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CASE REPORT

Accuracy of pre-surgical fMRI confirmed by subsequent crossed aphasia

Paolo Vitali · Nina Dronkers · Alexander Pincherle · Anna Rita Giovagnoli · Carlo Marras · Ludovico D'Incerti · Francesco Ghielmetti · Roberto Spreafico · Flavio Villani

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Abstract Atypical patterns of language activation in functional MRI (fMRI) are not unusual, particularly in patients with severe epilepsy. Still, the functional significance of these activations is under debate. We describe a case of a right-handed patient affected by drug-refractory right temporal lobe epilepsy in whom pre-surgical fMRI showed bilateral language activations, greater in the right hemisphere (RH). After surgery, a right subdural hematoma caused epileptic status and severe aphasia. This post-surgical complication of a crossed aphasia confirmed the prior fMRI findings of RH language thus stressing the value of pre-surgical fMRI evaluations, even when surgery is planned in the RH of a right-handed patient.

Keywords Language · Hemispheric dominance · Crossed aphasia · Temporal lobe epilepsy · Functional MRI

P. Vitali · L. D'Incerti · F. Ghielmetti
Division of Neuroradiology, Department of Diagnostics and Applied Technology, Foundation IRCCS National Neurological Institute "C. Besta", Milan, Italy

P. Vitali
Division of Neuroradiology, Neurological Institute "C. Mondino", Pavia, Italy

N. Dronkers
Center for Aphasia and Related Disorders, VA Northern California Health Care System, Mather, USA

N. Dronkers
Department of Neurology, University of California, Davis, Davis, USA

A. Pincherle · R. Spreafico · F. Villani (✉)
Division of Clinical Epileptology and Experimental Neurophysiology, Department of Diagnostics and Applied Technology, Foundation IRCCS Neurological Institute "C. Besta", Milan, Italy
e-mail: fvillani@istituto-besta.it

A. R. Giovagnoli
Laboratory of Neuropsychology, Department of Clinical Neurosciences, Foundation IRCCS Neurological Institute "C. Besta", Milan, Italy

C. Marras
Division of Neurosurgery III, Department of Neurosurgery, Foundation IRCCS Neurological Institute "C. Besta", Milan, Italy

Introduction

The determination of language lateralization before epilepsy surgery is critical in patients affected by drug-resistant temporal lobe epilepsy (TLE). Although most individuals have a left hemisphere specialization for the morphosyntactic, semantic and phonological aspects of language, seizures beginning early in childhood can cause atypical (i.e., bilateral or predominantly right) lateralization profiles [1–6].

Language lateralization can be determined by functional MRI (fMRI), which also maps the more precise cortical areas involved in language processing. The functional significance of these areas of activation in patients with atypical lateralization is still unclear, but becomes critical when using pre-surgical fMRI maps to plan surgical resection.

Here, we demonstrate the significance of atypical fMRI activations in a case of a right-handed patient affected by drug-refractory right TLE who developed a post-surgical

right subdural hematoma with epileptic status and severe aphasia.

Case report

A 31-year-old right-handed man affected by drug-resistant TLE associated with a right temporal–parietal cyst and hippocampal sclerosis (Fig. 1d) was admitted to our Epilepsy Surgery Unit to undergo reduction in the mass effect of the cyst (through fenestration) and resection of the mesial temporal structures.

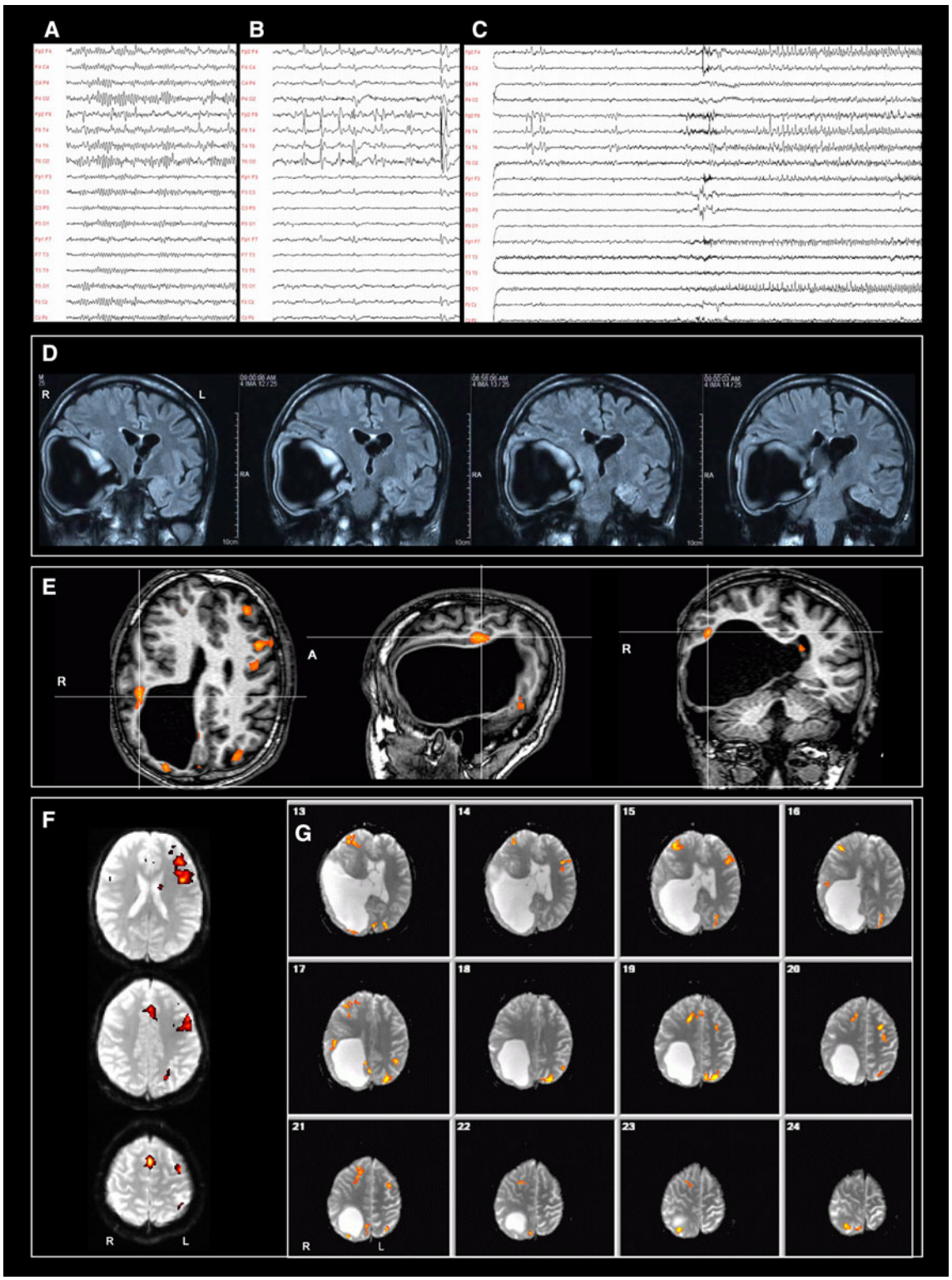
His clinical history began at the age of 11 years with daily focal seizures, characterized by tachycardia, loss of contact, and oral/limb automatisms, and were never controlled by therapy. At the time of surgery, while the patient was taking valproate, oxcarbazepine, clobazam and tiagabine, about 25–30 seizures per month were reported. EEG recordings showed asymmetric background activity, more stable in the left hemisphere, with epileptic and slow abnormalities over right temporal regions. The diagnosis was drug-resistant right TLE. Despite this diagnosis, the patient achieved a normal educational level, and was working at a railroad company.

At the pre-surgical evaluation, the neurological examination was normal. Neuropsychological assessment revealed only mild deficits in right hemisphere (RH) functions: constructional apraxia and visuospatial memory (Table 1). Language showed normal spontaneous initiative, comprehension, reading and writing, with mild deficits in semantic fluency. The video-EEG recording showed right temporal interictal epileptic activities and an ictal discharge arising from the right temporal lobe (Fig. 1a–c). The MRI showed a large cyst communicating with the ventricle, extending to the right temporal and parietal lobes, with mass effect on the frontal and anterior half of the temporal lobe. The superior temporal gyrus was displaced upward and the hippocampus was atrophic and hyperintense in T2-weighted images (Fig. 1d). The patient underwent routine pre-surgical fMRI with word fluency to assess language lateralization. This task, typically demonstrating strong left lateralization in normal subjects (Fig. 1f), showed bilateral frontal activations, greater in the RH (Fig. 1g), with additional right temporal activations (Fig. 1e). As a result, the surgical resection in this patient's RH was performed as though it were the language-dominant hemisphere.

The day after surgical resection of the right temporal pole and hippocampus, a CT scan showed a small right parietal subdural clot, stable at a repeat CT scan. However, during the following 2 weeks, the patient complained of worsening headache and presented with the brief episodes of confusion and progressively increasing global aphasia. After 2 weeks of surgery, an MRI scan showed a chronic subdural hematoma with mass effect on right temporal–parietal regions (Fig. 2d). The hematoma was drained immediately with headache resolution and partial language recovery. After 4 weeks of the first surgery, the patient developed a focal epileptic status, with agitated behavior and global aphasia. The EEG showed continuous epileptic activity in posterior quadrants of the RH (Fig. 2a). Lorazepam, 4 mg i.v., successfully stopped the status, with partial language recovery. After 5 days, the EEG still showed slow and epileptic activity in right temporal–parietal regions (Fig. 2b). After 6 weeks of the first surgery (4 weeks after hematoma drainage), the neuropsychological assessment still showed impaired performance in several cognitive areas, and spontaneous speech was characterized by poor prosody, articulation problems, anomias, paraphasias, and "conduit d'approche" (Table 1). Both phonemic and semantic fluency were impaired. The Aachener aphasia test (AAT) [8] revealed global aphasia involving both oral and written language. A second word fluency fMRI study, performed 6 weeks after the first surgery with the patient still aphasic, but able to produce few correct responses, revealed a reduction in the frontal activations, still with right lateralization, disappearance of the temporal activations, and new activations in the right inferior parietal lobe (Fig. 2f). In the same fMRI session, the response naming task still elicited activation of the right superior temporal sulcus, in the exact location activated in the pre-surgical fMRI study (Fig. 2e).

After 6 months of the first surgery, the patient was seizure-free, and language was significantly improved,

Fig. 1 Pre-surgical findings. **a** Interictal EEG (wakefulness). Abundant epileptic activity localized over the right temporal region (phase reversal on the F8 electrode). **b** Interictal EEG (NREM sleep). Epileptic activity increased and diffused. **c** Ictal EEG. Right temporal fast discharge, later involving the homolateral frontal regions and contralateral temporal regions. **d** Structural MRI (FLAIR). Large temporo-parietal cyst and the atrophic and hyperintense right hippocampus. **e** fMRI (word fluency). Right superior temporal sulcus activation. Three conditions were alternated in a six-cycle block design: phonemic fluency, semantic fluency, nonsense word repetition. To check online the performance, subjects pronounce aloud each word during each 1 s of pause between EPI scans. 100 EPI scans (TE 52 ms, TR 3,000 + 1 s interscan time, FOV 256 mm, 128 × 128 matrix, 25 contiguous 4-mm-thick axial slices) were acquired on a 1.5-T scanner with an eight channels phase-array coil. For the analysis (Brain Voyager software), after slice timing, motion correction, and smoothing with a gaussian filter (4-mm FWHM), the general linear model was applied to the time series of each voxel. Clusters of more than 16 contiguous voxels statistically correlated (significance threshold of $p < 0.00001$ uncorrected) with the model are considered activated. **f** fMRI (word fluency), group analysis of 10 normal right-handed controls (21–35 years). Striking left frontal dominance. **g** fMRI (word fluency). Bilateral frontal activation with right hemispheric dominance



even though spontaneous speech was still affected by occasional anomia and phonemic paraphasias. Semantic fluency, already affected at baseline, was the most impaired (Table 1). After 1 year of first surgery, language tests were normal, the patient was still seizure-free, and the EEG showed recovery of the background activity in the RH, with only mild slow abnormalities in right temporo-parietal regions (Fig. 2c).

Table 1 Neuropsychological assessment

Neuropsychology test results (raw scores)	Preoperative baseline	6 weeks after first surgery	6 months after first surgery
Abstract reasoning: Raven's matrices	33	25	32
Selective attention: attentive matrices	49	22[a]	43[b]
Divided attention: trail making test			
Part B	129	380[a]	134
Part A	70[b]	180[a]	47
Set shifting: Weigl sorting test	12	3[a]	10
Visual recognition: street completion test	10	2[a]	8
Constructive praxis: Rey complex figure copy	28.5[a]	9.6[a]	33
Ideomotor praxis: imitating gestures	20	17[b]	20
Orofacial praxis: imitating facial expressions	20	15[a]	20
Verbal short-term memory: digit span	5	3[a]	5
Visuospatial short-term memory: Corsi span	4[b]	3[a]	5
Verbal long-term memory: short story	15.5	0[a]	10[b]
Visuospatial long-term memory: Rey figure delayed	16.5[b]	0[a]	18[b]
Word fluency			
Phonemic cue	27	3[a]	24[b]
Semantic cue	31[b]	5[a]	28[a]
Verbal comprehension: token test	34	14[a]	33
Aachener aphasic test			
Token test		16	72
Repetition		107	148
Written language		26	88
Naming		65	117
Comprehension		71	112

The neuropsychological profile was assessed with the test battery for epilepsy patients used in our institution [7]. No overt seizures occurred before or during the tests in any session. Test scores were compared with single cut-off scores after transformation into age- and education-adjusted scores

In comparison with the normative data, patient's scores indicating a very low performance[a] and a borderline performance[b] are marked

Discussion

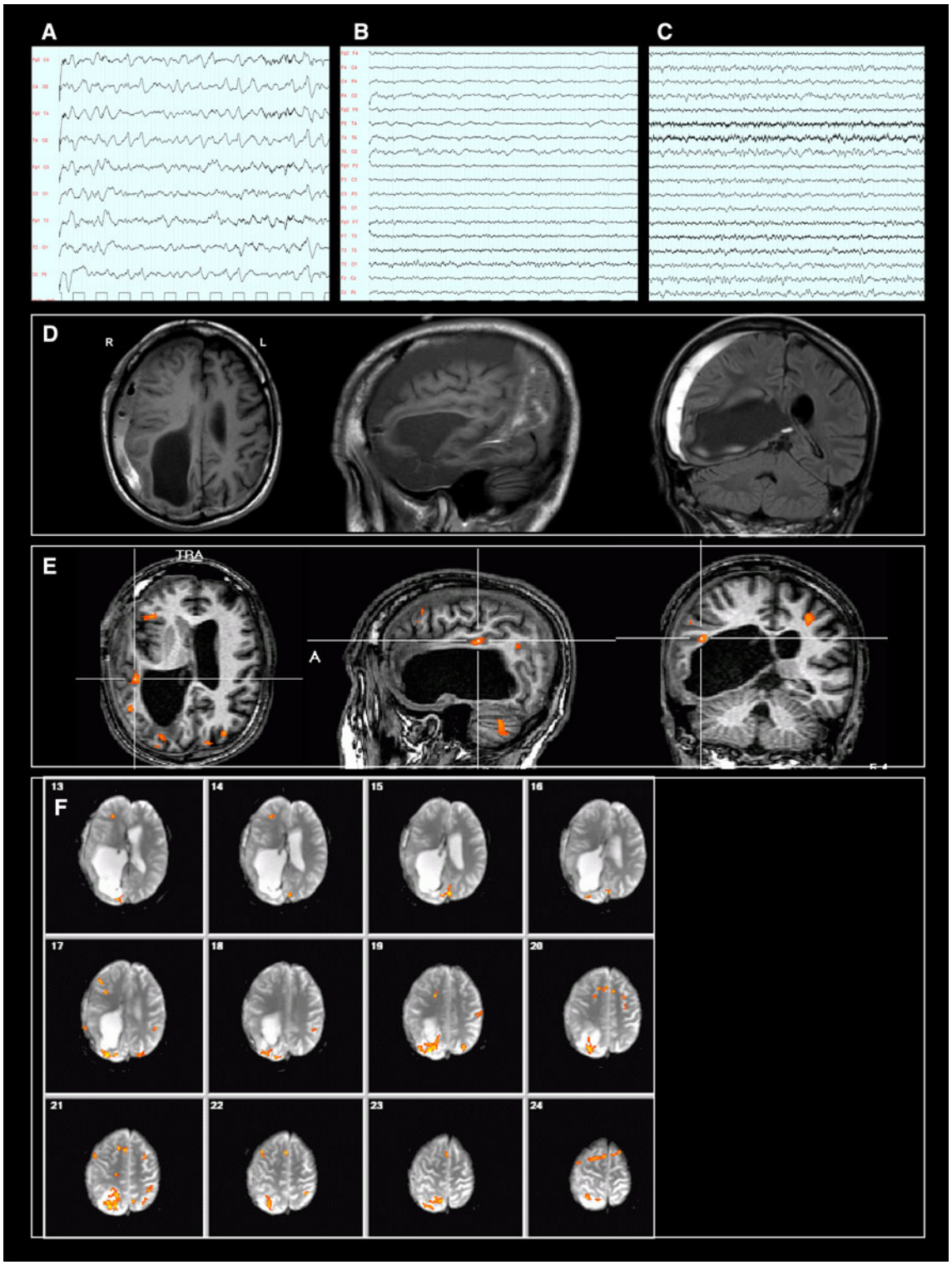
Right hemisphere language is generally considered rare, although in a large transcranial Doppler study, it was found in 7.5% of right handers [9]. This percentage is higher in left TLE, due to the prolonged effect of seizures on the brain and/or to pre-existing brain pathology [2–6]. When a RH lesion in a right hander causes language deficits, it is considered a "crossed aphasia" and it is estimated to occur in <3% of all aphasics [10]. To our knowledge, only three such cases underwent fMRI evaluations: one with a large right frontal meningioma [11], one with a right hemispheric seizure secondary to a temporal astrocytoma [12], and one with neurodegeneration of the RH causing primary progressive aphasia [13]. In each case, language had likely developed in a normal RH.

The present case is particularly rare because language developed in a dysmorphic and dysfunctional RH. Focal epilepsy was caused by a RH malformation that likely developed in the perinatal period, well before language acquisition. Why the affected RH continued to develop

Fig. 2 Post-surgical findings. **a** EEG (reduced montage) at the onset of status epilepticus, with psychomotor agitation and mutism. Bilateral slowing of background activity, and irregular rhythmic delta and sharp activity on the temporal and posterior regions of the right hemisphere, with some contralateral diffusion. **b** EEG 5 days after the onset of the status epilepticus, with the patient still aphasic. Irregular θ–δ activity still visible on the temporal and posterior regions of the right hemisphere. On the left hemisphere, the background activity is now more organized. **c** EEG 1 year after first surgery. Background activity is well organized in both hemispheres. The θ–δ irregular activity is still evident on the right posterior temporal regions. **d** Structural MRI 2 weeks after first surgery. Right temporal–parietal subdural hematoma. **e** fMRI (response naming) 6 weeks after first surgery. Consistent activation of the right superior temporal sulcus, as in Fig. 1e. Acquisition parameters as forward fluency. Three conditions were alternated in a six-cycle block design: auditory response naming, visual response naming, stereotyped phrase completion. **f** fMRI (word fluency) 6 weeks after first surgery. Poor frontal activation, still right dominance

language is unclear, although chances are it was predisposed to do so, and the cyst mass effect and epilepsy had no effect in diverting this course. An alternative explanation is that co-occurring unseen left hemisphere abnormalities forced a partial right ward shift in language lateralization which, again, was not affected by the RH pathology.

The functional significance of the right-sided fMRI activations was not fully appreciated until the unexpected complications of the subdural hematoma and consequent



epileptic status. The compression of the hematoma on the right temporal lobe (Fig. 2d) likely suppressed normal functioning, as EEGs performed at the onset of the language impairment (Fig. 2a) showed localized severe abnormalities in right temporo-parietal regions. Thus, MRI, fMRI, and EEG supported the clinical suspicion of RH language, further supported by the partial reversal of the aphasic symptoms after hematoma drainage, resolving to a residual semantic fluency deficit 6 months later, and normal language 1 year after surgery.

As expected in crossed aphasia, aphasia was the clinically dominant deficit due to the RH dysfunction, but not the only cognitive abnormality. Visuospatial reasoning, attention, constructive praxis, and longterm memory were also impaired. As reviewed in a metanalysis of crossed aphasia case reports, "typical right hemisphere (i.e., non-language-dominant) symptoms were frequent, but rarely carefully reported or assessed" [10].

This case emphasizes the need for caution during neurosurgical planning in the presence of fMRI atypical activations, even when seen in atypical locations.

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