Recovery from vascular aphasia is a major issue that implies functional reorganization of the language system in the brain. Several neuroimaging studies have pointed to the critical role of the immediate surroundings of the infarction in recovery capabilities, whereas others have suggested an essential role for the contralateral undamaged hemisphere. Those discrepancies should make us take into account the dynamic changes observed across time during the recovery course and draw a distinction between different language components (eg, semantic and phonological processes), depending on partially distinct networks that can be differently damaged depending on aphasia type.

The present study aimed at (1) developing a reproducible functional MRI (fMRI) paradigm that could be used for follow-up of different types of mild or moderate aphasia, and (2) documenting relationships between recovery and evolution of activation in the left perilesional cortex and homologous areas.

Brain activation was studied using 2 language tasks: (1) in a group of healthy subjects who underwent 2 fMRI sessions to evaluate the reproducibility; and (2) in an aphasic patient named PL with conduction aphasia, who was scanned twice (1 month and 1 year after stroke).

Materials and Methods

Case History
PL, a 44-year-old highly educated (postgraduate), right-handed man (Edinburgh Inventory), experienced a left sylvian stroke involving Wernicke's area, the posterior part of the insula, and the inferior part of the supramarginal gyrus (SMG) without motor impairment. Language evaluation was conducted at 1 month and 1 year after stroke. His aphasia was characterized using the Montreal–Toulouse battery (MT86).

Quantitative tests evaluating comprehension (token test), picture-naming abilities (Boston Naming Test [BNT]), and word fluency were performed.

MT86 showed mild conduction aphasia with preserved semantic access, contrasting with difficulties of word-form retrieval. Reading and writing from dictation were the most impaired tasks, with many phonological errors. The token test showed impairment increased with length of instructions. These 2 tests showed significant improvement during follow-up (Table). BNT, showing mild naming impairment (concerning word-form access), and fluency test, showing important evocation impairment without difference between literal and categorical evocation, did not show significant improvement.

Control Subjects
Ten healthy right-handed subjects (4 men, 6 women, mean age 44±9.7) matched for educational level participated in this study as controls. To assess intrasubject reproducibility, fMRI experiments were performed.
were performed twice for 7 of them (with a minimal 3-month interval).

MRI Protocol

MRI Acquisition

Each subject underwent a high-resolution T1-weighted anatomic scan on a 1.5-T Gyroscan ACSNT Power Track 6000, including 30 slices parallel to intercommissural line (no gap; thickness 3.5 mm; repetition time [TR]/echo time [TE]=274/25 ms; matrix=256×256; field of view =260 mm). Then, echo planar imaging was performed (30 slices; no gap; thickness 3.5 mm; TR/TE=3000/60ms; flip angle=90°; matrix=64×64). The blocked design fMRI paradigm comprised 5 baseline blocks alternating with 4 activation blocks, each lasting 30 seconds.

fMRI Stimuli

Each scanning session consisted of 2 separate tasks that involved a combined visual and auditory stimulation. Visual stimuli consisted of line drawings chosen from the Snodgrass Corpus and were projected via a video system; auditory stimuli were digitized spoken words presented via magnet earphones. Word–picture pairs were presented every 3 seconds (Figure 1).

The 2 tasks consisted of (1) a word–picture rhyming (“phonological”) task, in which subjects had to decide whether the picture and the simultaneously heard word rhymed or not; and (2) a word–picture semantic matching task, in which subjects had to decide whether the items belonged to the same semantic category or not.

For both tasks, active blocks included 10 pairs of items (with 40% of matching pairs). Subjects were instructed to respond to matching pairs by pressing a computer key with their right hand. Responses were recorded via the Psycscope Button box system. During “baseline” blocks, subjects were presented with a visual stimulus composed of 3 dots inserted in a square.

Image Processing

Images were analyzed with SPM99 (Wellcome Department of Cognitive Neurology, London, UK). The 90-volume images of each run were realigned to the first image to correct for head movement and normalized into Talairach’s space using the intercommissural line as reference plane. Data were thereafter expressed in terms of standard coordinates in the x, y, z axes. Transformed functional data were smoothed with a Gaussian kernel of 10 mm (full-width half maximum).

Statistical Analysis

Individual statistical maps of significant relative regional blood oxygenation level–dependent response changes were generated using a box car model convoluted by hemodynamic response function. For the control group, data were analyzed using the “random effect” model for contrasts between each task and baseline, with a spatial extent k>20 voxels and an amplitude threshold set at P<0.007 (r=3), uncorrected for multiple comparisons.

Compound contrasts involving “task baseline” main contrasts between the 2 sessions or groups (ie, the patient PL as a “group of 1” and the control group) were performed by using 2-sample t tests using the random effect model. For instance, these compound contrasts allowed us to compare PL at 1 month and 1 year after stroke (PLMRI1, PLMRI2) or control subjects at 1 month and 3 months later (CTMRI1, CTRMI2).

For each brain region (superior frontal, inferior frontal, parieto-temporal, occipitotemporal, and parietal cortices), a lateralization index (LI) [(right activation volume–left activation volume)/(right activation volume+left activation volume)] was calculated.

Results

fMRI Performances Analysis

Semantic Task

No significant difference in terms of hits or errors (false-positive [FP], false-negative [FN], bilateral Z test for proportion comparison) was observed between PL and controls, whatever the session. The PL’s response times (RTs) were significantly shorter than those of controls (P=0.008; bilateral Student t test) at session 1, but this difference disappeared at session 2.

Figure 1. fMRI paradigm. In rhyme task, subjects had to decide whether “picture–heard word” pair rhymes (then they pushed a button) or not. In baseline task, they had to look at 3 dots on a square. Semantic pairs are identically built. The headphones symbol represents heard words.
Word–Picture Rhyming Task
FP rates were significantly different between PL and controls at session 1 (10% versus 1%; \(P = 0.0001\)) and session 2 (5% versus 1%; \(P = 0.024\)). FN rates were significantly different only at session 1 (33% versus 12%; \(P = 0.025\)). PL’s RTs were not significantly different from those of controls, whatever the session.

Intertask Difficulty
Controls did not show any performance difference either in terms of responses or in terms of RTs, whatever the tasks or the sessions, whereas PL showed more difficulties in rhyme detection at both sessions (session 1: RTs 1950 ms for rhyming versus 1650 ms for semantic, \(P = 0.019\); session 2: RTs 2000 ms for rhyming versus 1860 ms for semantic, \(P = 0.014\)).

fMRI Results
Semantic Task
In controls (Figure 2a), the activation pattern observed at session 1 in the semantic task included right superior dorsolateral frontal (Brodmann’s area 9 [BA9]), left superior temporal (Heschl gyrus, Wernicke’s area, with an extension to the anterior temporal pole; LI = −1) and bilateral inferior occipitotemporal (BA18–BA19, 37; LI = −0.29) regions.

Two-sample \(t\) tests between first and second sessions (CT MRI1−CT MRI2 and PL MRI1−PL MRI2) did not show any activation at our usual group study thresholds (\(t = 3; \ P = 0.006\) uncorrected for multiple comparisons; voxel extent \(k = 20\)).

For PL (Figure 2a), the activation pattern observed at session 1 in the semantic task involved left frontal (supplementary motor area [SMA], BA47) and bilateral, although rather predominantly right-sided, parietotemporal regions (LI = 0.27). Posterior occipitotemporal regions were activated bilaterally (LI = 0.20), as well as cerebellar hemispheres. At session 2, the pattern included middle bilateral temporal (middle temporal gyrus [MTG] BA21–BA22; LI = 0.04) and right SMG. The contrast PL MRI2−PL MRI1 (Figure 3a) showed significant clusters in the left superior temporal gyrus (STG; BA21–BA22; LI = −1).

Comparisons between controls and PL at session 1 (CT MRI1−PL MRI1 and PL MRI1−CT MRI1; Figure 3a) showed more activation in the left SMG (BA7–BA40) and in the left STG (BA22) for controls and more activation in the right SMG for patient (LI = 1 in parietotemporal region).

At session 2, areas that were more activated for PL (PL MRI2−CT MRI2) were not only in the right SMG but also in the left MTG (BA21–BA22; LI = −0.55 in parietotemporal region).

Rhyming Task
In controls (Figure 2b), the activation pattern at session 1 included frontal cortex (LI = −0.66) in right and left motor–premotor areas, left dorsolateral frontal cortex (BA9–BA46), right anterior insula and BA47, and SMA. Parietotemporal cortices were involved, with a left predominance (BA41, BA21–BA22; SMG; LI = −0.71). Occipital regions were activated bilaterally (BA18–BA19), with a left extension to the fusiform gyrus (BA37–BA20). As for semantic task, 2-sample \(t\) tests between first and second sessions did not show any significant changes of activation.

For PL (Figure 2b), the activation pattern observed at session 1 showed a right parietotemporal predominance (SMG; STG; LI = 0.66), with the perilesional anterior tempo-
rall cortex being only weakly activated (anterior part of BA22, BA38). Moreover, dorsolateral frontal cortices (BA9–BA46) were activated bilaterally, as well as SMA, motor, and premotor areas (LI=0.49). Frontal activations also concerned right ventral regions (BA13, BA47, and BA10). Occipitotemporal as well as cerebellar regions were involved bilaterally.

At session 2, only right BA6, extending to BA4, was activated in dorsofrontal cortex. Temporal areas remained strongly activated, with an increase in left perilesional areas (MTG; BA21–BA22; LI=0.55). Occipitotemporal cortices still showed a bilateral activation confluent with a cerebellar one.

The contrast PLMRI2/PLMRI1 (Figure 3b) showed strong activations in the left hemisphere, particularly in the anterior parts of STG and MTG (LI=−1), occipitotemporal (LI=−0.59), and cerebellar regions. Superior and inferior frontal regions (BA6, BA10–BA22) were bilaterally involved with a right predominance (LI=0.75 and 0.36, respectively).

Comparisons between controls and PL (Figure 3b) at session 1 (CTMRI1–PLMRI1) showed more activation in the left SMG and STG, and in the left dorsolateral frontal cortex for controls. The reverse comparison showed a strong activation of SMG in the right hemisphere (LI=1).

At session 2, in parietotemporal regions, higher activation was observed in the right SMG (as at session 1) and the left MTG and STG (BA21–BA22) for PL (LI0.25).

**Discussion**

In the current study, brain activation was examined during 2 language tasks (“rhyme” and “semantic”) in a group of 10 healthy subjects. The intersubject robustness and the intrasubject reproducibility of these tasks were demonstrated, thus entailing their validity in a patient follow-up study over a stroke recovery time course. Indeed, we showed feasibility of this paradigm in a patient as early as 1 month after stroke, and the longitudinal study during the first 12 months of rehabilitation evidenced spatiotemporal characteristics of changes in brain activation pattern in relation to language recovery. Feasibility of this paradigm will have to be demonstrated further in different types and degrees of aphasia, comprehension of instructions and difficulty in performing a long-lasting fMRI session being the critical points for patients.

In controls, both tasks exhibited different distributed networks (Figure 2a and 2b). Semantic task especially involved 2 regions: (1) left STG, including Wernicke’s area, classically considered critical for decoding auditory verbal information,\(^\text{19–24}\) semantic access being reported to involve an anterior, ventral temporal pathway,\(^\text{25}\) as observed here; and (2) bilateral occipital and postero inferior temporal cortices (fusiform gyri), which are related to identification of visual items, reflecting the necessary implicit picture naming underlying word–picture comparison.\(^\text{26–28}\)
Phonological task also involved left STG, but with an extension to its posterior part, and SMG. It could be related to the hypothesis of a dorsal way for decoding auditory verbal information, involving posterior part of Wernicke’s area, planum temporale, and SMG as interface between external auditory perception (and internal word representation), and production, allowing for internal rehearsal according to the cognitive models of verbal working memory.10,25,29,30

In both tasks, an involvement of prefrontal cortex (BA9–BA46 and mesial cortex) was noticed, more pronounced for phonological task, especially in the left side, suggesting a higher attentional load for this task31 or a higher involvement of the articulatory loop.32

Language testing for PL showed numerous phonemic mistakes, contrasting with good access to the semantic target, as evidenced by MT86 testing. Indeed, PL presented similar performance scores to controls on semantic task during fMRI session but differed in rhyme task performance, with an improvement between first and second sessions. These data are in agreement with mild conduction aphasia and with lesion topography.33

In contrast with controls, whatever the task and the session, PL’s fMRI exhibited 3 more activated regions as follows: (1) right parietotemporal region, homologous of damaged left areas; (2) bilateral prefrontal areas, including BA9–BA46 (Figure 3a and 3b), medial BA6 (SMA), extending to anterior cingulum, particularly in rhyming task. Prefrontal cortex has been proved to play a critical role in coping strategies.34 Activation of this region could be attributed to the non-specific “attentional and executive control load,” which was expected (especially in phonological task) because the patient found tasks much harder to perform than the control subjects.31 This hypothesis is supported by the decreasing trend of prefrontal overactivation during recovery, when PL presented an improvement of language abilities. In addition, it could represent enhanced recruitment of verbal rehearsal system of the articulatory loop to compensate the failing of the articulatory perception and phonological task, especially in the left side, suggesting a higher attentional load for this task31 or a higher involvement of the articulatory loop.32

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