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Factors predicting language lateralization in patients with perisylvian vascular malformations

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Abstract

Object—The authors conducted a study to determine the factors associated with right-sided language dominance in patients with cerebrovascular malformations.

Methods—Twenty-two patients with either arteriovenous malformations (AVMs [15 cases]) or cavernous malformations (7 cases) underwent functional MR (fMR) imaging studies of language function; a 3.0-T head-only unit was used. Lateralization indices were calculated separately for Broca and Wernicke areas. Lesion size, Spetzler-Martin grade, and the distance between the lesion and anatomically defined language cortex were calculated for each patient.

Results—Right-sided language dominance occurred in 5 patients, all of whom had AVMs within 10 mm of canonical language areas. Three patients had right-sided language dominance in the Wernicke area alone whereas 2 had right-sided language dominance in both Broca and Wernicke areas. Wada testing and intraoperative electrocortical stimulation were performed as clinically indicated to corroborate fMR imaging findings.

Conclusions—The primary factor associated with right-sided language dominance was the AVM being within 10 mm of anatomically defined language areas. The lesion size and the Spetzler-Martin grade were not significant factors. Anomalous fMR imaging laterality was typically confined to the language area proximate to the lesion, with the distal language area remaining in the left hemisphere dominant. This study emphasizes the need to map each case individually in patients with left perisylvian AVMs. Assumptions about eloquent cortex based on anatomical landmarks (a key component of Spetzler-Martin grading) may have to be reconsidered.

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Disclosure
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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Keywords

cerebrovascular malformation; functional magnetic resonance imaging; language cortex lateralization

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Left hemispheric language dominance has been reported in 95% of right-handed[28] and approximately 75% of left-handed individuals.[9,21] Intracranial pathology, however, may significantly alter both inter- and intrahemispheric language representations. Language reorganization can occur in the setting of various pathological entities including medial temporal lobe epilepsy and other early-onset brain lesions.[1,3,4,8,12] Arteriovenous malformations have also been associated with both intra-[15] and interhemispheric language reorganization.[18,27] Given the well-documented possibility of anomalous language organization in patients with intracranial pathology, the optimal management of patients with cerebrovascular malformations, such as AVMs and CMs, in or near canonical language areas should incorporate preoperative language mapping.

Clinically available techniques for preoperative language mapping include fMR imaging, MEG, and intraarterial Amytal injection (Wada test). The noninvasive nature of fMR imaging and MEG make these modalities preferable for preoperative patient evaluation. In patients with vascular malformations, fMR imaging offers topographic maps of language function with very high sensitivity and acceptable specificity.[5,14,24] Although MEG is noninvasive like fMR imaging, it cannot provide topographic maps like fMR imaging (without applying sophisticated interpolation algorithms based on numerous assumptions) and may produce mapping errors if multiple areas of the brain are concurrently active.[10,17] Although Wada testing has long been considered the gold standard for preoperative assessment of language dominance, it is invasive and does not provide the topographic specificity offered by fMR imaging.[3] Given these constraints, fMR imaging, with corroborating evidence from Wada testing, intraoperative ESM, and clinical outcomes, likely offers the best opportunity to study language distribution and organization in patients with vascular malformations.

Although language lateralization and dominance in patients with vascular malformations has been previously studied, prior reports have focused on global laterality indices as a measure of language dominance.[18,27] However, the reports indicated that Broca and Wernicke areas can be asymmetrically lateralized in the setting of intracranial pathological entities.[27] Moreover, little is known about lesion characteristics that may help predict atypical lateralization.

In this study, we used fMR imaging of language function to evaluate language dominance in 22 patients with cerebrovascular malformations. In each case, laterality indices were calculated separately for Broca and Wernicke areas. We evaluated the effects of lesion size and location, as well as Spetzler-Martin AVM grade, on language lateralization.

Methods

Patient Population

We investigated 22 patients with cerebrovascular malformations (14 female and 8 male patients; mean age 35 ± 13 years) who underwent presurgical fMR imaging between 1999 and 2006. Fifteen patients had AVMs and 7 had CMs. Twenty-one patients had left hemispheric lesions, 18 of whom were right handed. One patient had a right hemispheric lesion and was left handed. Of the 15 patients with an AVM, all underwent preoperative angiography, 6 underwent Wada testing prior to fMR imaging, and 4 underwent ESM language confirmation; of the 7 patients with a CM, 1 underwent preoperative angiography, 2 Wada testing, and 2 ESM language confirmation. In all patients, initial presentation included seizures, hemorrhages, migraines, syncope, diplopia, hemiparesis, paresthesias, photophobia, and/or visual field deficits.

Intraarterial Amytal Injection (Wada Test) and Angiographic Assessment

Wada testing was indicated in 6 patients with AVMs and 2 patients with CMs. Hemispheric, selective, and/or superselective Amytal injections were performed in the presence of a neurologist, neuropsychologist, and neuroradiologist. In each case, 125 mg amobarbital was injected into the left internal carotid artery; language and memory tests were conducted over 4 minutes and rated for language dominance of expression and comprehension.

Magnetic Resonance Imaging

Blood oxygen level–dependent fMR imaging was performed on a 3.0-T head-only unit (Siemens Allegra). Multislice echo planar imaging was used with a gradient echo planar imaging sequence (TR 2500 msec, TE 35 msec, flip angle 90°, 64 × 64 pixels, field of view 20 × 20 cm). The in-plane resolution was 3.1 mm with a slice thickness of 3.0 mm. We acquired up to 4 sets of 96 whole-volume images while the patient performed 4 different language tasks. These tasks included an auditory responsive naming task, a reading comprehension task, a covert object naming with generation task, and a word generation task. During the auditory responsive naming task, the patient listened to a 3-word verbal description of a concrete noun and silently generated the names. For the reading comprehension task, the patient read descriptions of words and generated the names of these words. The covert object naming with generation task required the patients to view objects and generate their names and appropriate actions. The word generation task involved generating a list of words that either started with a specific letter or were included in a particular category. Each task was presented in a blocked design with 4 activation blocks interspersed with 4 rest-fixation blocks each lasting 30 seconds (4 minutes per task total). This protocol was approved by the UCLA Office for Protection of Human Subjects internal review board (no. 92–12–069).

Magnetic Resonance Imaging Analysis

Images were reconstructed in real time and analyzed for motion. Scans with evidence of excessive head motion were rejected and studies were repeated. Individual maps of fMR imaging activation were obtained by convolving the block paradigm with a model of the hemodynamic response function,[7] generating a Pearson correlation coefficient between this model and the MR imaging signal intensity at each voxel. Expression and comprehension maps were generated using a conjunction analysis for assessment of Broca and Wernicke areas, as previously described.[19] Briefly, maps were generated by identifying all voxels that exceeded a predetermined significance threshold ($p < 0.05$) and overlaying these "active" voxels on a anatomical T2-weighted MR image.[19]

Language cortex organization was studied in the inferior frontal (Broca) and superior temporal (Wernicke) areas separately. Because physiological language cortex is variable throughout the normal population, anatomical landmarks were used to define 2 geographic language cortices. The Broca area was defined as the posterior inferior frontal gyrus, including the pars triangularis and pars opercularis. The Wernicke area incorporated a broader region, including the posterior temporal-parietal region from the middle temporal gyrus through the temporalparietal junction posterior to the transverse temporal gyrus.[2] The angular gyrus was excluded from this measurement because it is not activated consistently across all language tasks.

The lateralization index was used to quantify the degree of language lateralization and dominance. It was calculated for each language region of interest (Broca and Wernicke) separately using the following formula: $LI = (V_L - V_R) / (V_L + V_R)$, where V_L denotes the number of voxels activated in the left hemisphere and V_R denotes the number of voxels activated in the right hemisphere. Although language dominance lies along a spectrum, for the purposes of discussion and analysis, language activation patterns were categorized into 1 of 3 patterns. An LI less than or equal to −0.2 is designated as right-sided dominance, whereas an LI greater than or equal to 0.2 signifies left-sided dominance (corresponding to 22% more voxels activated on one side than the other). An LI between −0.2 and 0.2 suggested no clear hemispheric preference.

An LI less than or equal to −0.2 could be due to either one of the following: 1) a shift in activation from left to right (that is, language reorganization), or 2) an artifactual decrease in observed left-sided fMR imaging without a concomitant increase in right hemisphere activation. To differentiate these scenarios, we compared the total number of voxels activated in the whole brain and right hemispheres of left-dominant and right-dominant patients. If the maps represented true reorganization, one would expect the total number of activated voxels to be equivalent in the 2 groups and the right hemisphere–dominant patients to have a greater number of activated voxels in the right hemisphere than the left hemisphere–dominant patients. Conversely, if an LI less than or equal to −0.2 (right-sided dominance) is artifactual, one would expect that the total number of activated voxels in patients deemed to be right-hemisphere dominant would be less than the other patients and that the total number of right hemisphere–activated voxels would be equivalent in the 2 groups.

Lesion size, distance from eloquent cortex, and Spetzler-Martin grade were determined from angiographic and/or MR imaging studies.[25] Lesion size was defined by the greatest diameter of the vascular malformation. The location of the lesion was measured as the shortest distance from the proximate edge of the cerebrovascular nidus to the proximate edge of the anatomically defined language region. When a vascular malformation was adjacent to both

Broca and Wernicke areas, the malformation was considered to be adjacent to the language area with the shortest measured distance.

Treatment

Of 15 patients with AVMs, 11 underwent craniotomy and resection, 3 were treated with radiosurgery, and 1 underwent conservative therapy. Of the 7 patients with CMs, all underwent surgery.

Electrocortical Stimulation Mapping

Intraoperative functional mapping using electrocortical stimulation was performed in 6 patients based on prior studies indicating the proximity of the language cortex map to the lesion.[5] Anesthesia for craniotomy was administered using an asleep-awake-asleep protocol.[11] We performed ESM of language function using a bipolar electrode and Grass instruments stimulator. Five- to 7-second trains of stimulation were administered, beginning at 4 mA (50-Hz stimulation with 50-µsec pulse width) and increasing by 2-mA increments until a maximum of 16 mA was reached. Each stimulation was paired with continuous intracranial electrocorticography to monitor afterdischarge activity.[20]

Results

Five patients (23%) had right-sided language dominance in the Wernicke area or in both Wernicke and Broca areas. Only 1 of these patients was left handed.

Analysis of Overall Activation Patterns

Of the 5 patients with right-sided language dominance, 3 had right-sided dominance of both Broca and Wernicke areas and 2 had right-sided dominance of only Wernicke area. Patient details and LIs are detailed in Table 1. The total number of activated voxels in the entire brain of patients with left dominance was equivalent to that seen in patients with right dominance (127.0 vs 125.2 voxels, $p = 0.97$, 2-tailed t-test) and the number of activated voxels in the right hemisphere of right-dominant patients was equivalent to the number of activated voxels in the left hemisphere of left-dominant patients (73.0 vs 96.4 voxels, $p = 0.25$, 2-tailed t-test). Moreover, the number of right hemisphere–activated voxels was significantly greater in the right-dominant patients than in left-dominant patients (73.0 vs 30.6 voxels, $p = 0.02$, 2-tailed t-test). Similar analyses were conducted in the Wernicke area. The total number of activated voxels bilaterally in the Wernicke area was not significantly different in patients with left- and right-hemisphere dominance (51.8 vs 62.4 voxels, $p = 0.64$, 2-tailed t-test). However, patients with right dominance–activated voxels had significantly more voxels in right-sided the Wernicke area than left-dominant patients (44.0 vs 13.0 voxels, $p = 0.01$, 2-tailed t-test). Meaningful comparisons could not be made in Broca area because only 2 patients exhibited rightsided dominance of the Broca area.

Factors Affecting Dominance

The data were interrogated to identify factors that correlated with right-sided dominance, including pathology type, size of malformation, the closest language area, and the distance from language areas. Although all 5 patients with right-sided dominance had AVMs and no patients with CM had right-sided dominance, the type of malformation was not significantly associated with rightsided dominance ($p = 0.13$, Fisher exact test). The lack of significance is likely attributable to the small sample size considering all patients with right dominance had AVMs. No particular symptoms or chief complaints were unique to patients with nonleft dominance. The only significant factor was distance from language cortices: the lesions in the 5 patients with right dominance were on average 2.6 ± 2.6 mm from language cortices whereas in those with left dominance the lesion was 19.2 ± 20.6 mm from language cortices ($p = 0.0046$, 2-tailed t-test). Subanalysis of patients with AVMs revealed similar results. Spetzler-Martin grade, nidus size, and the closest language area were not correlated with right-sided dominance (Fig. 1). Distance from language areas, however, remained significantly different between those with right-sided and left-sided dominance (1.8 ± 2.1 vs 17.5 ± 11.5 mm, respectively, $p = 0.002$, 2-tailed t-test) (Fig. 2). Subanalysis of patients with CMs was not possible as all patients had left-sided dominance.

To better characterize patterns of brain activity and organization we divided individuals into 3 groups based on the lesion type and its distance from functional cortex.

Group 1 included patients with AVMs within 10 mm of anatomically defined language cortex (8 cases). Figure 3 upper schematically illustrates the approximate location of the AVMs relative to Broca and Wernicke areas in the subset of Group 1 patients with right-sided language dominance. All patients with right-sided language dominance in this study were contained in this group, corresponding to 63% of all Group 1 patients. Three of these patients (Cases 1–3) had AVMs adjacent to the Wernicke area and had right dominance exclusively of Wernicke area (LI = −0.46 ± 0.26). The other 2 patients (Cases 4 and 5, with lesions adjacent to Broca area and Wernicke area, respectively) had right dominance of both Broca area (LI = −0.73 ± 0.12) and Wernicke area (LI = −0.50 ± 0.14). Figure 4 shows the fMR imaging representation of anomalous language cortex dominance in Cases 1, 2, 4, and 5. The remaining 3 patients had left-sided language dominance, as detailed in Table 1.

Group 2 included 7 patients with AVMs greater than 10 mm from anatomically defined language cortex. Two patients (Cases 10 and 15) had lesions near the Broca area, whereas 5 (Cases 9 and 11–14) had lesions adjacent to the Wernicke area. The location of the AVMs in all patients with left-sided language dominance is represented in Fig. 3 lower. All of these patients had left dominance of both Broca area and Wernicke area (LI = 0.73 ± 0.39 and 0.50 ± 21, respectively). Figure 4A illustrates left hemispheric language dominance in one such patient (Case 15).

Group 3 comprised all 7 patients with CMs. These patients all had left dominance (Broca LI = 0.66 ± 0.33; Wernicke LI = 0.72 ± 0.37). The lesions ranged from 0 to 90 mm from geographically defined language cortex areas (mean 22 ± 31 mm). There was 1 patient (Case 16) in this group with a right hemispheric lesion who was left handed and who exhibited left dominance in both Broca and Wernicke areas.

Multimodality Corroboration

Corroborating evidence of accurate language localization was provided by Wada testing, CSM, and clinical outcomes. Wada testing confirmed language dominance found in fMR imaging studies in 7 of 8 cases. In one patient (Case 2), fMR imaging indicated right-sided dominance in the Wernicke area and left-sided dominance of the Broca region. However, Wada testing indicated left language function in the superior temporal branches. Intraoperative ESM confirmed the absence of perinidal essential language cortices, allowing safe resection of the AVM. All patients who underwent resection had intact language, both preoperatively and by 1 month postoperatively.

Discussion

Previous studies have shown that right-sided language dominance can occur in patients with cerebrovascular malformations.[18,27] For example, Vikingstad and colleagues[27] reported greater right-hemisphere recruitment during language tasks in patients with AVMs than in those with adult-onset left-hemisphere brain injury due to stroke. Although they qualitatively noted an importance of the perisylvian location in determining right-hemisphere language dominance, our current study confirms that the primary variable associated with the identification of right-sided language dominance was proximity of the lesion (within 10 mm) to a primary language area. Furthermore, we found than the Broca and Wernicke areas can have asymmetrical dominance across language cortices. The recognition of nonright dominance and bilateral language representations has significant implications for surgical planning and possibly for the recovery of language after neurosurgical intervention.

There are several possible explanations for right-sided language dominance in patients with AVMs adjacent to language cortices. First, the congenital nature of AVMs may render adjacent canonical language areas unable to completely acquire language, resulting in contralateral (that is, right) language acquisition. Second, language representations may have partially or completely shifted from the left to the right hemisphere due to progressive enlargement or hemodynamic changes associated with AVMs. Third, right-sided dominance may be due to an artifactual decrease in observed left-sided fMR imaging activations due to flow-related changes interfering with the perfusion-dependent fMR imaging response or because of flow-related MR susceptibility artifact. If this were indeed the case, one would expect the total number of activated voxels to be decreased (due to artifacts) without an increase in right-sided activations in the right-lateralized cases. In fact, we observed the opposite. Overall activation patterns (that is, number of activated voxels) were equivalent in the 2 groups and there was a statistically significant increased number of right hemisphere–activated voxels in the right-lateralized cases. This pattern is consistent with true right-sided representation (either due to reorganization or differential acquisition) and is inconsistent with an imaging-related artifact. These findings corroborate those of Pouratian et al.,[19] who demonstrated that fMR imaging is highly sensitive and specific for determining language localization in patients with vascular malformations, even directly adjacent to these lesions. Finally, the distribution of lateralization in this population (23% with right-sided language) may be a variant of the normal distribution of language dominance. This is unlikely, however, given that only 1 patient in the current study was left handed and 95% of right-handed patients are left-hemisphere dominant.[9,21,28] In fact, the distribution of lateralization reported in this study more closely mirrors that in other studies of patients with left hemisphere pathology.[12,15] For example, Rasmussen and Milner[22] found that in patients with left-hemisphere injury, 81% of right-handed patients and 33% of left-handed patients were left-hemisphere dominant.

Two patients were found to have right-hemisphere dominance of both Broca and Wernicke areas (Cases 4 and 5). Both had lesions that were well positioned to interfere with or disrupt the arcuate fasciculus. We hypothesize that right language dominance of both regions may be due to disruption of the arcuate fasciculus, which connects the 2 key language areas (that is, Broca and Wernicke areas). The disruption of the primary input or output tracts of the critical language areas may have rendered the putative left-hemisphere language areas incapable of acquiring language.

Impact of Pathological Entity on Lateralization

Only patients with an AVM exhibited right-hemisphere dominance, despite 3 patients with CMs having lesions within 10 mm of language areas. The reason is unclear but may be that CMs have a lower flow rate than AVMs and are therefore less disruptive of the hemodynamics of adjacent cortices.[16] Alternatively, the differential effect on lateralization may be due to histopathological differences between AVMs and CMs: whereas AVMs characteristically include normal brain parenchyma within the nidus, CMs rarely have neural tissue within the tangle of vessels. Finally, although size was not a significant factor in the overall analysis, the smaller overall size of CMs compared with AVMs (17.9 ± 7.7 vs 35.6 ± 10.6 cm, $p = 0.0004$, 2-tailed t-test) may in part influence the functional properties of adjacent cortices.

Functional MR Imaging Reliability

Functional MR imaging offers a relatively rapid and reliable means of topographically mapping multiple functions. It can therefore reliably assist in preoperative decision making and help expedite intraoperative ESM.[6,19,23,26] The equivalent overall activation patterns in right- and left-dominant patients in this study support the notion that AVM hemodynamics do not significantly alter or interfere with the detection of clinically significant fMR imaging activations. Consistent with the current findings, several studies have indicated that it can be a useful technique for predicting language lateralization.[21,28] Still, because of the hemodynamic changes associated with AVMs, the reliability of fMR imaging for assessment of lateralization has been called into question.[18] The Wada test has long been considered the gold standard for evaluating lateralization, but its inability to map specific cortices (rather than vascular territories) can be a significant limitation. Moreover, whereas the Wada test will identify areas that are essential, fMR imaging will identify all areas that are active during a given task (that is, high sensitivity and acceptable specificity).[19] These technical differences may account for the discordant findings in Case 2, in which fMR imaging indicated right dominance of the Wernicke area while Wada testing suggested language in the left superior temporal region. Both techniques may indeed be correct and provide clinically relevant information. Functional MR imaging indicates a preponderance of right-sided activation (Fig. 2C), suggesting a right-greater-than-left dominance but does not preclude the presence of essential language cortices within the left hemisphere, as confirmed by Wada testing. Because a right-hemisphere injection was not performed (not clinically indicated), it is unclear if Wada testing would have also confirmed right-sided language function. Finally, the reliability of fMR imaging maps can be compromised in the setting of recent seizures (that is, seizures within 24 hours of fMR imaging).[13] To maximize its reliability, fMR imaging mapping should be performed during a seizure-free period (≥ 24 hours after the last seizure). These findings emphasize that the use of fMR imaging alone is not sufficient and that intraoperative electrocortical stimulation is still necessary to interrogate and identify which cortical areas are essential for language function.[5,19]

Limitations of Study

While the data suggests that right-sided language dominance is associated with AVMs within 10 mm of anatomically defined language areas, the sample size is relatively small. A small sample size may erroneously result in false-negative findings. For example, the absence of right-hemisphere language function in any patients with CMs may be due to the small population studied. Studies composed of a larger sample size need to be conducted to confirm these findings. Furthermore, the confirmatory tests, ESM, and Wada testing were not conducted in all patients, which would be useful for corroboration of results.

Conclusions

This study emphasizes the need to map each case individually in patients with left perisylvian AVMs. Assumptions about “eloquent” location based on anatomical landmarks (a key component of Spetzler-Martin grading) may have to be reconsidered. The potential for right-sided language function in patients with left-hemisphere AVMs within 10 mm of anatomically defined language areas suggests that grading and operative decision making should be based on functional maps generated for individual patients rather than anatomy alone. Further largescale studies of the impact of individual functional maps on the management of outcomes of patients with vascular malformations are warranted.

Abbreviations used in this paper

AVM	arteriovenous malformation
CM	cavernous malformation
ESM	electrocortical stimulation mapping
fMR	functional MR
LI	lateralization index
MEG	magnetoencephalography

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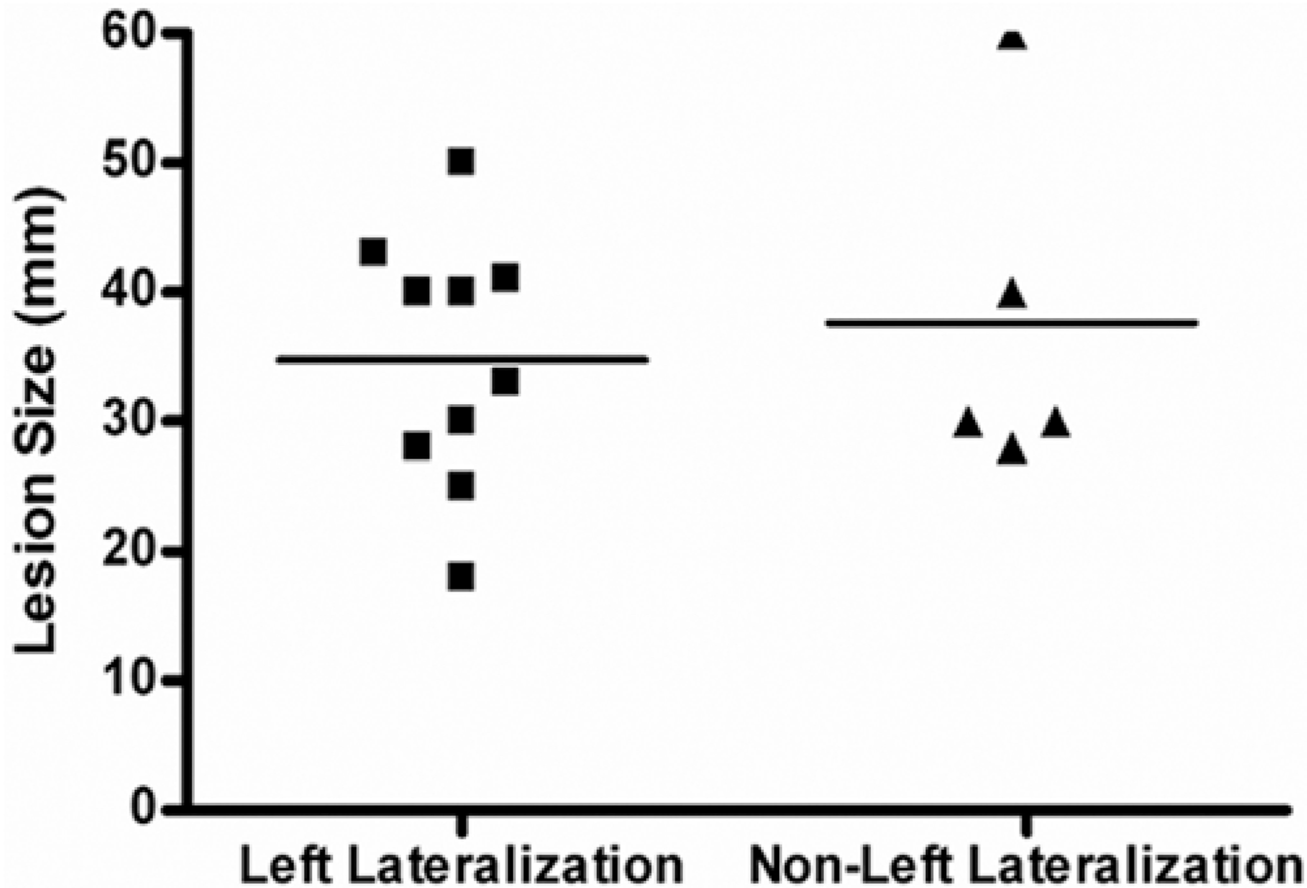

Fig. 1.

Relationship of AVM size and lateralization. There is no significant difference between patients with left dominance *(squares)* and nonleft dominance *(triangles)* with respect to the size of the lesion ($p > 0.05$).

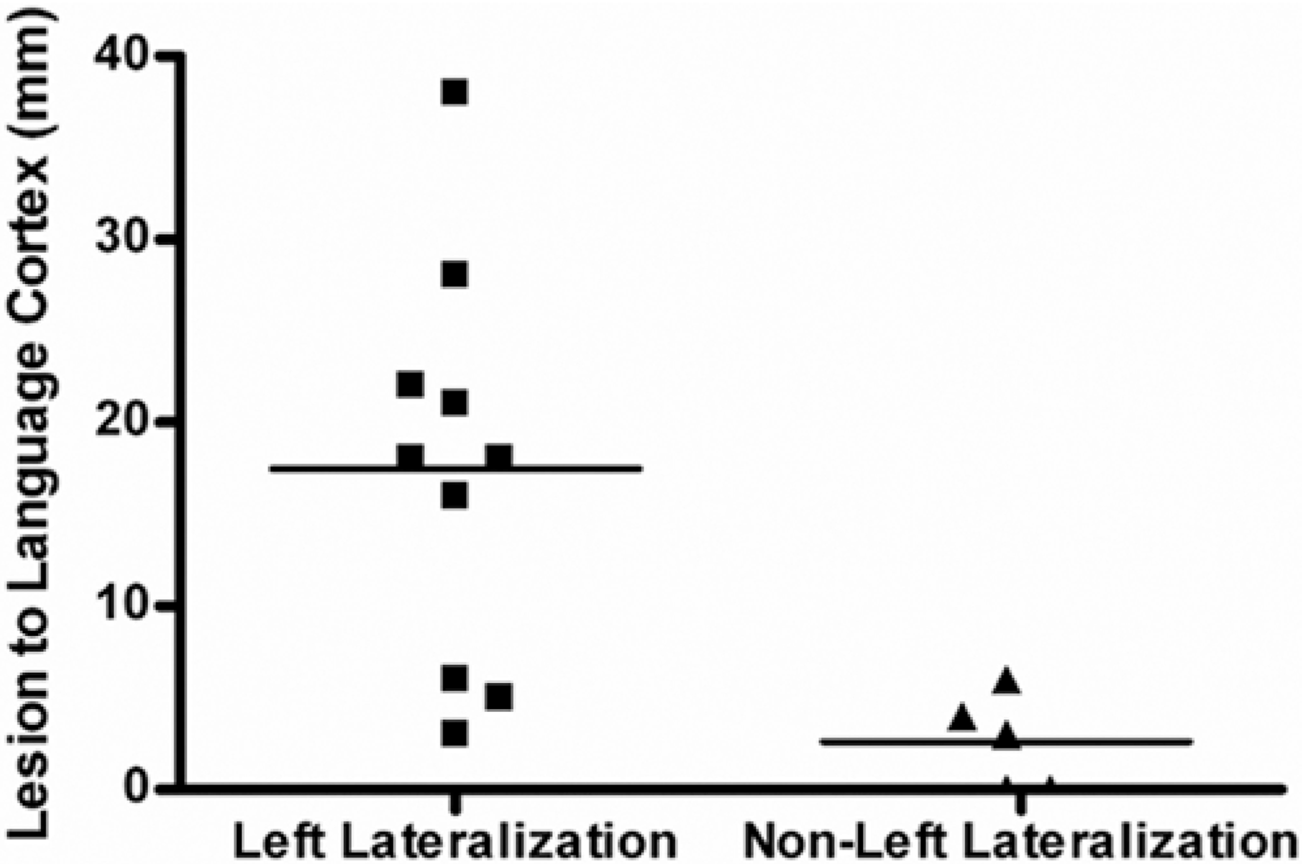

Fig. 2.

Relationship of AVM distance from language and lateralization. Lesions in patients with nonleft dominance were on average significantly closer to anatomically defined language cortices than those with left dominance (1.8 ± 2.1 vs 17.5 ± 11.5 mm, respectively; p = 0.002, 2-tailed t-test).

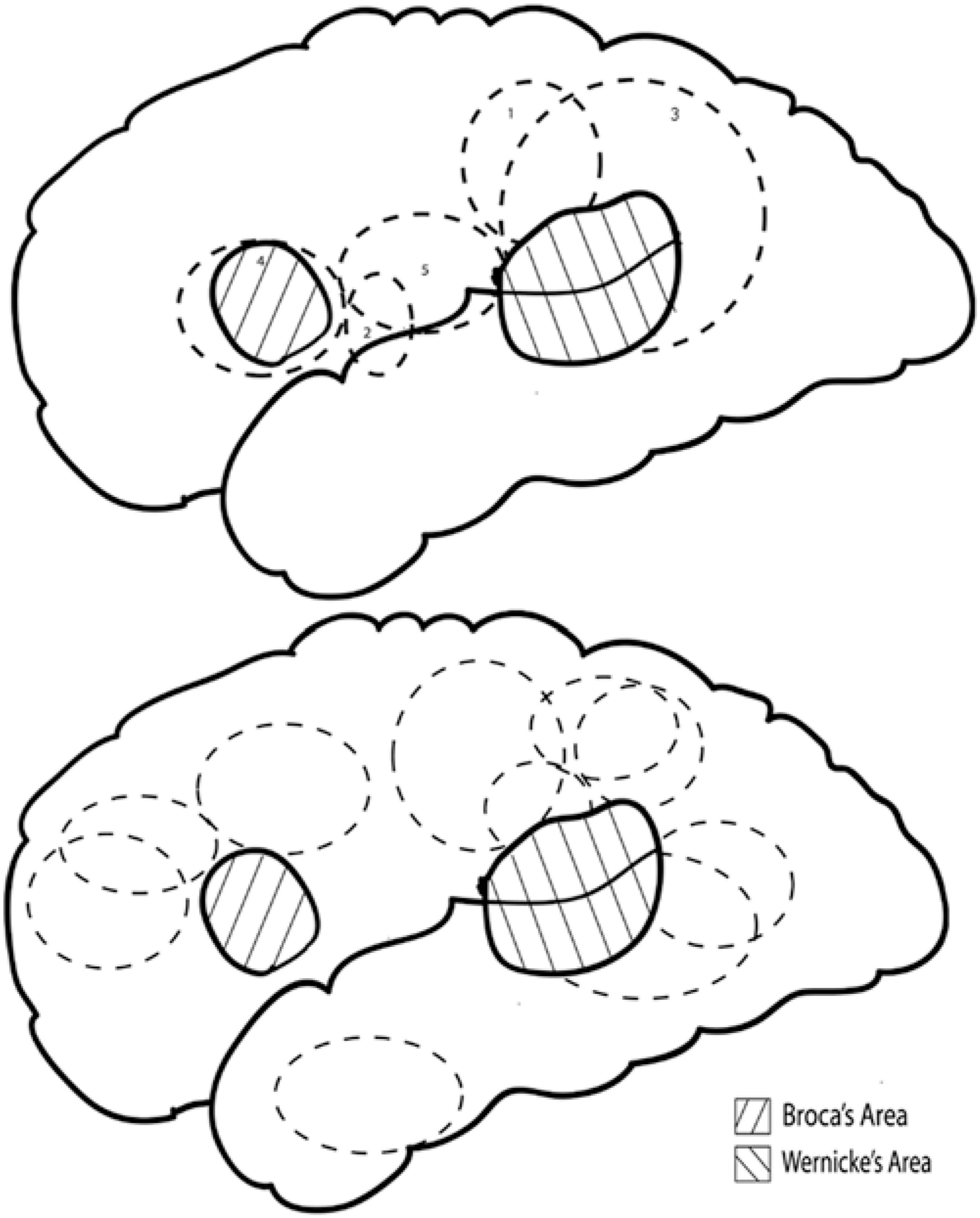

Fig. 3.

Schematic representation of approximate location of AVMs in patients with right-sided language dominance **(upper)** and left-sided language dominance **(lower)** relative to anatomically-defined Broca area and Wernicke area. Numbers in the schematic for right-sided language dominance **(upper)** correspond to case numbers as described in Table 1.

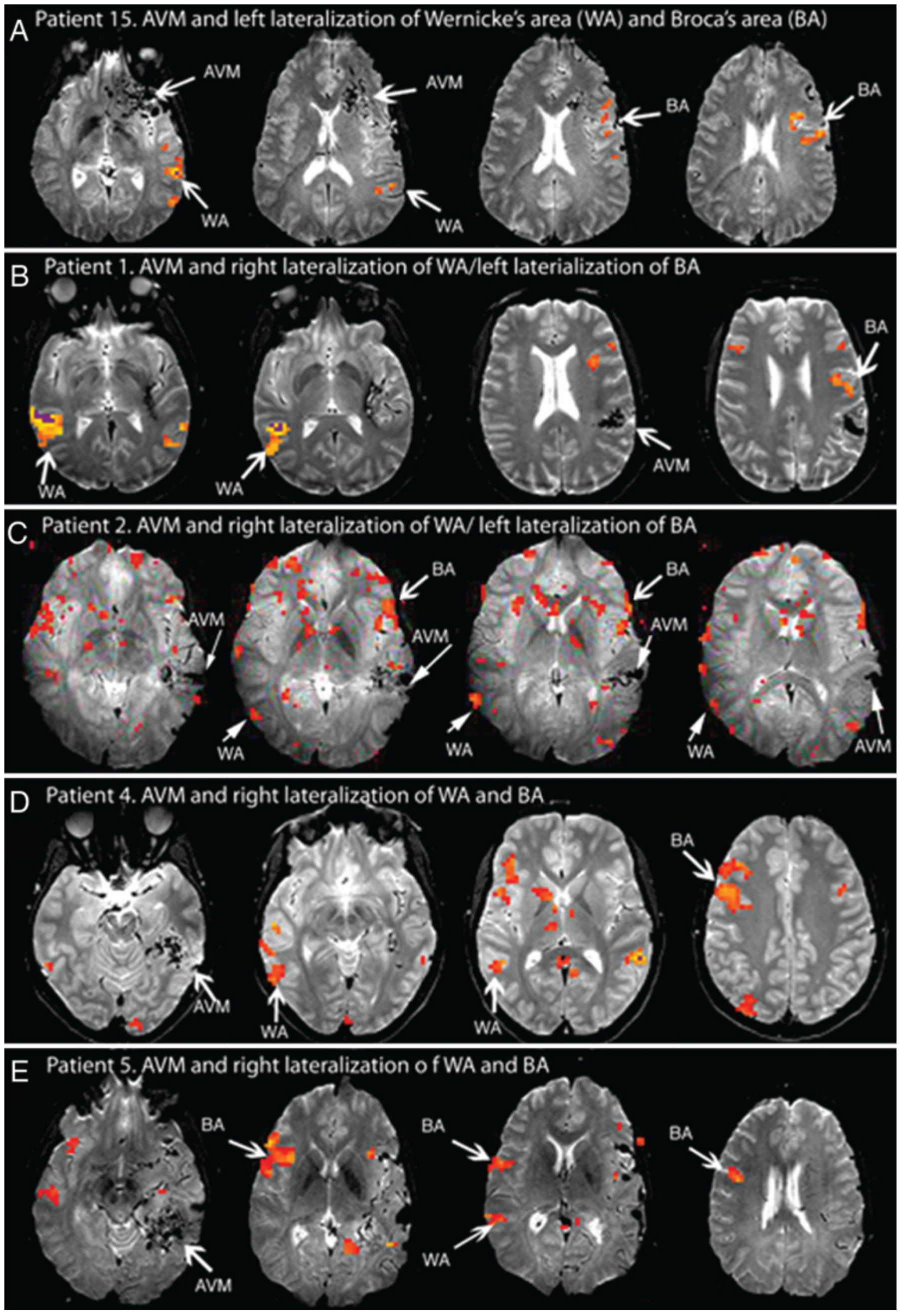

Fig. 4.

Example fMR imaging language activations. **A:** Case 15 (Group 2) exhibits left dominance of both the Broca area (BA) and Wernicke area (WA). **B and C:** Cases 1 and 2 (Group 1) demonstrate right dominance of Wernicke area and left dominance of Broca area. **D:** Case 4 (Group 1) has an AVM that potentially disrupts the arcuate fasciculus. There is right dominance in both Wernicke area and Broca areas. **E:** Case 5 (Group 1) has a lesion that also likely disrupts the arcuate fasciculus. The patient exhibits right dominance of both Wernicke area and Broca areas.

TABLE 1

Summary of patient characteristics and language lateralization[*]

Case No.	Age (yrs), Sex	Hand Dom	S-M Grade	Lt-Sided Lesion Location	Lesion Diameter (mm)	Distance From Language Cortex (mm)	Language Lateralization: fMRI WA (LI)	Language Lateralization: fMRI BA (LI)	Language Lateralization: Wada Test	Procedure
Group 1: AVMs w/in 10 mm of language cortex										
1	55, F	rt	2	WA	28	6	rt (−0.27)[†]	lt (0.55)		SRS
2	13, F	rt	3	WA	40	4	rt (−0.70)[†]	lt (0.77)	lt	SRS
3	29, M	rt	3	WA	60	0	rt (−0.20)[†]	lt (0.72)		observe
4	19, F	lt	3	BA	30	3	rt (−0.40)[†]	rt (−0.81)[†]	rt	surgery
5	40, M	rt	4	WA	30	0	rt (−0.60)[†]	rt (−0.64)[†]		surgery
6	32, F	rt	3	WA	41	5	lt (0.38)	lt (1.00)		SRS
7	19, F	rt	2	BA	28	3	BA (0)	lt (0.42)		surgery
8	38, F	rt	3	WA	40	6	lt (1.00)	lt (0.79)	lt	surgery
Group 2: AVMs >10 mm from language cortex										
9	59, F	rt	2	WA	18	16	lt (0.83)	lt (1.00)		surgery
10	34, M	rt	2	BA	25	28	lt (0.45)	lt (0.45)	lt	surgery
11	17, M	rt	3	WA	40	38	lt (0.44)	lt (0.82)		surgery
12	43, F	rt	3	WA	43	22	lt (0.41)	lt (0.35)		surgery
13	48,M	rt	3	WA	33	18	lt (0.55)	lt (0.55)		surgery
14	31, F	lt	4	WA	30	18	lt (0.26)	lt (0.34)	lt	surgery
15	26, M	rt	4	BA	50	21	lt (1.00)	lt (1.00)	lt	surgery
Group 3: CMs										
16	35, F	lt	–	WA	14	90	lt (0.73)	lt (0.20)		surgery
17	46, F	rt	–	WA	18	0	lt (1.00)	lt (0.30)	lt	surgery
18	49, F	rt	–	BA	13	12	lt (0.31)	lt (0.73)		surgery
19	43, F	rt	–	BA	15	7	lt (0.90)	lt (0.86)		surgery

Case No.	Age (yrs), Sex	Hand Dom	S-M Grade	Lt-Sided Lesion Location	Lesion Diameter (mm)	Distance From Language Cortex (mm)	Language Lateralization			Procedure
							fMRI		Wada Test	
							WA (LI)	BA (LI)		
20	42, M	rt	–	BA	15	15	lt (0.11)	lt (1.00)		surgery
21	37, F	rt	–	BA	15	10	lt (1.00)	lt (0.53)		surgery
22	19, M	lt	–	BA	35	18	lt (1.00)	lt (1.00)	lt	surgery

*BA = near Broca area; Dom = dominance; S-M = Spetzler-Martin; SRS = stereotactic radiosurgery; WA = near Wernicke area.

†Values represent atypical findings—namely right-sided language dominance.