Epilepsy & Behavior 79 (2018) 34–41

Contents lists available at ScienceDirect

Epilepsy & Behavior

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

The clinical impact of integration of magnetoencephalography in the presurgical workup for refractory nonlesional epilepsy

Ismail S. Mohamed [a,b], Alain Bouthillier [c], Arline Bérubé [d], Patrick Cossette [d], Patrice Finet [c], Jean-Marc Saint-Hilaire [d], Manon Robert [e], Dang Khoa Nguyen [d,*]

[a] IWK Health Center, Department of Pediatrics, Division of Neurology, Halifax, Canada
[b] University of Alabama, Department of Pediatrics, Division of Neurology, Birmingham, AL, USA
[c] Division of Neurosurgery, Notre-Dame Hospital (CHUM), University of Montreal, Canada
[d] Division of Neurology, Notre-Dame Hospital (CHUM), University of Montréal, Canada
[e] Neuropsychology and Cognition Research Center, Psychology Department, University of Montreal, Canada

ARTICLE INFO

Article history:
Received 26 August 2017
Revised 11 October 2017
Accepted 27 October 2017
Available online xxxx

Keywords:
Magnetoencephalograpy
Nonlesional
Refractory
Epilepsy

ABSTRACT

Objective: For patients with nonlesional refractory focal epilepsy (NLRFE), localization of the epileptogenic zone is more arduous, and intracranial electroencephalography (EEG) (icEEG) is frequently required. Planning for icEEG is dependent on combined data from multiple noninvasive modalities. We report the negative impact of lack of integration of magnetoencephalography (MEG) in the presurgical workup in NLRFE.
Methods: Observational MEG case series involving 31 consecutive patients with NLRFE in an academic epilepsy center. For various reasons, MEG data were not analyzed in a timely manner to be included in the decision-making process. The presumed impact of MEG was assessed retrospectively.
Results: Magnetoencephalography would have changed the initial management in 21/31 (68%) had MEG results been available by reducing the number of intracranial electrodes, modifying their position, allowing for direct surgery, canceling the intracranial study, or providing enough evidence to justify one. Good surgical outcome was achieved in 11 out of 17 patients who proceeded to epilepsy surgery. Nine out of eleven had MEG clusters corresponding to the resection area, and MEG findings would have allowed for direct surgery (avoiding icEEG) in 2/11. Six patients had poor outcome including three patients where MEG would have significantly changed the outcome by modifying the resection margin. Magnetoencephalography provided superior information in 3 patients where inadequate coverage precluded accurate mapping of the epileptogenic zone.
Conclusion: In this single center retrospective study, MEG would have changed patient management, icEEG planning, and surgical outcome in a significant percentage of patients with NLRFE and should be considered in the presurgical workup in those patients.

1. Introduction

Epilepsy surgery is recommended when medication fails and the seizures are confined to one area of the brain where tissue can be safely removed [1]. Detection of an epileptogenic lesion on a brain magnetic resonance study (MRI) substantially improves surgical outcome, since the location of the lesion is usually congruent with the epileptogenic zone (EZ) [2]. Unfortunately, one-quarter of drug-resistant focal epilepsies have no identifiable lesions [3]. In these patients with nonlesional refractory focal epilepsy (NLRFE), approximation of the EZ must rely heavily on the remaining available tools: scalp video-EEG, ictal and interictal single-photon emission computed tomography (SPECT), and positron emission tomography (PET) [4]. While generally useful in medial temporal lobe epilepsy, most of these tools lack adequate spatiotemporal resolution to accurately localize the EZ in neocortical epilepsy, and many will require invasive intracranial electrode studies. Because chronic implantation of intracranial electrodes carries a risk of infection and hemorrhage, it is best to limit the number of electrodes without compromising the ability to localize the EZ adequately. The limitations listed above translate into a poor surgical outcome for patients with NLRFE: ~51% for nonlesional temporal lobe epilepsy and ~35% seizure-free for nonlesional extratemporal lobe epilepsy [2].

Magnetoencephalography (MEG) is being used with increasing frequency in the presurgical evaluation of patients with epilepsy [5–8]. Magnetoencephalography spike sources are overlaid on the subject's MRI creating magnetic source images (MSI). Magnetic source image results are then combined with results from other noninvasive modalities to guide the surgical decision, including the choice of surgery type and the number and location of intracranial electrodes. In that context, MSI results have been compared with other conventional noninvasive

* Corresponding author at: Division of Neurology, Notre-Dame Hospital (CHUM), 1560 Sherbrooke East, Montreal, Quebec H2L 4M1, Canada.
E-mail address: d.nguyen@umontreal.ca (D.K. Nguyen).

https://doi.org/10.1016/j.yebeh.2017.10.036
1525-5050/

presurgical evaluation tools (PET and SPECT). A presurgical evaluation including MSI has been shown to provide clinically pertinent and complementary information about the EZ in about 20–30% of patients with refractory focal epilepsy, leading to better patient selection, increased accuracy of intracranial EEG (icEEG), and potentially better postsurgical outcome [9–12]. As information from all modalities is often utilized to guide the surgical decision, the impact of lack of availability or omission of any of these modalities on the surgical outcome cannot be directly assessed.

In the present study, we report on the negative impact of the lack of utilization of MSI on the surgical outcome in a group of patients with NLRFE.

2. Methods

2.1. Study context

An MEG system was purchased and installed in 2006 by a group of researchers on neuropsychology and cognition. Benefiting from this platform, our group set up a research project to evaluate the value of MEG for patients with NLRFE. The study was approved by our institutional ethics committee, and all patients signed a consent form. For various reasons (limited funding, personnel recruitment and training, pipeline set-up, exploration of different source analysis methods, learning curve for interpretation of results, etc.), MEG results were not included in the preoperative consensus decision until January 2010, as the acquired MEG data could not be analyzed in a timely fashion and/or were felt to still be experimental. In those patients, the surgical decision was based on the epilepsy surgery conference consensus after review of the standard presurgical workup. The latter consisted in 3.0 Tesla high-resolution brain MRI, video-scalp EEG recording of seizures, ictal SPECT, and ^{18}Fluroro-deoxy-glucose-PET.

2.2. Participants

Between April 2006 and January 2010, 31 consecutive patients (mean age: 36 years; range: 13–68) with NLRFE investigated for potential epilepsy surgery were recruited for the study. Based on the standard presurgical evaluation, 12/31 patients (39%) were presumed to have nonlesional temporal lobe epilepsy and the remaining 19 (61%), nonlesional extratemporal lobe epilepsy. Magnetic resonance imaging was totally normal in 26 subjects. The remaining five subjects had MRI abnormalities, which were nonspecific or were not felt to be epileptogenic nor localizing at the time of the evaluation (Table 1).

2.3. Magnetic source imaging (MSI)

Magnetoencephalography studies were generally performed while patients were admitted for long-term video-EEG monitoring as part of their presurgical evaluation. In that context, antiepileptic drugs had frequently been tapered off or dosages lowered. Furthermore, patients were in a state of mild sleep deprivation (4 h) for the MEG study.

A CTF whole-head 275-sensor MEG system in a heavy magnetically shielded room was used for the recordings (CTF, Coquitlam, BC, Canada). The total average recording time was 90 min, typically in multiple datasets, each 5 min in duration. Both EEG and MEG data were collected at a sampling rate of 600 Hz and band pass filtered at 1–70 Hz. The MEG data were analyzed by an epileptologist (IM) who was experienced in MEG interpretation and only had access to a sample of the morphology of scalp-EEG spikes recorded during prior video-EEG recordings. Interictal epileptiform discharges (IEDs) were identified by examining the MEG recordings and cross-referencing them with the simultaneous EEG recording. Source localizations of epileptic events were obtained using the single equivalent current dipole (ECD) model applied to the earliest peak of each IED with a multiple sphere conductor head model in which a single sphere was fit to the digitized head shape for each MEG sensor in each patient. Interictal epileptiform discharges were analyzed if they demonstrated a stable topography map over the rising phase of the spike, and dipole fits were considered valid when the goodness of fit was >70% and with a dipole moment of 50–400 nAm. Equivalent current dipoles were then superimposed on the coregistered patient's MRI.

Magnetoencephalography datasets were classified into four categories [13,14]: 0) No or <6 MEG spike sources; 1) Single cluster (≥6 spike sources ≤ 1 cm apart); 2) Multiple clusters; and 3) Scatter (i.e., ≥6 spike sources > 1 cm apart). Temporal lobe ECDs were defined as localized to the mesiobasal temporal regions if located predominantly in the anterior half of the temporal lobe and had horizontal or anterior vertical dipole orientation. Dipole sources located exclusively to the posterior half of the temporal lobe with vertical orientation were classified as localized to the lateral temporal lobe [15].

2.4. Assessment of MSI contribution to patient management

To determine whether MSI influences patient management, results of the standard presurgical evaluation for all patients were presented randomly to a multidisciplinary epilepsy surgery team (unaware of MSI results). This team included three epileptologists (AB, PC, and JMSH) who had not previously been involved in the care of the patients discussed. For each patient, the presumed (p) localization of the EZ (pTemporal, pExtratemporal) and the plan of action (A- focal resective surgery without icEEG, B- icEEG recordings, or C- rejected because considered poor surgical candidate) were determined. When icEEG was planned, the electrode locations were anatomically determined, and the total number of contacts was calculated. In general, the results of this evaluation were similar to the actual plan of management of the patient adopted at the epilepsy conference. If there was a discrepancy between the number of icEEG contacts determined by this blinded process and the actual number of contacts used, the latter number was used. In a second step, MSI results were presented by a fourth epileptologist (DKN) who had not taken part in the decision-making process. Any changes in the initial patient plan management or changes in initial icEEG planning to add or remove electrodes were noted. Clinical relevance of changes in patient management related to MSI findings was evaluated on a case-by-case basis (Fig. 1).

2.5. Correlation between MSI, icEEG findings, and surgical outcome

We also compared MSI results with icEEG findings on a case-by-case basis for the subset of patients who eventually underwent an icEEG study. Magnetic source image findings were considered concordant with ictal icEEG if interictal spikes were found in the same sublobar region(s): frontal polar, dorsal lateral frontal (superior), dorsal lateral frontal (inferior), mesial frontal, anterior parietal, posterior parietal (superior), posterior parietal (inferior), mesial parietal, lateral occipital, mesial occipital, lateral temporal, temporal polar, mesial temporal, and insula [16]. Ictal icEEG was considered nonlocalized if ictal onset involved multiple contiguous sublobar regions and multifocal if multiple noncontiguous regions were involved. We then evaluated surgical outcome among patients who had surgery. An Engel I or II outcome was considered good, while an Engel III or IV outcome was deemed poor [17].

3. Results

3.1. Magnetic source imaging findings

Magnetoencephalography showed spikes in 28/31 patients (90%) (Table 1). No MSI results were available for the three remaining patients due to a coregistration error (1), absence of spikes (1) or fewer than 6 MEG spike sources in one patient (MSI type 0). Twenty-two out of