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Brief Communication

"What is it?" A functional MRI and SPECT study of ictal speech in a second language

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ABSTRACT

Neuronal networks involved in second language (L2) processing vary between normal subjects. Patients with epilepsy may have ictal speech automatisms in their second language. To delineate the brain systems involved in L2 ictal speech, we combined functional MRI during bilingual tasks and ictal – interictal single-photon emission computed tomography in a patient who presented L2 ictal speech productions. These analyses showed that the networks activated by the seizure and those activated by L2 processing intersected in the right hippocampus. These results may provide some insights both into the pathophysiology of ictal speech and into the brain organization for L2.

1. Introduction

Patients with epilepsy may exhibit ictal speech. Ictal speech automatisms are usually uttered in the patient's native language [1], but rare cases of second language (L2) ictal speech production have been reported [2–4]. Distinct networks may be involved in generating ictal speech in the first or second language. These different networks cannot be accounted for by a simple contrast between dominant and nondominant hemispheres.

Functional imaging analysis in healthy subjects has provided some insights into the variability of networks activated in different languages. In highly proficient bilingual individuals with early acquisition of L2, both languages activate essentially identical cortical networks [5], and the selection and control of the output language are thought to involve subcortical structures, notably the left caudate [6]. In contrast, for subjects with low proficiency or late acquisition (after the age of 6) of L2, cortical regions activated by L2 are more extended [7,8], with an occasional right hemispheric predominance [9].

Native language (L1) and L2 ictal speech automatisms generally result from partial seizures that originate in the nondominant hemisphere [1–4]. Driver et al. distinguished two possible explanations of this lateralization pattern: either ictal speech in L2 results from release of the dominant hemisphere from the inhibitory action of the nondominant one, or ictal speech results directly from overactivation of the nondominant hemisphere. To assess these hypotheses, we studied a patient who produced L2 ictal speech. We used functional MRI (fMRI) during bilingual tasks and interictal – ictal single-photon emission computed tomography (SPECT) to delineate and compare the network involved in L2 processing and the epileptic network.

2. Methods

2.1. Case history

The patient, a 34-year-old right-handed French man, had pharmacologically intractable partial epilepsy that began at the age of 8 [4]. At age 1, he had suffered a brain injury with a right hemispheric subdural hematoma that was surgically removed. The

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patient was later evaluated for surgery because he continued to have two or three partial seizures per month with conventional carbamazepine and phenobarbital treatment. Seizures started with epigastric sensations, followed first by loss of consciousness and then by rhythmic vocalizations, as well as oral, motor, and speech automatisms. Speech automatisms were stereotyped, with the patient repeating the English sentence "What is it?" for about 10 seconds. Finally, in response to any question, he would answer "yes." There were no postictal speech disorders. Interictal EEG revealed epileptic spikes on the right temporal lobe. Ictal EEG showed a right temporal discharge. Brain MRI revealed a T2-weighted signal increase in the right hippocampus and partial loss of gray–white matter demarcation in the right temporal pole, an abnormality often associated with hippocampal sclerosis [10].

The first language of the patient and his parents was French. He had studied English as a foreign language at school from 11 to 18 years of age, without taking a particular interest in it. At the time of the presurgical evaluation, the patient had not spoken English for 16 years, except during rare English business training, and his overall proficiency was low. His level of oral comprehension and speech production was limited to simple sentences, although his grammar and reading ability were somewhat better. A Wada test was not performed, as the neuropsychological evaluation showed typical dysfunction of the right mesial temporal region, that is, an impairment of the nonverbal memory.

A right amygdalo-hippocampectomy associated with an anterior temporal lobe resection was performed after the present brain functional imaging studies. Pathological examination revealed hippocampal sclerosis. The patient was seizure free 1 year after surgery.

2.2. SPECT study of the seizure-related network

To localize the epileptogenic focus, ^{99m}Tc-ECD perfusion SPECT was performed both during a seizure-free interictal period and during a typical seizure under video/EEG monitoring (26 seconds after clinical onset of the seizure and 10 seconds before ictal speech), using a triple-head camera equipped with low-energy, high-resolution parallel hole collimators (Irix, Philips). Reconstructed volumes were normalized with respect to the mean regional cerebral blood flow (rCBF) value, normalized to Talairach space, and smoothed (8 mm). An image of relative rCBF increase was obtained by subtraction of both scans and thresholded at 50%.

2.3. Functional MRI study of the first and second languages

The patient was presented with four auditory stimulus sequences, each comprising 12 French, 12 English, and 6 Danish sentences, plus 6 silent trials, organized in a pseudo-random order. One trial started every 15 seconds. The patient was asked to press the right key if the French or English sentences were semantically true (e.g., "cigarettes are not smoked by animals") or the left key if they were semantically false (e.g., "plane crashes no longer happen at night"), and to press both keys for Danish sentences. We expected that this comprehension task with complex sentence stimuli would activate a large part of the L2 network.

For each sequence, 216 functional volumes sensitive to BOLD contrast were acquired with a T2-weighted gradient echo, echo planar imaging sequence on a 1.5-T Signa Imager (TR = 2500 ms, $\alpha = 90°$, TE = 60 ms, field of view = 240 $\times$ 240 mm, resolution = 5 $\times$ 3.75 $\times$ 3.75 mm^3). Six additional volumes were acquired at the beginning of each sequence to reach signal equilibrium, but were not analyzed. Functional images were corrected for movement, spatially normalized, and smoothed (5 mm), using the SPM99 software. Temporal filters were applied (high-pass 120 seconds, low-pass 4 seconds). Activation for each type of trial was modeled by a convolution of the time series of trials (each represented by a 3-second epoch), with the standard SPM hemodynamic function. Additional variables of noninterest modeled constant differences across sequences. Differences between conditions were assessed by contrasting each language versus silence, and L2 versus L1.

3. Results

3.1. SPECT

Comparison of the ictal and interictal SPECT images revealed a right-lateralized temporo-insular network, which included the right hippocampus (Fig. 1). The ratio of activated volume in the right relative to the left hemisphere was 12.2.

3.2. Functional MRI

English sentences (L2) activated bilateral frontotemporoparietal networks, relative to silence. We derived activations associated with English language processing by computing the critical contrast of English minus French sentences (voxelwise threshold $P < 0.01$; extent threshold $P < 0.05$ corrected for multiple comparisons across the whole brain). This comparison was masked inclusively by the contrast of English minus silence, to be sure that true activations were measured ($P < 0.05$). This revealed a strongly right-lateralized English-related network. Overall the ratio of activated volume in the right relative to the left hemisphere was 4.43 (ratio of the number of suprathreshold voxels in the right to that in the left hemisphere). This network included the right hippocampus (Talairach coordinates 27 −33 −9, $Z = 4.26$) (Fig. 1).

We then delineated the intersection of the fMRI network activated by the English language and of the epileptic network as delineated by SPECT. This showed a single area of overlap localized to the right hippocampal region (Fig. 1).

4. Discussion

We have shown, in a patient with ictal speech automatisms in a second language, an anatomical overlap between the seizure-activated network and L2 processing areas in the right hippocampus. Driver et al. [3] described a case, similar to the present one, of a Polish patient who uttered in English "I beg your pardon" during electrical stimulation of the right amygdala. Driver and colleagues suggested two hypotheses to explain the L2 speech automatisms, emphasizing either disinhibition of the left hemisphere or direct activation of the right hemisphere by the epileptic discharge [3]. The present results, derived from a combination of ictal SPECT and fMRI studies, suggest that L2 speech automatisms may result from direct activation of the brain areas affected by the ictal discharge.

The right hippocampus participated in the patient's ictal behavior, but may not itself underlie verbal production in L2, as simple partial seizures limited to the hippocampus are associated primarily with dysmnestic or vegetative phenomena. Possibly, the hippocampus is a key area in the propagation of ictal discharges to more distant networks that eventually yield the utterance of the simple English sentence we report here. Both in normal subjects and in patients with left or right temporal lobe epilepsy [11], the hippocampus is consistently and bilaterally activated during word comprehension tests. Activation, at coordinates similar to those reported in this study, is associated with the successful encoding of word lists and with the intelligibility of degraded sentences [12]. The hippocampus is also the source of electrical potentials induced by sentences with anomalous semantic terminations [13]. In late bilingual patients, ictal

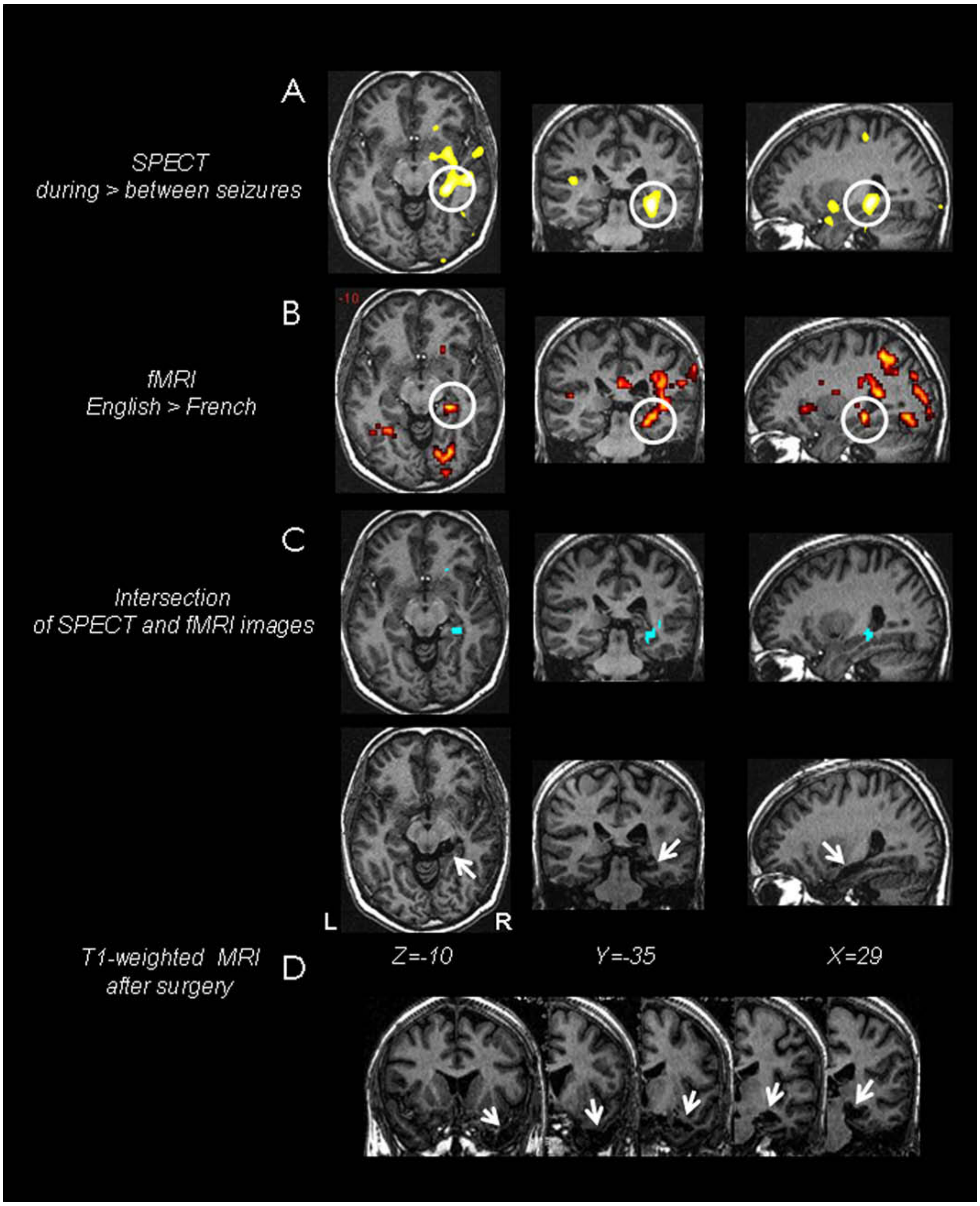

Fig. 1. (A) Subtraction of interictal from ictal SPECT images reveals a largely right temporo-insular epileptic network with a rCBF increase >50% during a seizure. (B) Functional MRI activation when the patient was listening to English as compared with French sentences shows a predominantly right hemisphere network. (C) Intersection of the ictal and the L2 networks in the right hippocampus (intersection of SPECT (A) and fMRI (B) images). (D) The surgical resection of the right temporal pole (performed after the brain functional imaging studies) extended caudally to the hippocampus, region of overlap of the SPECT and fMRI networks.

speech automatisms may occur if the L2-related widespread network is correctly activated, explaining the rarity of this symptom in comparison with ictal automatisms in native language elicited by a more restricted brain area. The fMRI study of L2 consisted of comprehension tasks, because production tasks were not possible in this patient. It is therefore important to underline that the critical region for L2 ictal speech production might lie beyond the hippocampus within the right temporo-insular network demonstrated on ictal SPECT.

Our approach in a single patient may be especially revealing as both the areas associated with L2 and epileptic networks show a wide variability across individuals. The spatial overlap between activated brain regions may provide some insights into the pathophysiology of ictal speech and the organization of brain areas involved in processing a second language.

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