Epilepsy & Behavior 81 (2018) 49–54

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

Adapting a memory fMRI research protocol in clinical routine: Feasibility and results

Ovidio Solano Cabrera [a,b], Stéphane Lehéricy [c,d,e], Véronique Masson [a], Séverine Samson [f], Sophie Dupont [a,d,e,g,*]

[a] Epilepsy unit, AP-HP Groupe hospitalier Pitié-Salpêtrière–Charles Foix, F-75013 Paris, France
[b] Epilepsy Clinic, Neurology department, Social Security Salvadoran Institute, San Salvador, El Salvador
[c] Neuroradiology unit, AP-HP Groupe hospitalier Pitié-Salpêtrière–Charles Foix, F-75013 Paris, France
[d] Inserm U 1127, CNRS UMR 7225, UMR S 1127, Institut du Cerveau et de la Moelle épinière - ICM, Centre de Neuroimagerie de Recherche - CENIR, F-75013 Paris, France
[e] Sorbonne University, UPMC Univ. Paris 06, F-75005 Paris, France
[f] Laboratoire PSITEC (EA 4072), Université de Lille, F-59000 Lille, France
[g] Rehabilitation unit, AP-HP Groupe hospitalier Pitié-Salpêtrière–Charles Foix, F-75013 Paris, France

ARTICLE INFO

Article history:
Received 19 September 2017
Revised 10 November 2017
Accepted 19 November 2017
Available online xxxx

Keywords:
Medial temporal lobe epilepsy
fMRI
Episodic memory
Neuropsychological testing
Postoperative outcome

ABSTRACT

Objective: The objective of this study was to test the reliability of functional magnetic resonance imaging (fMRI) evaluation of memory function in clinical practice to predict postoperative memory decline in patients with refractory medial temporal lobe epilepsy (MTLE) candidate to surgery.
Methods: Twenty-six consecutive patients with MTLE who underwent a complete presurgical evaluation were included. All patients underwent fMRI memory study and complete neuropsychological assessment. Lesions consisted in hippocampal sclerosis in 18 patients (12 right and 6 left), dysembryoplastic neuroepithelial tumor (DNET) in 5 cases (4 right, 1 left), epidermoid cyst in one patient (right). Two patients had no lesion (2 left).
Results: Nineteen patients (73%) underwent surgery. The other seven patients (27%) declined surgery, mainly because of the risk of memory deficit. The fMRI procedure correctly predicted both verbal and nonverbal memory postoperative outcome in 13 of the patients (72%), failed to predict a postoperative memory worsening in only two patients (12%), and predicted worsening in three patients (17%) that remained stable (versus 44%, 39%, and 17% with the sole neuropsychological testing). The reliability of the fMRI procedure was not influenced by the type of lesion, the side of the epileptic focus, or the type of preoperative memory profile (typical or atypical).
Significance: Appearing as a valuable clinical tool to predict postoperative memory outcome, fMRI may add information over and above other available tests.

1. Introduction

Surgery is an effective therapy for refractory medial temporal lobe epilepsy (MTLE) [1]. Candidate patients with epilepsy to the surgery are usually concerned by the following two major points: i) seizure freedom after surgery and ii) after effects following surgery, especially the risk of memory decline. Indeed, a substantial number of patients with MTLE experience a worsening of episodic memory following surgery [2]. Several studies intended to identify clinical factors that are associated with a significant postoperative memory decline. These factors include surgery in the dominant hemisphere for language, low preoperative memory function, later age of seizure onset, low verbal IQ, persistence of seizures after surgery, persistence of interictal epileptiform discharges on postoperative electroencephalography (EEG), postictal memory deficit, mood disturbance before surgery, and magnetic resonance imaging (MRI) findings other than exclusively unilateral medial temporal sclerosis [2–13]. To date, the "gold standard" prediction of potential postoperative memory deficits is still based on neuropsychological measures and the Wada test. But recent studies have pointed out the interest of functional imaging studies to improve the prediction of postoperative memory outcome. Firstly, studies have demonstrated the ability of memory functional MRI (fMRI) protocols to replace the Wada test and accurately predict memory outcome [14–18]. Further studies have confirmed the potential of fMRI as a preoperative predictor of postsurgical memory decline. Most of these studies suggested that the functional capacity of the resected hippocampus, rather than the functional reserve of the contralateral hippocampus, was what determined the postoperative memory decline [19–25]. In other terms, patients with a consistent fMRI activation of the hippocampus to be resected were at high risk of postoperative memory decline. In 2010, our team has conducted a study to determine which of fMRI or Wada test were the best predictors of postoperative changes in memory and could help to provide to patients a precise counseling before surgery [26]. We found that the equation based on left fMRI

* Corresponding author at: Epileptology Unit and Rehabilitation Unit, Hôpital de la Salpêtrière, 47, boulevard de l'Hôpital, 75651 Paris cedex 13, France.
E-mail address: sophie.dupont@aphp.fr (S. Dupont).

https://doi.org/10.1016/j.yebeh.2017.11.018
1525-5050/© 2017 Published by Elsevier Inc.

medial temporal lobe (MTL) activation during delayed recognition, side of the epileptic focus and preoperative global verbal memory score correctly determined the worsening of verbal memory in 90% of the patients. Wada test data were not predictive of changes in either verbal or nonverbal memory. Based on these promising preliminary results, we decided to implant our research protocol in clinical routine in order to validate its feasibility and reliability. We wanted to test the reliability of our protocol research that had been validated in patients with MTLE with hippocampal sclerosis with atypical memory profiles in consecutive patients with MTLE with and without hippocampal sclerosis, with typical or atypical memory profiles. We also aimed to study the impact of the fMRI results on the surgical decision.

2. Methods

2.1. Subjects

The study population included 26 patients with consecutive MTLE who underwent a complete presurgical evaluation in our epilepsy center from September 2014 to September 2015.

This retrospective study was approved by the local ethics committee, in agreement with the Declaration of Helsinki. Informed written consent was obtained from all patients.

Inclusion criteria were the following:

1 Well explored unilateral MTLE with at least a prolonged surface video-EEG and a structural MRI;
2 Complete neuropsychological assessment including episodic verbal and visuospatial tests (Full Scale IQ, (digit)-span, verbal memory testing (Jones-Gotman verbal learning (MJG) and/or Rey auditory verbal learning test) and nonverbal testing (Rey/Taylor complex figure, and/or Aggie's figures visual learning);
3 Decision of surgery for epileptic reasons subject to memory assessment.

The degree of deficit of learning and recognition in verbal and nonverbal memory for every patient was categorized as normal, slight, moderate, and severe.

2.2. Protocol

We used the fMRI memory protocol validated by our team [26]. Memory tasks included episodic memory encoding and recognition tasks. Patients are tested on two consecutive days to create two recognition conditions that differed in relation to the delay of recognition as follows: immediate recognition or 24-hour-delayed recognition. For each session, a sequential task-activation block paradigm was employed alternating an experimental condition and a control condition. Session 1 was performed outside the scanner.

In Session 1, the encoding task consisted of three blocks of 12 study stimuli repeated over the 3 blocks alternating with four blocks of 12 control stimuli. Stimuli consisted of color photographs of simple objects, such as fruit, flowers or animals that may be encoded by both verbal and nonverbal strategies. Each stimulus was presented during 3 s. Each block lasted for 36 s. Control stimuli were obtained by degrading study stimuli with a random-rectilinear algorithm from Adobe Photoshop 6.0. Patients were explicitly instructed to try to remember the studied stimuli for a later test.

After a delay of 60 s, patients performed the recognition task. During this task, subjects were presented with 24 stimuli consisting in 12 novel stimuli and the 12 previously learnt stimuli, displayed in blocks of 8 stimuli (4 new/4 study) alternating with four blocks of 8 control stimuli. Each stimulus was presented during 3 s. Each block lasted for 24 s.

In Session 2, the following day, subjects began the fMRI session by a 24-hour-delayed recognition of stimuli encountered the previous day followed by new encoding and immediate recognition tasks.

2.3. fMRI acquisition

The MRI data were acquired from an MRI machine 3T GE Signa. The subjects were placed in supine position. Their heads were immobilized with cushions to reduce movement artifacts. The images were projected onto a mirror located at the end of the bore of the imager. For each subject, a classic structural T1-weighted three-dimensional (3D) Brain Volume imaging (BRAVO) was first collected to provide detailed anatomical information. Then functional imaging was performed using 39 continuous slices using single shot gradient echo planar imaging covering the entire brain in the coronal plane perpendicular to the long axis of the hippocampus (repetition time = 3 s, echo time = 35 ms, flip angle = 90°, matrix = 64 × 64, field of view = 20 × 20 cm^2, slice thickness = 3 mm). The encoding task included 84 images (acquisition time = 4 min and 12 s) and the delayed and immediate recognition tasks included 56 images (acquisition time = 2 min and 48 s). Four dummy scans were added at the beginning of each fMRI acquisition. MRI acquisitions including both structural and functional images lasted 45 min.

2.4. Data analysis

Data processing was performed using Brainwave software® based on an advantage workstation (General Electrics, Milwaukee). The fMRI scans were corrected for head movements using a six-parameter rigid body motion correction via registration to the first volume. The realigned functional images were realigned to the anatomical reference in the native space and smoothed with a 4-mm Gaussian filter. General linear models were defined individually across runs, each with one regressor per condition. The task regressors were defined as a box-car convolved with the canonical hemodynamic response function. Voxels were considered to be significantly activated in comparison with the reference task at z-score > 3, uncorrected for multiple comparisons. This individual analysis focused on MTL activations (hippocampus proper and parahippocampal cortices, Brodmann areas 27, 28, and 34–36). Only individual analysis was performed for each subject.

2.4.1. fMRI lateralization

To evaluate MTL lateralization, we considered the presence or absence of activation within the left and right hippocampal and parahippocampal regions. Images were visually inspected for activations in these areas as usually done during the regular neuroradiological reading in a clinical setting. Activation was considered lateralized in the right or left MTL if it was clearly predominant in one hemisphere and bilateral if activation was symmetrical or mildly asymmetric.

2.5. Surgical decision

After the neuropsychological and fMRI assessments, each patient was reviewed during the neurological staff to take the surgical decision according to both neuropsychological and fMRI activation data. The surgical indication was retained in case of the following:

1) perfect congruence of electroclinical data from video-EEG and MRI imaging
2) no risk of postoperative amnesia

When a memory decline was predictable, enlightened information was provided to the patient, so that he could make his decision.

2.6. Postoperative evaluation

One year after surgery, all patients were systematically hospitalized during 5 days to undergo a complete postoperative evaluation including clinical visit, MRI, EEG, and a neuropsychological assessment including