34. Duquette P, Pleines J, Girard M, Charest L, Senecal-Quevillon M, Masse C. The increased susceptibility of women to multiple sclerosis. Can J Neurol Sci 1992;19:466–471.
35. Duquette P, Girard M. Hormonal factors in susceptibility to multiple sclerosis. Curr Opin Neurol Neurosurg 1993;6:195–201.
36. Azzimondi G, Stracciari A, Rinaldi R, D'Alessandro R, Pazzaglia P. Multiple sclerosis with very late onset: report of six cases and review of the literature. Eur Neurol 1994;34:332–336.
37. Hawkins SA, McDonnell GV. Benign multiple sclerosis? Clinical course, long term follow-up, and assessment of prognostic factors. J Neurol Neurosurg Psychiatry 1999;67:148–152.
38. Bashir K, Whitaker JN. Clinical and laboratory feature of primary progressive and secondary progressive MS. Neurology 1999;53:765–771.
39. Lević ZM, Dujmović I, Pekmezović T, et al. Prognostic factors for survival in multiple sclerosis. Mult Scler 1999;5:171–178.
40. Confraveux C, Vukusic S, Moreau T, Adeleine P. Relapses and progression of disability in multiple sclerosis, N Engl J Med 2000;343:1430–1438.
41. Trojano M, Liguori M, Zimatore GB, et al. Age-related disability in multiple sclerosis. Ann Neurol 2002;51:475–480.

Face encoding and psychometric testing in healthy dextrals with right hemisphere language

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Abstract—*Objective:* To document how right hemisphere language dominance in neurologically normal right-handed individuals affects lateralization of face encoding and level of performance in neuropsychological tests. *Methods:* Three healthy right-handed adults with predominantly right hemisphere language activation during single-word or sentence-level processing were identified from 210 consecutive right-handed subjects studied using blood oxygenation level-dependent contrast fMRI. These three study subjects (S1 to S3) underwent a second scanning session where they performed word and face encoding. Their functional scans were contrasted with those obtained from six healthy control subjects (C1 to C6) with left hemisphere language dominance. Psychometric tests were performed on the study subjects. *Results:* Right hemisphere-dominant language activation was reproduced in the second scanning session in the three study subjects. The extent to which the lateralization of face encoding was reversed varied. Right hemisphere language was associated with lower (but within normal) verbal IQ compared with performance IQ in two of three volunteers. Verbal and nonverbal memory scores were normal and did not differ appreciably. *Conclusion:* Right hemisphere-dominant language in healthy dextrals exists but is rare. The extent to which face encoding is reversed in these individuals is variable. Cognitive function does not appear to be significantly compromised even though some psychometric test scores are asymmetric in favor of nonverbal performance when the reversal of lateralization of face and word memory is not complete.

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Left hemisphere dominance for language is a robust brain functional asymmetry. Ninety-one percent of dextrals in an intracarotid amobarbital-based study[1] and 94% in a large fMRI-based series[2] demonstrated left cerebral hemisphere dominance for language. Right hemisphere language dominance has been reported in normal individuals using a variety of techniques including visual half-field studies, dichotic listening,[3,4] transcranial Doppler (TCD) sonography,[5-7] and fMRI,[8-10] as well as in the setting of early neurologic disorders.[11] Several studies have reported a negative impact on verbal and nonverbal functions when language is right hemisphere dominant. For example, epileptic individuals in whom right hemisphere dominance for language arose as a result of surgical or destructive lesions of the left hemisphere showed improvement in language function over time, but this never recovered to normal.[12,13] Deleterious effects on visuospatial skills have been reported when language function lateralizes to the right hemisphere as a result of neurologic disease. This has been attributed to the "crowding" of cognitive functions.[14-16] In patient-based studies, the negative impact on cognitive functions reported in association with right hemisphere language may reflect the effects of reorganization rather than development under nonpathologic conditions. It is therefore of interest to investigate if cognitive functions in neurologically normal individuals are similarly affected in the setting of right hemisphere language dominance.

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How common is right hemisphere language in neurologically intact dextrals? The existence of crossed aphasia in which aphasia develops following right hemisphere stroke suggests that a small percentage (ranging from 1 to 13%) of apparently normal right-handed individuals have right hemisphere language dominance.[17] Although supporting the occurrence of right hemisphere language, these studies are limited in assessing its impact on cognition as the performance at study may be affected by the stroke. Visual half-field and dichotic listening studies of cerebral lateralization provide evidence for the lateralization of specialized functions, but the transcallosal transmission in normal subjects makes these techniques less than ideal for studying this issue.[3,4,18] A systematic evaluation of 326 healthy individuals using TCD sonography found that 4% of strongly right-handed individuals have right hemisphere language.[6] Further, in contrast to patients who are found to have right hemisphere language in the context of neurologic disease, these healthy individuals were reported to have preserved verbal and nonverbal cognitive functions. This might be a result of their having a mirrored representation of other lateralized brain functions such that "crowding" does not occur. Such reversal of hemispheric functional asymmetry for several higher cortical functions has been suggested by clinical–behavioral correlations,[19] but the functional anatomy and cognitive performance of such individuals prior to sustaining a neurologic deficit have not previously been documented.

In this communication, we evaluated three neurologically intact dextrals who were found to have right hemisphere language dominance. Using fMRI, we determined their cerebral lateralization of face memory encoding, a function that has been documented to involve the right frontal region. We sought to determine the extent to which functional cerebral asymmetries might be inverted in these apparently healthy individuals.[20,21] Our expectation was that if face memory encoding and language were lateralized to opposite hemispheres such that the usual lateralization of functions were reversed, normal psychometric test performances would be obtained. As a corollary, departure from such "mirrored representation" of cerebral functional asymmetry could be expected to result in some asymmetry of performance in verbal and nonverbal skills.

Materials and methods. *Identification of study individuals.* Three healthy individuals with no history of neurologic illness were identified as having right hemisphere-dominant language from 210 consecutive, neurologically normal, right-handed volunteers between 19 and 30 years of age. About 65% of these individuals were women. All 210 underwent fMRI employing different language tasks in the course of language-related brain-imaging studies.[22-25] The language tasks used in various experiments were cued word generation in two languages[25] (English and Mandarin), sentence comprehension in two languages,[23] a word classification task in English,[24] and a semantic association task.[22] Each individual performed only one type of language task.

Right hemisphere lateralization of language was discovered on inspecting serial axial sections of the brain in these various studies and finding a pattern of activation that mirrored the usual pattern of left hemisphere-dominant activation. The right hemisphere language dominance in the reported individuals was unequivocal, appearing as if the data had been laterally inverted. Formal lateralization of language asymmetry was not performed on the other 207 individuals except those involved in a previous study.[25]

Handedness was determined by adapting the Briggs and Nebe variant of the Edinburgh Handedness Questionnaire,[26] where a score of +24 indicates complete right-handedness and a score of −24 complete left-handedness. Two subjects with handedness scores of +19 and +9 were identified as having right hemisphere language during a sentence comprehension task, and the third, with a handedness score of +23, was identified during the evaluation of word semantic associations. One of the subjects had sinistral relatives. Two of the study subjects were undergraduates at the time of testing, and one was an executive secretary. All three were women aged between 20 and 25 years.

Second standardized fMRI study. The three study subjects (S1 to S3) were re-evaluated with a second standardized fMRI study involving face and word encoding to ensure that the right hemisphere lateralization for language was reproducible. The lateralization of face memory was also examined.

A "face- and word-encoding" task was selected because right hemisphere dominance for face encoding has been verified by fMRI,[27] by intracarotid amobarbital testing,[21] and by examining patients with frontal lobe lesions.[28]

The face-encoding task used a block design in which faces and word blocks alternated. Unfamiliar faces (with hair masked out) were shown for 2 seconds every 2.5 seconds. Both sexes and persons from different age groups and races were represented in the 72 nonfamous faces used for the experiment. The word-encoding task involved the presentation of single concrete words that were displayed for 2 seconds every 2.5 seconds. Interleaved between blocks of faces (and words) were 25-second intervals during which the volunteers were told to fixate on a cross. Volunteers were instructed to remember the presented faces for a subsequent test. To facilitate remembering, they were asked to determine if the faces were happy or not (the faces were all emotionally neutral). In the word-encoding task, similar instructions to remember the presented words for subsequent testing were given. In addition, an instruction to make a semantic judgment (living/nonliving) was added to facilitate encoding.[29] Face encoding has previously been shown to preferentially activate the right prefrontal region and word encoding the left prefrontal region.[27]

To verify that the laterality of activation in our study population was atypical, we compared six neurologically normal dextrals (C1 to C6), five women and one man, of comparable age (range 20 to 24 years) and education to the study subjects. They had handedness scores ranging from +14 to +24. All six were undergraduates at a local university with above-average scholastic performance.

Table 1 *Laterality indexes in control (C1–C6) and study (S1–S3) volunteers*

	Word/sentence judgment		Face encoding	Word encoding	
Subject	Frontal	Temporal	Frontal	Frontal	Temporal
S1	−0.77	−1.00	0.44	−0.96	−1.00
S2	−0.37	−1.00	0.08	−1.00	NA
S3	−0.80	−1.00	0.05	−0.70	−0.99
C1	ND	ND	−0.42	1.00	NA
C2	ND	ND	−0.62	0.95	NA
C3	ND	ND	−0.40	0.63	NA
C4	ND	ND	−1.00	1.00	1.00
C5	ND	ND	−0.03	1.00	NA
C6	ND	ND	−0.76	1.00	1.00

The laterality index was calculated by summing voxels in each prefrontal and lateral region above the threshold correlation coefficient of 0.4 and using the formula ($[L - R]/[L + R]$). The range of values is from −1 to +1; the former represents complete right hemisphere dominance and the latter complete left hemisphere dominance.

ND = data not collected; NA = absence of activation in region of interest.

Imaging and image analysis. fMRI was performed in a 2.0 T scanner (Bruker, Karlsruhe, Germany). Visual stimuli were presented using an MR-compatible fiberoptic system (Avotec, Jansen Beach, FL). Functional images were acquired using a gradient-echo echo-planar imaging sequence with a repetition time of 2 seconds and an effective echo time of 40 milliseconds. Fifteen oblique axial slices parallel to the intercommissural plane were obtained. Image processing was performed with Brain Voyager 2000 (version 4.4; Brain Innovation B.V., Maastricht, The Netherlands) using previously described methods.[22] Statistical maps for individual participants were created using a correlation coefficient threshold of 0.4.[30] The use of more conservative thresholds can give the appearance of stronger functional asymmetry, although this effect is modest.[9]

Right hemisphere dominance for language was formally quantified by two measures. The first involved computing an fMRI-based laterality index[30] obtained by counting voxels activated above threshold in the frontal and lateral temporal regions (table 1), and the second involved a region of interest (ROI)-based analysis of signal change in each frontal region.[31]

The frontal region included in the determination of the laterality index lay within the inferior and middle frontal gyri corresponding approximately to Brodmann areas 44/45 and 9. In the temporal region, the volume of interest lay in the posterior third of the superior and middle temporal gyri corresponding to Brodmann areas 21 and 22. The laterality index was defined as ($[L - R]/[L + R]$), where L and R denote voxel counts above threshold in each of the ROI. We note that previous work has shown better correlation of fMRI-based language laterality and Wada testing when the frontal activation (relative to temporal activation) was assessed.[32]

The specific methodology to determine signal change in the frontal region involved determining the percentage signal change in the ROI and has been previously described.[31] The percentage signal change associated with face and word encoding was displayed in a manner consistent with the original work reporting the functional asymmetry related to word and face encoding.[27]

Neuropsychological testing. Each of the three right hemisphere-dominant individuals then underwent neuropsychological testing by a neuropsychologist. This was performed using several tests including the Wechsler Adult Intelligence Scale–Revised,[33] which measured verbal (verbal IQ [VIQ]) and nonverbal (performance IQ [PIQ]) cognitive function, the Warrington Recognition Memory Test for words and faces,[34] the Rey–Osterrieth Complex Figure-Copying Test, and the Wechsler Memory Scale–Revised[35] test of memory. The test composition followed tests used in a previous work documenting cognitive performance in individuals with temporal lobe epilepsy who were right hemisphere dominant for language.[16] The tests were performed in one sitting in a quiet room with adequate rest intervals between subtests.

All three volunteers use English in daily life so that vocabulary and sociocultural confounds in administering this test to the study subjects were not significant. The possible exception to this point is that S2's educational background may have had a minor negative effect on verbal test scores. In general, the administered tests are used routinely in the local English-speaking clinical population with results comparable to those obtained in published normative data.

Results. *Imaging findings.* In the experiments that detected individuals in the study group, predominantly right frontal, posterotemporal, and parietal activation was present in all three study subjects while judging semantic associations (two subjects; see table 1 and figure 1A) or sentence comprehension (one subject). Right hemisphere language dominance was reflected in the laterality indexes showing negative values for language (see table 1). The difference in the lateralization index between study and control subjects was significant.

In the face- and word-encoding experiment, control subjects showed predominantly left prefrontal activation with word encoding and predominantly right frontal activation during face encoding (figure 2). This was true whether or not voxel-counting or percentage signal change analysis

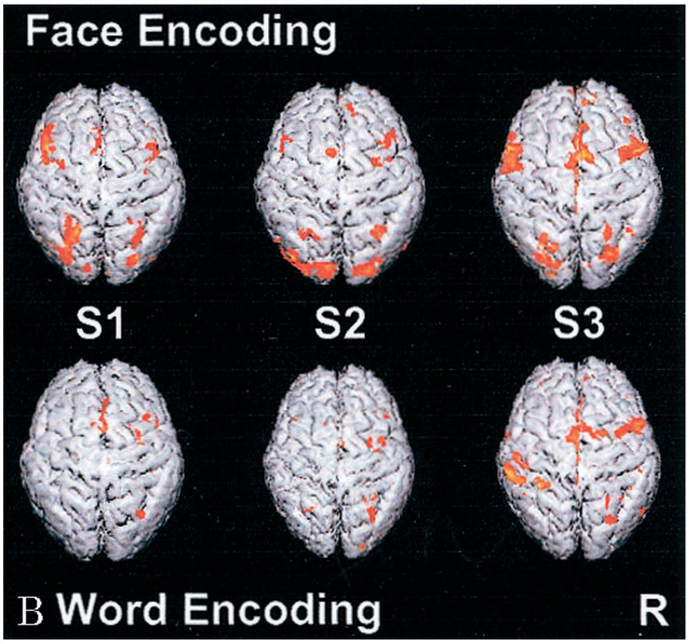

Figure 1. (A) Superior view of volume-rendered brain images shows activation associated with performance of language tasks in the three study subjects (S1 to S3). S1 performed a semantic judgment task. S2 and S3 performed a sentence judgment task. The brains are oriented such that the anterior-facing portion of the brain is anterior. (B) Activation associated with face and word encoding in the three study subjects (S1 to S3).

was used (figure 3). All three study subjects with right hemisphere language dominance showed greater right hemisphere activation during word encoding (see table 1 and figures 1B and 3), reproducing the finding of right hemisphere dominance for language processing obtained in prior experiments. The differences in laterality indexes for face and word encoding between test subjects and control subjects were significant ($t[7] = 2.68$, $p < 0.05$ for face encoding; $t[7] = 16.8$, $p < 0.0001$ for word encoding). Lowering the significance threshold of detection of activation led to a secondary display of left frontal activation for word encoding in the three study subjects, but this did not alter the right hemisphere-biased asymmetry of activation for words. Subject S1 activated predominantly the left frontal

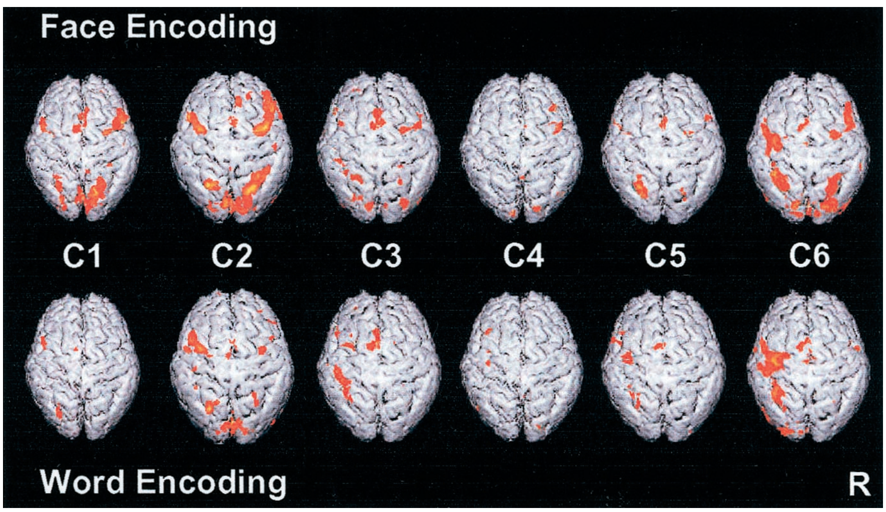

Figure 2. Activation associated with face and word encoding in the six age-matched, right-handed control subjects (C1 to C6).

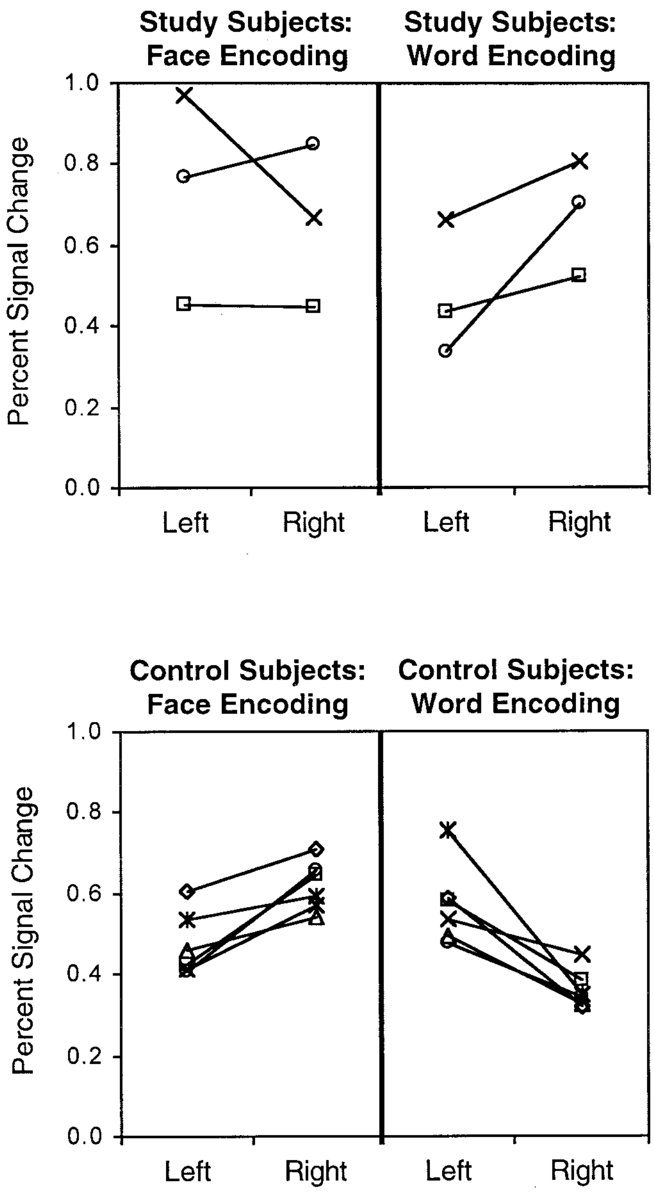

Figure 3. Percentage signal change graphs obtained from frontal regions of interest showing relative asymmetry of brain activation during word and face encoding in three study subjects (S1 to S3; top) and six control subjects (C1 to C6; bottom). Top: X = S1; -□- = S2; —○— = S3; Bottom: X = C1; -□- = C2; —○— = C3; —△— = C4; —◇— = C5; ✳ = C6.

region during face encoding. Subjects S2 and S3 showed bilateral activation for face encoding.

Neuropsychological data. PIQ was in the normal range in the study subjects. The difference between VIQ and PIQ was >1 SD (determined from historical normative data) in S2 and S3. However, these individual's VIQ scores were within 1 SD of the VIQ index score of 100 in all three individuals (table 2). The relative difference in VIQ and PIQ was least in the individual with left hemisphere-predominant activation for face encoding (S1). A lower VIQ score for S2 may have been contributed by limitations with vocabulary, given that she was the only nonundergraduate in the study and control groups. The Warrington Word Memory and Wechsler Verbal Memory scores in WMS-R

Table 2 *Study subject characteristics and neuropsychological test scores*

Study subject characteristics and test scores	S1	S2	S3
Age, y	23	25	24
Sex	F	F	F
Education	College	High school	College
Handedness score	+23	+9	+19
Verbal IQ	103	90*	104*
Performance IQ	114	108	129
Full-scale IQ	107	97	116
Block design	10†	15†	19†
Digit symbol	15†	14†	16†
Word memory (Warrington)	49/50 (~90)	48/50 (~90)	48/50 (~90)
Face memory (Warrington)	44/50 (62)	42/50 (50)	45/50 (68)
Immediate recall (VRI)	37/41 (76)	40/41 (96)	40/41 (96)
Delayed recall (VRII)	38/41 (86)	40/41 (99)	40/41 (99)
Logical memory I (immediate)	30/50 (73)	26/50 (50)	29/50 (60)
Logical memory II (delayed)	28/50 (57)	24/50 (57)	28/50 (75)
Verbal memory index	109	98	102
Visual memory index	120	113	101
Rey–Osterrieth figure	34†	26†	27†

IQ and memory index scores are quotient scores. Values in parentheses are percentile scores. Subcomponents of the WMS-R for visual (VRI, VRII) and verbal (logical memory I and II) are reported.

* Significant differences between verbal and performance IQ scores.

† Scaled scores.

subtests for the three study subjects were normal. None of the study subjects appeared to have problems with verbal communication in the course of their work or academic activities.

The Warrington Face Memory Test scores shown in table 2 are raw and percentile scores. The raw scores of 44, 42, and 46 (of 50) for S1, S2, and S3 in that order were quite closely clustered. We interpret these scores as being within normal.

The PIQ scores together with normal scores in the Rey–Osterrieth complex figure reproduction task (recall phase) lend further support to the notion that nonverbal skills were intact in all the study subjects.

Discussion. Lateralization of language function for surgical decision making has been traditionally been performed using intracarotid amobarbital (Wada) testing. However, in recent years, fMRI-based lateralization of language function has been shown to produce results in good agreement with those obtained with intracarotid amobarbital testing[30,32,36-38] and electrical stimulation.[37,39] Most fMRI-based studies determined language lateralization on the basis of frontal cortical activation, and two studies have further suggested restricting this to the inferior frontal gyrus.[9,32] Right hemisphere-dominant language in right-handers is rare and has, to date, been reported in 5 of 50 neurologically normal sinistrals[40] and in 3 of 50 epileptic patients.[2] Neither of these studies detected right hemisphere language in healthy dextrals. There have, to date, been only three cases of right hemisphere language in dextrals using fMRI,[8,10,41] two of whom were patients. As it is not ethical to confirm the right hemisphere dominance of language in healthy volunteers with either intracarotid amobarbital testing or electrical stimulation, assurance that the language lateralization obtained from fMRI in the current report was not a spurious finding was obtained by replicating the right hemisphere-dominant language using a second standardized word-encoding task. Replication of evidence of right hemisphere language function in the individual volunteers is important because different tasks reveal somewhat different extents of language lateralization.[9]

Functional TCD (fTCD) sonography has revealed functional lateralization of language that corresponds closely with results reported with intracarotid amobarbital testing.[42] Much valuable information regarding the relationship between handedness, cerebral functional asymmetry, and psychometric performance has been gleaned from studying normal individuals. FTCD sonography has shown a higher frequency of right hemisphere dominance (about 10%) for language[6] than intracarotid amobarbital, fMRI, or crossed aphasia data would suggest. One contribution of the current report lies in that it provides an independent source of information supporting the inferences drawn from fTCD studies.

This report demonstrates the notion that the cognitive impact of right hemisphere language in healthy individuals may differ from that of individuals with neurologic disorders. This notion is supported by the absence of significant differences in mastery of foreign languages, artistic talent, or verbal fluency when healthy individuals with left, bilateral, and right hemisphere language representation (as defined by TCD sonography) were compared.[7] Notably, in a subset analysis of the same cohort of individuals, four persons were subsequently found to have right hemisphere-dominant language and spatial attention.[43] As opposed to what would be expected from the "crowding hypothesis,"[14] these healthy individuals were found to have average to superior verbal and nonverbal abilities.

On the other hand, the large difference in VIQ and PIQ that was seen in two individuals in whom word encoding and face encoding were not as extensively reversed as in the remaining individual could be interpreted as weak support for the crowding hypothesis. While noting this, we believe it inappropriate to draw firm conclusions until more cases are studied. Certainly, in relative terms, two study subjects had considerably higher PIQ than VIQ. However, in absolute terms, both VIQ and verbal memory scores were within normal. Although some may take issue with our conservative interpretation of the psychometric score asymmetries, we justify our interpretation of the data by erring on the side of caution, given the limited sample size and noting that functionally all the study individuals are unimpaired (one of the individuals is now an engineer, the second a professional secretary, and the third a lawyer). One contrast of clinical interest is the point that, if anything, right hemisphere language in apparently normal dextrals does not negatively affect nonlanguage performance, whereas right hemisphere language in individuals with temporal lobe epilepsy appears to do so.[16]

The observation that language and face memory encoding was mirrored in one individual but not in two others is consistent with the suggestion that in individuals with right hemisphere language, functional cerebral asymmetries may segregate independently rather than be simply reversed. Work on signals for left–right patterning suggests that different signals control the expression of asymmetry and the specific pattern of lateralization of particular structures, although the specific manner in which asymmetric cerebral functions are determined is currently unknown.[44] It has been proposed that right-handedness and left cerebral dominance of language occur if an individual receives a particular gene. Failure to receive this gene is proposed to lead to a randomized lateralization of components of language processing (such as a dissociation of semantic and phonologic aspects of word processing) and limb praxis.[17,45] Our observations suggest that randomization of functional lateralization could also occur for nonlinguistic task processing (such as face processing), but, clearly, more cases are required before meaningful conclusions can be drawn.

In this report, all three persons with right hemisphere language were women. Numerous reports suggest that women, on average, have slightly better verbal skills than men. Earlier functional neuroimaging studies reported more left-lateralized frontal lobe activation in men than in women performing a visual phonologic task[46] and a semantic processing task.[47] However, subsequent imaging studies have not replicated sex differences in cerebral lateralization for language.[48,49] Further, an earlier report where fMRI was utilized to document right hemisphere language in a healthy dextral involved a male volunteer.[10]

In conclusion, varying degrees of lateralization of face memory were found in association with right hemisphere language. Nonverbal cognitive function in these individuals is not impaired. While verbal memory was normal and verbal skills were not functionally impaired, an impressive asymmetry in verbal and performance IQ scores when face and word memory lateralization are not completely reversed merits further investigation in a larger study.

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References

1. Loring DW, Meador KJ, Lee GP, et al. Cerebral language lateralization: evidence from intracarotid amobarbital testing. Neuropsychologia 1990;28:831–838.
2. Springer JA, Binder JR, Hammeke TA, et al. Language dominance in neurologically normal and epilepsy subjects: a functional MRI study. Brain 1999;122:2033–2046.
3. Bryden MP, McManus IC, Bulman–Fleming MB. Evaluating the empirical support for the Geschwind–Behan–Galaburda model of cerebral lateralization. Brain Cogn 1994;26:103–167.
4. Hugdahl K. Lateralization of cognitive processes in the brain. Acta Psychol (Amst) 2000;105:211–235.
5. Knecht S, Deppe M, Drager B, et al. Language lateralization in healthy right-handers. Brain 2000;123:74–81.
6. Knecht S, Drager B, Deppe M, et al. Handedness and hemispheric language dominance in healthy humans. Brain 2000; 123:2512–2518.
7. Knecht S, Drager B, Floel A, et al. Behavioural relevance of atypical language lateralization in healthy subjects. Brain 2001;124:1657–1665.
8. Spreer J, Quiske A, Altenmuller DM, et al. Unsuspected atypical hemispheric dominance for language as determined by fMRI. Epilepsia 2001;42:957–959.
9. Hund-Georgiadis M, Lex U, von Cramon DY. Language dominance assessment by means of fMRI: contributions from task design, performance, and stimulus modality. J Magn Res Imag 2001;13:668–675.
10. Chee MW, Buckner RL, Savoy RL. Right hemisphere language in a neurologically normal dextral: a fMRI study. Neuroreport 1998;9:3499–3502.
11. Rasmussen T, Milner B. The role of early left-brain injury in determining lateralization of cerebral speech functions. Ann NY Acad Sci 1977;299:355–369.
12. Woods RP, Dodrill CB, Ojemann GA. Brain injury, handedness, and speech lateralization in a series of amobarbital studies. Ann Neurol 1988;23:510–518.
13. Woods BT, Carey S. Language deficits after apparent clinical recovery from childhood aphasia. Ann Neurol 1979;6:405–409.
14. Teuber HL. Why two brains? In: Schmitt FO, Worden FG, eds. The neurosciences. Third study program. Cambridge, MA: MIT Press, 1974:71–74.
15. 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.
16. Loring DW, Strauss E, Hermann BP, et al. Effects of anomalous language representation on neuropsychological performance in temporal lobe epilepsy. Neurology 1999;53:260–264.
17. Alexander MP, Annett M. Crossed aphasia and related anomalies of cerebral organization: case reports and a genetic hypothesis. Brain Lang 1996;55:213–239.
18. Bryden MP, Bulman-Fleming MB. Laterality effects in normal subjects: evidence for interhemispheric interactions. Behav Brain Res 1994;64:119–129.
19. Fischer RS, Alexander MP, Gabriel C, Gould E, Milione J. Reversed lateralization of cognitive functions in right handers. Exceptions to classical aphasiology. Brain 1991;114:245–261.
20. McDermott KB, Buckner RL, Petersen SE, Kelley WM, Sanders AL. Set- and code-specific activation in frontal cortex: an fMRI study of encoding and retrieval of faces and words. J Cogn Neurosci 1999;11:631–640.
21. Kelley WM, Ojemann JG, Wetzel RD, et al. Wada testing reveals frontal lateralization for the memorization of words and faces. J Cogn Neurosci 2002;14:116–125.
22. Chee MW, Weekes B, Lee KM, et al. Overlap and dissociation of semantic processing of Chinese characters, English words, and pictures: evidence from fMRI. Neuroimage 2000;12:392–403.
23. Chee MW, Caplan D, Soon CS, et al. Processing of visually presented sentences in Mandarin and English studied with fMRI. Neuron 1999;23:127–137.
24. Chee MW, Sriram N, Soon CS, Lee KM. Dorsolateral prefrontal cortex and the implicit association of concepts and attributes. Neuroreport 2000;11:135–140.
25. Chee MW, Tan EW, Thiel T. Mandarin and English single word processing studied with functional magnetic resonance imaging. J Neurosci 1999;19:3050–3056.
26. Briggs GG, Nebes RD. Patterns of hand preference in a student population. Cortex 1975;11:230–238.
27. Kelley WM, Miezin FM, McDermott KB, et al. Hemispheric specialization in human dorsal frontal cortex and medial temporal lobe for verbal and nonverbal memory encoding. Neuron 1998;20:927–936.
28. Rapcsak SZ, Nielsen L, Littrell LD, et al. Face memory impairments in patients with frontal lobe damage. Neurology 2001;57:1168–1175.
29. Logan JM, Sanders AL, Snyder AZ, Morris JC, Buckner RL. Under-recruitment and nonselective recruitment: dissociable neural mechanisms associated with aging. Neuron 2002;33: 827–840.
30. Binder JR, Swanson SJ, Hammeke TA, et al. Determination of language dominance using functional MRI: a comparison with the WADA test. Neurology 1996;46:978–984.
31. Chee MW, Hon NH, Caplan D, Lee HL, Goh J. Frequency of concrete words modulates prefrontal activation during semantic judgments. Neuroimage 2002;16:259–268.
32. Lehericy S, Cohen L, Bazin B, et al. Functional MR evaluation of temporal and frontal language dominance compared with the Wada test. Neurology 2000;54:1625–1633.
33. Wechsler D. Wechsler Adult Intelligence Scale-Revised manual. New York: Psychological Corporation, 1981.
34. Warrington EK. Recognition Memory Test. Windsor: NFER-Nelson, 1984.
35. Wechsler D. Wechsler Memory Scale–Revised manual. San Antonio: Psychological Corporation, 1987.
36. Desmond JE, Sum JM, Wagner AD, et al. Functional MRI measurement of language lateralization in Wada-tested patients. Brain 1995;118:1411–1419.
37. FitzGerald DB, Cosgrove GR, Ronner S, et al. Location of language in the cortex: a comparison between functional MR imaging and electrocortical stimulation. AJNR Am J Neuroradiol 1997;18:1529–1539.
38. Benson RR, FitzGerald DB, LeSueur LL, et al. Language dominance determined by whole brain functional MRI in patients with brain lesions. Neurology 1999;52:798–809.
39. Rutten GJ, van Rijen PC, van Veelen CW, Ramsey NF. Language area localization with three-dimensional functional magnetic resonance imaging matches intrasulcal electrostimulation in Broca's area. Ann Neurol 1999;46:405–408.
40. Pujol J, Deus J, Losilla JM, Capdevila A. Cerebral lateralization of language in normal left-handed people studied by functional MRI. Neurology 1999;52:1038–1043.
41. Hund-Georgiadis M, Zysset S, Weih K, Guthke T, von Cramon DY. Crossed nonaphasia in a dextral with left hemispheric lesions: a functional magnetic resonance imaging study of mirrored brain organization. Stroke 2001;32:2703–2707.
42. Deppe M, Knecht S, Papke K, et al. Assessment of hemispheric language lateralization: a comparison between fMRI and fTCD. J Cereb Blood Flow Metab 2000;20:263–268.
43. Floel A, Knecht S, Lohmann H, et al. Language and spatial attention can lateralize to the same hemisphere in healthy humans. Neurology 2001;57:1018–1024.
44. Yost HJ. Left–right development from embryos to brains. Dev Genet 1998;23:159–163.
45. Annett M. Handedness and cerebral dominance: the right shift theory. J Neuropsychiatry Clin Neurosci 1998;10:459–469.
46. Shaywitz BA, Shaywitz SE, Pugh KR, et al. Sex differences in the functional organization of the brain for language. Nature 1995;373:607–609.
47. Shaywitz BA, Pugh KR, Constable T. Location of semantic processing using functional magnetic resonance imaging. Hum Brain Map 1995;2:149–158.
48. Buckner RL, Raichle ME, Petersen SE. Dissociation of human prefrontal cortical areas across different speech production tasks and gender groups. J Neurophysiol 1995;74:2163–2173.
49. Frost JA, Binder JR, Springer JA, et al. Language processing is strongly left lateralized in both sexes. Evidence from functional MRI. Brain 1999;122:199–208.