Functional MR evaluation of temporal and frontal language dominance compared with the Wada test

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Article abstract—*Objective:* To evaluate the reliability of temporal and frontal functional MRI (fMRI) activation for the assessment of language dominance, as compared with the Wada test. *Patients and Methods:* Ten patients with temporal lobe epilepsy were studied using blood oxygen level dependent fMRI and echoplanar imaging (1.5-T). Three tasks were used: semantic verbal fluency, covert sentence repetition, and story listening. Data were analyzed using pixel by pixel autocorrelation and cross-correlation. fMRI laterality indices were defined for several regions of interest as the ratio (L − R)/(L + R), L being the number of activated voxels in the left hemisphere and R in the right hemisphere. Wada laterality indices were defined as the difference in the percentages of errors in language tests between left and right carotid injections. *Results:* Semantic verbal fluency: The asymmetry of frontal activation was correlated with Wada laterality indices. The strongest correlation was observed in the precentral/middle frontal gyrus/inferior frontal sulcus area. Story listening: The asymmetry of frontal, but not temporal, activation was correlated with Wada laterality indices. Covert sentence repetition: No correlation was observed. *Conclusions:* There was a good congruence between hemispheric dominance for language as assessed with the Wada test and fMRI laterality indices in the frontal but not in the temporal lobes. The story listening and the covert sentence repetition tasks increased the sensitivity of detection of posterior language sites that may be useful for brain lesion surgery. **Key words:** Functional MRI—Language—Epilepsy—Hemispheric dominance.

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Presurgical evaluation of language functions in patients with brain lesions is usually performed using the Wada test, originally designed to study hemispheric language dominance before proceeding with temporal lobe resection.[1] This test is invasive as it requires the successive injection of amobarbital in the two internal carotid arteries to induce a temporary inactivation of each hemisphere. Hemispheric dominance can also be assessed using morphometric or functional imaging. Anatomic asymmetries have also been documented in frontal and temporal language areas and seem to correlate with lateralized language functions.[2-4] Using functional MRI (fMRI), several studies have shown a concordance between the degree of asymmetry of activation during language tasks and hemispheric dominance as determined with the Wada test.[5-9]

These studies mostly resorted to productive tasks such as verbal fluency,[7] verb generation,[9] or semantic decision tasks,[5,6] predominantly activating the frontal language areas. These tasks may not be optimal in patients with posterior temporo-parietal lesions. Tasks exploring speech perception are associated with predominant temporal lobe activations.[10-12] The value of such temporal activation for assessing language dominance has not been studied.

The aim of the current work was to study the asymmetry of frontal and temporal fMRI activation in patients performing three different language tasks to assess the value of asymmetry indices for determining hemispheric dominance for language. For that purpose, fMRI asymmetry indices were correlated with asymmetry indices derived from the Wada test. Tasks were designed to encompass a large range of language functions thought to involve both frontal and temporal areas. Lesions of Broca's area produce a nonfluent aphasia with relative preservation of auditory comprehension. In contrast, lesions of Wernicke's area produce a fluent aphasia with auditory comprehension deficits. These two regions have thus been considered critical speech–language areas, although they mediate somewhat different functions. Given this background and the importance of lateralizing language functions in presurgical epileptic patients, we were interested in learning whether 1) fMRI indices for language production tasks, selectively activating portions of Broca's area, would better correlate with Wada indices

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Table 1 Description of the patients and their lesions (all lesions were temporal)

Patient no.	Sex	Age, y	Age at seizure onset, y	Handedness*	Brain lesion	Lesion side
1	M	43	3	18	HS	R
2	M	55	46	18	HS	R
3	F	33	17	18	HS	R
4	M	34	1	18	HS	L
5	M	34	11	18	HS	L
6	F	18	8	18	HS	L
7	F	53	20	18	HS	L
8	F	48	6	18	Dysplasia	R
9	M	34	26	18	Dysplasia	R
10	M	19	14	88	Trauma	R

* Handedness scores ranged from 18 (max score for right handers) to 90 (max score for left handers). Ambidextrous subjects score 30.

HS = hippocampal sclerosis.

for production tasks, and 2) fMRI indices for language perception tasks, selectively activating posterior language areas, would better correlate with Wada indices for perception tasks.

Methods. *Patients.* Ten consecutive patients referred for surgical treatment of severe refractory epilepsy of temporal lobe origin were studied (six men and four women; mean age = 37 years; range 18 to 55 years, table 1). The study was approved by the National Ethics Committee and all patients gave their informed consent. The temporal lobe origin of epilepsy was established by noninvasive parameters, comprising natural history, early event, standard video/EEG, and routine MRI. Seven patients had hippocampal sclerosis ipsilateral to the epileptogenic focus, two had temporal dysplasia, and one had sequelae of a cranial trauma involving the antero-lateral surface of the right temporal lobe. Lesions were right-sided in six patients and left-sided in four patients (see table 1).

Handedness was assessed using a standardized questionnaire (see table 1).[13] Nine patients were right handed, one was left handed. The results of the neuropsychological assessment are summarized in table 2. The mean revised Full-Scale IQ was 87 ± 16.[14] The mean educational level was 9.8 years. All patients were submitted to semantic and phonemic Word Fluency tasks[15] and items of the Wechsler Memory Scale (normative data are provided in table 2). The mean number of words produced during 3 minutes was 24.5 ± 6.5 for the phonemic index and 42.5 ± 7.7 for the semantic index.

Table 2 Summary of the neuropsychological evaluation and lateralization indices (LI)

Subjects	Education, y	VIQ	PIQ	GIQ	Phonemic fluency	Semantic fluency	Immediate verbal memory*	Delayed verbal memory†	Wada LI			Frontal LI (fluency)	Temporal LI (story listening)
									Global	Comprehension	Production		
Patients													
1	9	92	96	93	39	59	19.1	19.3	−0.22	−0.33	0.08	−0.54	0.29
2	9	106	110	110	22	42	21.4	20.0	0.44	0.50	0.58	0.56	0.78
3	12	98	83	89	28	41	21.8	12.8	0.83	1.00	0.83	0.56	0.37
4	11	82	75	75	18	34	13.8	8.8	0.61	0.75	0.58	0.88	0.68
5	9	92	73	82	14	32	—	—	0.67	0.84	0.67	0.59	1.00
6	9	81	89	84	25	44	16.9	14.8	0.69	0.58	0.83	1.00	1.00
7	9	85	79	83	26	44	14.8	6.5	0.69	0.50	0.83	0.54	1.00
8	11	85	86	86	23	41	14.9	11.3	0.81	0.87	0.91	1.00	0.57
9	8	58	57	55	25	38	11.6	10.8	0.48	0.46	0.38	0.19	1.00
10	11	107	110	108	25	50	21.0	21.5	0.65	0.50	0.75	0.71	0.34
Controls (n = 20), mean ± SD‡	9.8				39.5 ± 5	57.8 ± 11.4	29.8 ± 3.5	27.9 ± 3.2					

* Score on the immediate recall of paired-associate words and of two stories (maximum score, 35).

† Score on the delayed recall (90 min) of paired-associate words and of two stories (maximum score, 35).

‡ Controls were 20 subjects matched in age, sex, and educational level.

VIQ = verbal IQ; PIQ = performance IQ; GIQ = general IQ.

On average, patients scored below normal values in neuropsychological tests, as shown in table 2, but were able to carry out the fMRI and Wada experimental tasks. They all responded adequately during the short instruction phase that preceded the imaging experiment. Patients were all capable of generating a number of words within the specified category. Their ability to repeat sentences was reflected in the immediate and delayed verbal memory tests.

Imaging. The MR protocol was carried out with a 1.5-T MR unit using blood oxygen level dependent (BOLD) fMRI. After sagittal scout sequence, the protocol included: 1) 12 axial gradient echo–echoplanar (EPI) images covering the whole frontal lobes (repetition time/echo time/α: 5000/60 msec/90°, 6-mm-slice thickness, no gap; in-plane resolution: 3.75 mm × 3.75 mm); and 2) axial inversion recovery three-dimensional fast spoiled gradient recalled acquisition for anatomic localization. Images were acquired over less than 45 minutes. To prevent involuntary head movements inside the magnet, the volunteer's head was taped on the forehead and firmly restrained on either side with foam pads.

fMRI tasks. Three different tasks were performed by the patients: semantic fluency, covert sentence repetition, and story listening. In the semantic fluency task, patients had to generate mentally as many words as possible from a given semantic category (fruits, vegetables, pieces of furniture, body parts, animals, sports). The name of a different category was presented aurally at the beginning of each activation period. Fluency was contrasted with a control rest condition. At the beginning of each control period, patients were asked aurally to stop generating words and to rest. In the covert sentence repetition task, patients were presented with short sentences (mean duration = 2.88 seconds, range 1.82 to 4.22 seconds), each followed by a silent period of the same duration. During the silent period, patients had to repeat the sentence mentally. Repetition was contrasted with a control rest condition. In the story listening task, patients listened to a story in French, segmented in three 30-second fragments. Story listening was contrasted with a control condition consisting of listening to the same story fragments played backward, in order to subtract the auditory component of the task. Task order was counterbalanced across patients. During the scan, patients lay in the dark. Stimuli were recorded on a digital audiotape and presented using standard headphones customized for fMRI experiments and inserted in a noise-protecting helmet that provided isolation from scanner noise. The paradigm consisted of seven epochs of 30 sec, alternating control (R) and language conditions (L) (R-L-R-L-R-L-R). Forty-two volumes of 12 sections were acquired over 3:30 minutes. The first four volumes of each sequence were discarded to reach signal equilibrium.

fMRI analysis. Data were motion corrected,[16] temporally filtered, and analyzed with a dedicated software (ACTIV, Service Hospitalier Frédéric Joliot, Commissariat à l'Energie Atomique, Orsay, France) written in Interactive Data Language (Research Systems International France, Paris), using pixel by pixel autocorrelation[17] and cross-correlation with a reference waveform[18] of the MRI signal time course. Motion was evaluated using cine mode and calculation of the displacement of the center of mass of the functional images over time in the three planes (<0.5 mm in all patients, corresponding to less than 15% of pixel size in the axial plane). Activated clusters were defined as follows: > 3 contiguous pixels, correlation coefficient > 0.40, autocorrelation coefficient > 0.20 ($p < 0.001$). Activated pixels were overlaid on axial anatomic images with a color scale representing the correlation coefficient. Pixels were then localized according to the individual anatomy of the patients using multiplanar analysis and three-dimensional surface rendering of the cortex (Voxtool, General Electric, Milwaukee, WI), and clustered in regions of interest (ROI): frontal lobe (including the entire frontal lobe, rostral to the central sulcus), insula (INS), inferior frontal gyrus (IFG, including the lateral and inferior surface of the gyrus, and the adjacent precentral sulcus posteriorly), middle frontal gyrus (MFG, including the adjacent precentral sulcus posteriorly, and the inferior frontal sulcus inferiorly), superior frontal gyrus (SFG, including the adjacent portion of the precentral sulcus and the superior frontal sulcus), medial frontal cortex including the supplementary motor area and the cingulum (SMA/CING), inferior parietal lobule and superior temporal gyrus (IPL/STG, including the supramarginal gyrus, the angular gyrus, the superior temporal gyrus and sulcus), middle and inferior temporal gyri (MTG/ITG, including the medial and inferior temporal gyri and the inferior temporal sulcus), temporal lobe (including the IPL/STG and MTG/ITG areas), superior parietal lobule and intraparietal cortex (SPL, including the two banks of the intraparietal sulcus and the superior parietal lobule), and precuneus (bounded by the marginal ramus of the cingulate sulcus rostrally, the subparietal sulcus inferiorly, and the parieto-occipital sulcus posteriorly). Regions boundaries were determined with reference to anatomic atlases of gyral anatomy[19] and individual gyral variations.[2,20]

For each ROI, we computed first the total number of activated pixels in the left (L) and right (R) hemispheres and second a lateralization index (LI) defined as the ratio (L − R)/(L + R) (LI range from −1 to +1). A positive index corresponded to a left-predominant activation (strong left lateralization: +0.5 to +1, weak left lateralization: +0.25 to +0.5), and a negative index to a right-predominant activation (strong right lateralization: from −1 to −0.5, weak right lateralization: from −0.5 to −0.25).[21] Symmetric activation was scored from −0.25 to +0.25.

Wada quantification of hemispheric dominance. Intracarotid amobarbital testing was performed in each patient as part of the presurgical evaluation. Amobarbital (140 mg in 3 mL saline) was injected in each carotid artery via a transfemoral approach. The two hemispheres were tested on 2 consecutive days. Patients received a battery of language tasks during the 15 minutes following injection using the procedure of the Montreal Neurologic Institute.[22] A set of nine tasks was repeated until all of the tasks had been correctly executed. These tasks included productive speech tasks, including serial speech (counting forward and backward, saying the days of the week in normal and reverse order), naming 12 visually presented objects and two pictures of objects; receptive speech tasks, including simple motor commands such as "stick out your tongue," and a simplified version of the token test (pointing at named objects and at targets of different colors and different shapes); and other speech tasks, including reading aloud 10 words and spelling six words. The first three runs

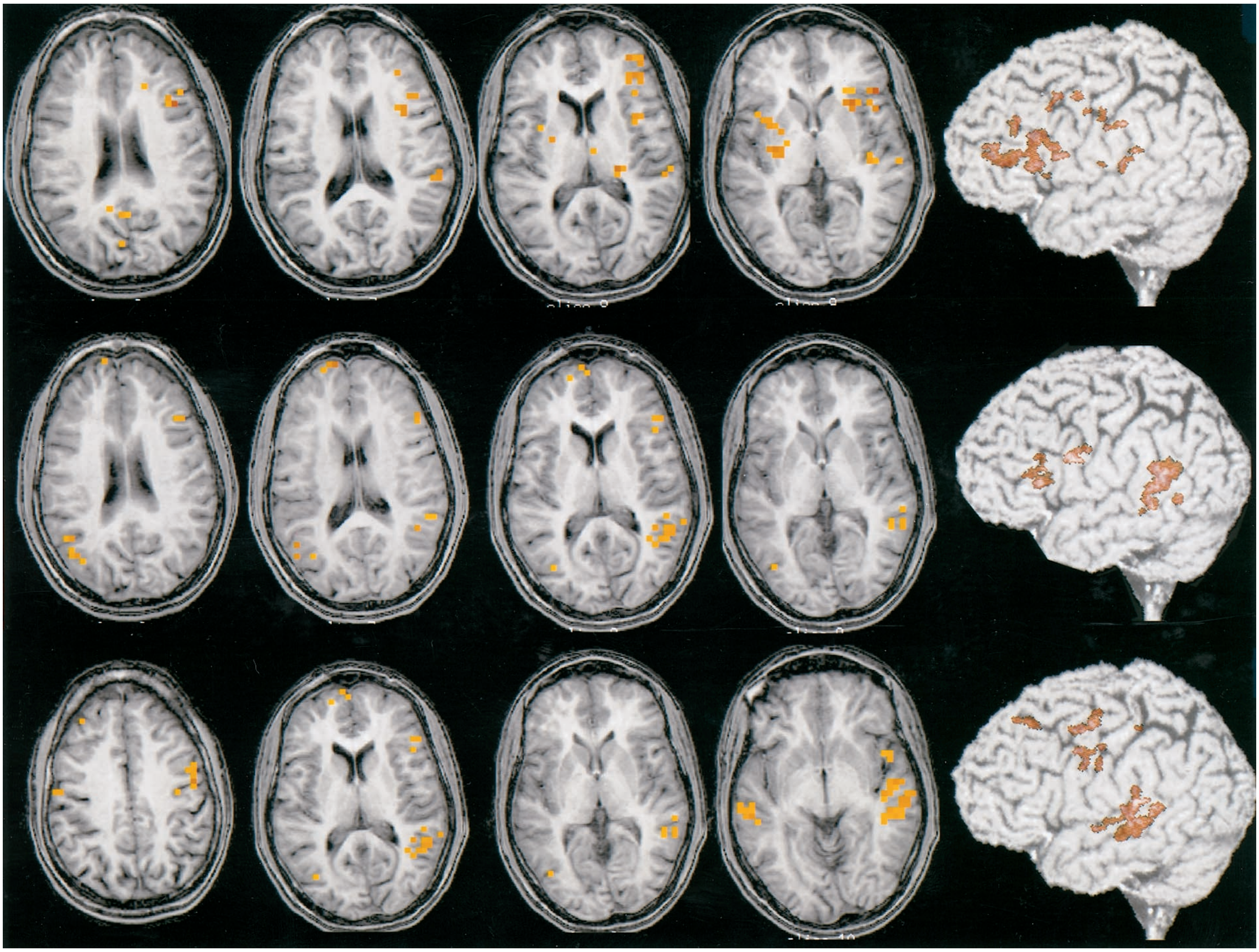

Figure 1. Functional images of Patient 3 performing the semantic fluency (upper row), the story listening (middle row), and the covert repetition tasks (lower row). Activated pixels are overlaid on axial anatomic images (inversion recovery T1-weighted) and on a three-dimensional surface rendering of the left hemisphere (right).

of each task were scored from 0 to 2 (0 = wrong, 1 = not perfectly executed, 2 = perfectly executed).

Wada LI were computed for productive tasks, receptive tasks, and for all tasks together as the difference between scores during left injection minus scores during right injection, divided by the maximum possible score (Wada LI range: from −1 to +1). As for fMRI indices, a positive index corresponded to a left-predominant lateralization (strong left lateralization: +0.5 to +1, weak left lateralization: +0.25 to +0.5), and a negative index to a right-predominant lateralization (strong right lateralization: from −1 to −0.5, weak right lateralization: from −0.5 to −0.25). Symmetric language representation was scored from −0.25 to +0.25.

Results. *Localization of language areas.* Figure 1 shows the different patterns of activation across the three tasks in a typical patient (Patient 3). Figure 2 shows the areas activated in all 10 patients, demonstrating a large variation in the total number of activated pixels across tasks and across individuals. Table 3 shows the mean number of activated pixels by regions for the three tasks.

Semantic fluency. Activation was found in the frontal lobes in all patients, including the inferior frontal gyrus and sulcus (10 patients), the anterior insular cortex (7 patients), the middle frontal gyrus (9 patients), and the supplementary motor/cingulate areas (8 patients). Activation was observed in posterior temporo-parietal areas in only five patients.

Covert sentence repetition. Activation was present bilaterally in the superior temporal gyrus/inferior parietal area (10 patients), the inferior and middle frontal gyri (5 patients), the supplementary motor/cingulate areas (4 patients), and in fewer than 4 patients in other regions. Activation was also observed bilaterally in the planum temporale, primary auditory areas, and the inferior part of the precentral gyrus.

Story listening. Activation was found in temporal areas and inferior parietal areas forming a continuous stream along the superior temporal sulcus extending in the angular gyrus without clear demarcation (10 patients). Activation was also found in the medial frontal gyri (6 patients), the supplementary motor/cingulate areas (6 patients), and in the superior (4 patients) and inferior frontal gyri (2 patients).

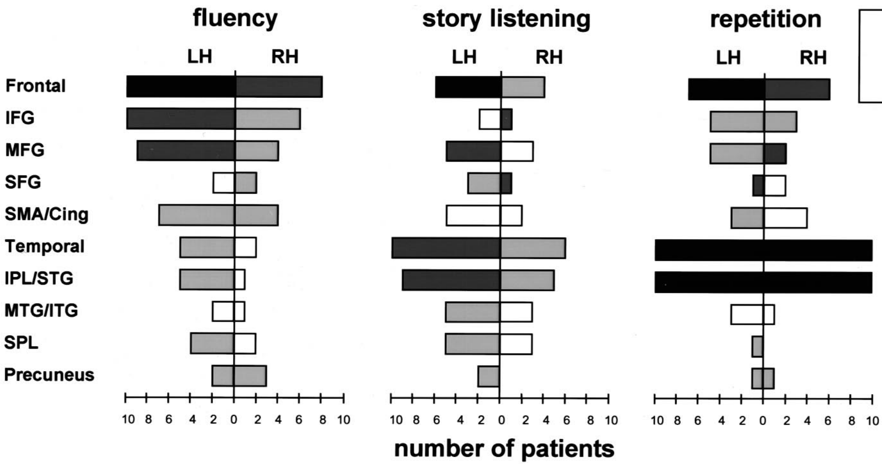

Figure 2. Average number of activated voxels in anatomic regions for each of the three tasks. IFG = inferior frontal gyrus; MFG = middle frontal gyrus; SFG = superior frontal gyrus; SMA/CING = supplementary motor area and the cingulum; IPL/STG = inferior parietal lobule and superior temporal gyrus; MTG/ITG = middle and inferior temporal gyri; SPL = superior parietal lobule and intraparietal cortex; LH = left hemisphere; RH = right hemisphere.

Hemispheric language dominance. Six patients (Patients 2 and 4 through 8) had a strong left lateralization in both the frontal lobes (on the basis of the global frontal index in the semantic fluency task) and the temporal lobes (on the basis of the global temporal index in the story listening task) (see table 2). Two patients (Patients 3 and 10) had a strong left lateralization in the frontal lobes and a weak left lateralization in the temporal lobes. Patient 1 had a strong right lateralization in the frontal lobes and a weak left lateralization in the temporal lobes. Patient 9 had a more symmetric pattern in the frontal lobes and a strong left lateralization in the temporal lobes. In the word generation task, the degree of leftward asymmetry was similar in the middle frontal (mean LI = 0.69) and in the superior temporal gyri (mean LI = 0.66) (table 4). In the covert repetition task, the asymmetry was higher in the medial frontal (mean LI = 0.53) than in the superior temporal gyri (mean LI = 0.06) (see table 3). In the story listening task, the leftward asymmetry was higher in the temporal (mean LI = 0.70) than the frontal lobes (mean LI = 0.47) (see table 4).

For the semantic fluency and the story listening tasks, a significant correlation between Wada and fMRI lateralization indices was observed in frontal but not in temporoparietal areas (see table 4, figure 3). In the semantic fluency task, the global, productive, and receptive Wada indices were significantly correlated with the fMRI indices computed for the middle frontal gyrus and for the anterior insula, but were not correlated with the fMRI index for the inferior frontal gyrus (see figure 3). For the story listening task, the global, productive and receptive Wada indices were correlated with the fMRI index for the middle frontal gyrus. The global and productive Wada indices were correlated with the fMRI index for the supplementary motor/cingulate areas (see figure 3). For the repetition task, no significant correlation was found between Wada and fMRI indices in any region.

No significant correlation was found between Wada and fMRI indices for posterior temporo-parietal areas in any task (see figure 3).

Discussion. The results of the current study may be summarized as follows: 1) lateralization of brain fMRI activation was more prominent in the semantic fluency and the story listening tasks than in the

Table 3 *Mean number of activated pixels by regions for the three tasks*

	SMA/Cing		SFG		MFG		IFG		Insula		Frontal		IPL/STG		MTG/ITG		Temporal		IPC/SPL		Precuneus	
Tasks	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R
Verbal fluency																						
Mean	5.1	2.4	1.1	2.0	14.9	3.5	14.3	3.7	3.7	1	35.4	11.6	3.9	0.4	0.5	0.2	4.4	0.6	3.2	0.7	1.7	2.1
SEM	6	3	5	1	12	8	16	3	3.1	1.8	23	12	3	*	1	*	3	1	3	1	5	4
Story listening																						
Mean	2.5	0.8	2.0	1.3	8.0	1.2	1.1	1.2	0	0	13.6	4.5	13.5	3.4	3.2	1.3	16.7	4.7	3.0	1.0	1.3	0.0
SEM	2	1	5	*	14	2	1	*	*	*	21	11	9	5	5	1	12	7	3	2	8	*
Repetition																						
Mean	1.9	2.2	1.5	0.9	4.9	2.9	5.3	1.9	0.7	0.3	13.6	7.9	37.5	35.5	1.5	0.2	39.0	35.7	0.7	0.0	0.6	0.6
SEM	3	3	*	2	5	13	5	4	2.2	0.9	15	18	18	19	3	*	18	19	*	*	*	*

* Not enough patients for calculation.

SMA/Cing = medial frontal cortex including the supplementary motor area and the cingulum; SFG = superior frontal gyrus; MFG = middle frontal gyrus; IFG = inferior frontal gyrus; IPL/STG = inferior parietal lobule and superior temporal gyrus; MTG/ITG = middle and inferior temporal gyri; IPC/SPL = intraparietal cortex/superior parietal lobule.

Table 4 Functional MRI (fMRI) lateralization indices (LI) and correlation between the global Wada index and fMRI indices for the main regions of interest

	Semantic fluency			Story listening			Covert repetition		
Region	LI	*r*	*p*	LI	*r*	*p*	LI	*r*	*p*
Frontal	0.548	0.88	0.00082	0.466	0.61	NS	0.312	0.07	NS
IFG	0.644	−0.21	NS	0.294	*	*	0.381	−0.44	NS
Insula	0.682	0.82	0.023	*	*	*	*	*	*
MFG	0.692	0.89	0.0015	0.510	0.87	0.023	0.532	0.35	NS
SMA/Cing	0.301	0.49	NS	0.528	0.91	0.013	*	*	*
Temporal	0.625	−0.07	NS	0.704	0.30	NS	0.056	−0.62	NS
IPL/STG	0.667	−0.06	NS	0.734	0.45	NS	0.057	0.04	NS

Correlations with selective production or comprehension Wada indices followed an almost identical pattern.

* Not enough patients for calculation (≤4).

NS = not significant; IFG = inferior frontal gyrus; MFG = middle frontal gyrus; SMA/Cing = medial frontal cortex including the supplementary motor area and the cingulum; IPL/STG = inferior parietal lobule and superior temporal gyrus.

covert sentence repetition task; 2) Wada test assessment of hemispheric dominance was correlated with activation asymmetry in the frontal lobes, but not with activation asymmetry in the temporal lobes; 3) the semantic fluency task was better at predicting language lateralization in individual patients than the two other tasks; and 4) as expected, the use of multiple tasks increased the sensitivity of the detection of areas associated with language, which may be useful in presurgical evaluation of patients with brain lesions.

Regional language activation during expressive and receptive language tasks. Tasks were designed to encompass many aspects of language function, such as passive sensory processing, speech comprehension, motor programming and output, and semantic processing. In the semantic fluency task, activation was extensive, including the operculum, the inferior and middle frontal areas (BA 44, 45, 9/46, and 47), the premotor cortex (BA 6), and the supplementary motor and cingulate areas. The most reproducible foci of activation were observed in the premotor cortex (posterior part of the middle frontal gyrus and the adjacent precentral sulcus), the dorsolateral prefrontal cortex, the inferior frontal sulcus, and the anterior part of the insula. Posterior activation in temporo-parietal areas was less frequently observed. These data are in agreement with several previous studies using productive tasks such as semantic or orthographic verbal fluency[7,23-25] or other word generation tasks.[6,26-31] The main foci of activation in these tasks were found in the left dorsal and ventral lateral prefrontal cortex (BA 44 through 47). Differences in the relative intensity of activation in these areas may largely be attributable to variations in task design, as suggested previously.[30] Thus, covert generation of words predominantly activated the premotor and dorsolateral prefrontal cortex,[23,24] whereas verb generation in response to a given noun activated predominantly the inferior frontal cortex of BA 47.[26,28] The role of these regions is still debated

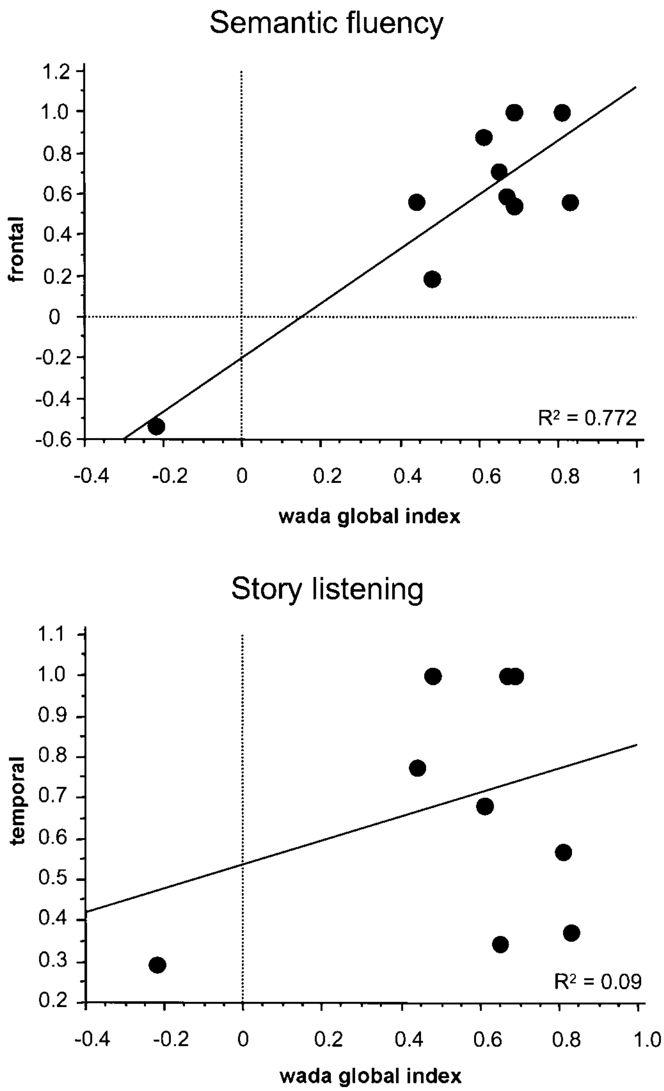

Figure 3. Pearson linear regression between the Wada global index and functional MRI (fMRI) global frontal index in the semantic fluency task (up) and fMRI global temporal index in the story listening task (down).

and may be related to the semantic components of the tasks,[26,32] the process of willingly retrieving verbal material ("willed action"),[23,27] the initiation of a strategy to identify words from memory,[33] components of verbal working memory corresponding to the articulatory loop,[34] and the preparation for the articulation of the response.[35]

The repetition task has received comparatively much less attention. In this task, activation was more extensive than in the other tasks, probably reflecting both sensory and output components of the task. In the temporal lobe, activation was found in the middle and superior temporal gyri as previously reported.[26,35,36] These areas are thought to be involved in word perception,[35] lexico-semantic,[37] and phonologic processing.[26,37] Posterior areas may be more specifically involved when words are combined into sentences as opposed to single words.[38] In the frontal lobes, activation predominated in the inferior part of the precentral gyrus (mouth region) and in the premotor and prefrontal cortex (BA 6 and 44 or Broca's area[26,28,34,35,39,40]) and is thought to be related to phonological processing and articulatory encoding. Activation in the inferior and middle frontal gyri and in the supplementary motor/cingulate areas was less frequently observed than in the semantic fluency task. Activation was also observed in primary auditory cortex.

In the story listening task, activation was constantly observed in the left temporal lobe along the superior temporal sulcus, and in neighboring portions of the superior and middle temporal gyri, often extending in the angular gyrus without clear demarcation. On the opposite, frontal areas were activated in few subjects. The use of backward speech as a control condition is thought to subtract early auditory processes.[12] Thus, activation in the superior temporal gyrus probably represents linguistic rather than auditory processing. A similar pattern of activation, independent of the modality of stimulation, has been reported in studies using similar tasks.[10-12] However, when rest is used as a control condition, as in our sentence covert repetition task, temporal lobe activation most probably encompasses areas of early auditory processing.[10,41,42]

Assessment of language dominance. Activations observed in the frontal and temporal lobes showed an overall asymmetry.[12,21,41,43] As expected, most patients were clearly left hemisphere dominant on the basis of fMRI indices. Leftward asymmetry was higher in the middle frontal than in the superior temporal gyri in the covert repetition task, but similar in these two regions in the word generation task. In contrast, the leftward asymmetry of activation was higher in the superior temporal gyri than in frontal areas in the story listening task. Temporal activation in the covert repetition task was not asymmetric, as these activations included the planum temporale and primary auditory areas, which are poorly lateralized.[36] Overall, the lateralizing value of the tasks was higher for the word generation than for the two other tasks. These data are in agreement with a previous study[9] reporting stronger lateralization with a productive task (verb generation) than with two other, predominantly receptive, tasks (reading and naming). Lastly, the possibility of a reorganization of language was examined in the two patients (Patients 4 and 6) who had left-hemispheric seizure foci and seizure onset below or at the age of 8. These two patients were strongly left-hemisphere dominant (see table 2). This finding was not suggestive of the presence of a reorganization of language areas. However, no firm conclusion can be drawn on that topic given the small number of patients studied.

Measures of language lateralization obtained with fMRI and with the Wada test were significantly correlated in the frontal lobe, confirming previous reports using various word generation[7-9] or semantic decision tasks.[5,6] Anatomic asymmetries of the inferior frontal lobe have also been related to language lateralization.[4] Such correlation did not prevail in temporal areas. The strongest correlation was found in the dorsolateral prefrontal cortex and the adjacent premotor cortex in the semantic fluency task. A weaker correlation was found in the same regions in the story listening task, although few patients activated this area in this task. Activation in the medial frontal cortex was also correlated with Wada indices in this task, although to a lesser extent. Activation in the inferior frontal areas was not correlated with Wada lateralization indices in any task. Inferior frontal indices included the opercular motor areas, which were less lateralized than the dorsolateral prefrontal/premotor area. One hypothesis is that some patients silently articulated the words they produced and therefore induced a bilateral activation of this region. This is particularly the case in the repetition task and may explain why no correlation was found in the frontal lobe in this task. However, a correlation was observed in the fluency task within a subregion of the inferior frontal area buried in the antero-medial part of the insular cortex. This area was specifically activated in the fluency task but not in the two other tasks. The insular region may be specialized in the planning and coordination of speech movements.[44]

Temporal lobe activation was not correlated with Wada indices in any of the tasks. In the semantic fluency task, temporal activation was too infrequent to allow for correlation analyses. That temporal activation was not as reliable as frontal activation in predicting language dominance has been suggested previously,[8] although anatomic studies have reported that asymmetries of the planum temporale may be related to language laterality.[3] The lack of correlation between lateralization of temporal activation during story listening and language dominance assessed with the Wada test remains incompletely understood. Several explanations may be proposed. First, fMRI may not be sensitive enough to detect brain asymmetry in temporal areas. Second, the characteristics of the task used may not be optimal.

Thus, as brain activation in right-hemisphere homologues of language areas may be modulated by sentence comprehension,[11] the difficulty of story comprehension may increase the amount of activation in the right hemisphere. However, temporal activation in this task was clearly lateralized in agreement with previous studies,[12,36,41,45] strongly arguing against these hypotheses. Third, in the covert repetition task, temporal lobe activation included early auditory processing areas, which are poorly lateralized in controls.[36] However, in the story listening task activation in these areas was subtracted by the paradigm design, and indeed no activation was found in primary auditory areas. Fourth, the number of patients may not be large enough to detect a weak correlation. Fifth, although temporal and frontal lobe language dominance are most often concordant, a dissociation between frontal and temporal areas, as evidenced in Patient 1, has been reported previously.[46] Aphasia induced by intracarotid amobarbital in the Wada test may be more related to frontal than temporal lobe inactivation.

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Sleep reactivity during acute nasal CPAP in obstructive sleep apnea syndrome

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Article abstract—*Objective:* To measure the readjustments of sleep macro- and microstructure in patients with obstructive sleep apnea syndrome (OSAS) after acute nasal continuous positive airway pressure (NCPAP) treatment. *Background:* The conventional polysomnographic analysis (macrostructure of sleep) does not necessarily provide the best measures of sleep disruption associated with OSAS. In contrast, microstructural methods of analyzing sleep (i.e., arousals and cyclic alternating pattern) may improve evaluation of patients with OSAS. *Method:* Ten patients with OSAS were monitored polygraphically before and during the first night of NCPAP therapy. The results were compared with those of 10 age- and sex-matched controls without sleep-related breathing disorders. Each nocturnal recording was followed by daytime observation using the multiple sleep latency test and Visual Analogue Scale (VAS). *Results:* The first night of ventilatory therapy was characterized by a remarkable expansion of stages 3 and 4 and of REM sleep. In addition, NCPAP suppressed the presence of cyclic alternating pattern (CAP) in REM sleep and induced an impressive rebound of arousals and of certain CAP variables—i.e., CAP rate, CAP time, number of CAP cycles—which dropped well below the physiologic values expressed by controls. A normal duration of phases A and B was re-established starting the first treatment night. When we matched sleep variables with the indices of daytime function, a significant correlation emerged only between the variations of CAP rate and VAS scores. In particular, improvement of daytime sleepiness was less evident when the ventilatory-induced drop of CAP rate was more pronounced. *Conclusions:* The application of CAP variables to the microstructural analysis of sleep may expand our knowledge regarding sleep and respiration. **Key words:** Sleep—Sleep apnea syndrome—Nasal CPAP—Arousals—Cyclic alternating pattern.
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Obstructive sleep apnea syndrome (OSAS) is a clinical disorder characterized by repetitive interruptions of airflow and severe fragmentation of sleep. In OSAS, respiratory events—i.e., apneas and hypopneas (AH)—recur every 20 to 40 seconds, with consequent transient asphyxia accompanied by heart rate deceleration and appearance of EEG theta-delta activities. In contrast, termination of each respiratory event is generally associated with an increase of muscle tone, tachycardia, and EEG arousal.[1] These cyclic changes reflect an unstable and poorly consolidated sleep that results in a marked alteration of the sleep structure.

Despite the severe sleep fragmentation, there may be no formal change in OSAS recordings by standard definition.[2] These findings indicate that the conventional polysomnographic analysis (macrostructure of sleep) may not provide the best measures of sleep disruption associated with OSAS, and more advanced methods of analyzing sleep, sleep fragmentation, and arousal are needed to improve evaluation of patients with OSAS.[3] Even conventional arousal criteria[4] may underestimate the severity of sleep disruption,[5] as many patients with OSAS have apneic events that do not end in conventionally established arousals. According to the American Sleep Disorders Association (ASDA) definition,[4] arousals are identified as rapid EEG frequency shifts. However, an increase of delta band amplitude starting before the apnea offset has been described in non-REM (NREM)

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