of handedness on VIQ in the three language dominant groups, PIQ was significantly lower for nondextral patients with bilateral language compared with right-handed patients with bilateral language. In contrast, PIQ was not affected by handedness in either the left or right language groups. A similar pattern was present in the bilateral language group for Block Design and Line Orientation, with higher performance present in dextral patients. Although these latter analyses were exploratory and based on small sample sizes, the consistency across tests suggests that handedness is one factor associated with the crowding effect in patients who do not display a complete transfer of language to the right hemisphere.

We speculate that nondextral patients in the left cerebral language group are composed primarily of patients whose handedness was biologically determined rather than resulting from cerebral injury (i.e., pathologic left-handedness). The 89% right-handed figure of the left language group is consistent with most estimates of handedness prevalence in the general population.[18] Because the overall group percentage of right-handedness in the left language group is the same as that of the general population, it is likely that handedness in this group was biologically determined. In contrast, a transfer of handedness (i.e., pathologic left-handedness) is present to a large degree in the other groups. Right-handedness occurred less frequently, decreasing to 69% in the bilateral language group and to 50% in the right language group ($\chi^2 = 71.0, p < 0.0001$). In both the bilateral and right language groups, the shift in language was accompanied by a shift in hand preference in some, but not all of the patients.

In patients with partial transfer of language to the right hemisphere, there is not an associated decline in visuospatial function unless there is also a shift in handedness. Conversely, when there is a complete shift of language to the right hemisphere, there appears to be no additional negative effect associated with nondextral handedness; both handedness groups perform more poorly on visuospatial tasks. Thus, a left hemisphere lesion that produces complete transfer of language will impair visuospatial ability regardless of the effects of handedness. In patients with bilateral language, a left hemisphere lesion that leaves hand preference intact is likely to be less disruptive than one that alters handedness. Only in the latter case is visuospatial function also compromised.

Two types of bilateral language representation demonstrated by Wada testing have been described.[19] One type demonstrates little if any language alteration following either the left or right hemispheric injection and is termed bilateral autonomous language representation. In the other pattern, termed bilaterally dependent language, patients display language impairment following both left and right hemisphere injections. Bilaterally dependent language is hypothesized to result from a shift in language toward the right hemisphere after early left hemisphere injury and is associated with poorer neuropsychological function. If this dichotomy is related to our findings, it would be expected that the dextral patients in our bilateral language group would be more likely to display the pattern of bilateral autonomous language and the nondextral patients to display a pattern of bilateral dependent language. Unfortunately, this information was not coded.

Owing to an incomplete data set, we were unable to use a multivariate approach to data analysis. Multiple univariate analyses increase the experimentwise Type I error rate in proportion to the number of analyses being conducted. To decrease the likelihood of capitalizing solely on chance facts, we established three principal variables before analyses as our primary dependent measures (i.e., VIQ, PIQ, and Block Design). These measures were chosen for three reasons. First, the summary IQ measures were based on the largest sample size available. Consequently, the absence of any group difference on VIQ could not easily be attributed to sample size and statistical power considerations. Second, PIQ was based on the same sample as VIQ. Although we did not expect PIQ to be the best available measure to assess right hemisphere function, being based on the same sample as VIQ ensured that we would avoid introducing a subject/group bias into our results. Third, Block Design was selected because it was expected to be the single most sensitive measure of right hemisphere impairment. The consistency of results across multiple measures also argues against findings being solely attributable to chance. Of the six statistically significant findings, all were associated with decreased visuospatial function.

The effect of the presence of a structural lesion could not be properly investigated because of small sample size and because structural lesions were coded in the database only as being present or absent. We did perform an analysis using PIQ with both language representation and lesion presence/absence as grouping factors and found no statistical interaction. However, future studies will be needed to more precisely determine what effects, if any, the presence of a structural lesion exerts on cognitive performance with atypical cerebral language lateralization. Results of this study confirm the presence of the "crowding" phenomenon in patients with right hemisphere language without extensive left hemisphere lesions and suggest that such a cost also extends to nondextral patients with bilateral language representation.

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References

1. Berker EA, Berker AH, Smith A. Translation of Broca's 1865 report: "Localization of speech in the third left frontal convolution." Arch Neurol 1986;43:1065–1072.
2. Basser L. Hemiplegia of early onset and the faculty of speech with special reference to the effect of hemispherectomy. Brain 1962;85:427–460.
3. Milner B. Psychological aspects of focal epilepsy and its neurosurgical management. Adv Neurol 1975;8:299–321.
4. Teuber HL. Why two brains? In: Schmitt FO, Worden FG, eds. The neurosciences. Third study program. Cambridge, MA: MIT Press, 1974:71–74.
5. Lee GP, Hamsher KdeS. Neuropsychological findings in toxicometabolic confusional states. J Clin Exp Neuropsychol 1988; 10:769–778.
6. Strauss E, Satz P, Wada J. An examination of the crowding hypothesis in epileptic patients who have undergone the carotid Amytal test. Neuropsychologia 1990;28:1221–1227.
7. Woods RP, Ojemann GA, Dodrill CB. Brain injury, handedness, and speech lateralization in a series of amobarbital studies. Ann Neurol 1988;23:510–518.
8. Wechsler D. WAIS-R manual. New York: The Psychological Corporation, 1981.
9. Kaplan EF, Goodglass H, Weintraub S. The Boston naming test. 2nd ed. Philadelphia: Lea & Febiger, 1983.
10. Spreen O, Benton AL. Neurosensory Center Comprehensive Examination for Aphasia. Victoria, B.C.: University of Victoria, Psychology Laboratory, 1997.
11. Rey A. L'examen psychologique dans les cas d'encéphalopathie tramatique. Arch Psychologie 1941;37:286–340.
12. Benton AL, Sivan AB, Hamsher KdeS, Varney NR, Spreen O. Contributions to neuropsychological assessment. A clinical manual. 2nd ed. New York: Oxford University Press, 1994.
13. Wechsler D. Wechsler Memory Scale-Revised manual. San Antonio, TX: The Psychological Corporation, 1987.
14. Lezak MD. Neuropsychological Assessment. 3rd ed. New York: Oxford University Press, 1995.
15. Spreen O, Strauss E. A compendium of neuropsychological tests. 2nd ed. New York: Oxford University Press, 1998.
16. Satz P, Strauss E, Wada J, Orsini DL. Some correlates of intra- and interhemispheric speech organization after left focal brain injury. Neuropsychologia 1988;26:345–350.
17. Meador KJ, Loring DW, Lee GP, et al. Hemisphere asymmetry for eye gaze mechanisms. Brain 1989;112:103–111.
18. Gilbert, AN, Wysocki CJ. Hand preference and age in the United States. Neuropsychologia 1992;30:601–608.
19. Benbadis SR, Dinner SD, Chelune GJ, Peidmonte M, Lüders HO. Autonomous versus dependent: a classification of bilateral language representation by intracarotid amobarbital procedure. J Epilepsy 1995;8:255–263.