Case Report

Praxis-induced seizures in a patient with juvenile myoclonic epilepsy: MEG-EEG coregistration study

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ABSTRACT

Purpose: Juvenile myoclonic epilepsy (JME) is one of the most common generalized idiopathic epilepsies of childhood and adolescence. In some patients with JME, mathematical calculus and praxis may induce myoclonic seizures.

Methods: A reflex myoclonic seizure was recorded by simultaneous magnetoencephalography (MEG) and electroencephalography (EEG) when a generalized spike–wave synchronous pattern at 3 Hz was observed.

Results: Source reconstruction localized the epileptogenic area to the right premotor frontal cortex.

Conclusions: The present study demonstrates that the origin of epileptiform activity in JME can be localized in brain areas associated with the premotor frontal cortex.

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1. Introduction

Mental activity, such as mathematical calculus, and diverse manipulative tasks can induce myoclonic seizures in some patients with JME [1–7]. The first authoritative report on praxis-induced JME was carried out by Inoue et al. [5] Later, Matsuoka et al. [1] also reported that the various processes underlying the precipitating events share common features and described them as “praxis-induced seizures” [1,2,8].

So far, however, the pathophysiological mechanism of this syndrome remains uncertain, although several studies suggest a hyperexcitability of the somatomotor frontal cortex in the framework of a diffuse cortical hyperexcitability [4,9–11].

In this work, the unusual case of a patient with JME with praxis-induced reflex seizures was studied. Magnetoencephalography was used to register one of these seizures. In addition, we conducted a literature review on the pathophysiology of JME.

2. Case presentation

A 29-year-old, right-handed male was diagnosed with JME on clinical grounds. He did not have a familial history of epilepsy. At 8 years of age, he began with myoclonic jerks in both arms, predominantly the left. The jerks were observed after waking up. He also presented tonic–clonic seizures and absences. The EEG showed 3-Hz generalized spike and wave patterns with photoparoxysmal response (Fig. 1).

At school, he began having jerks during mental tasks, especially with mental calculation. When he was older, he could not perform work as a waiter, because while calculating a sum, he often threw away the tray in his hands. He was treated with different combinations of levetiracetam, valproic acid, and lamotrigine. Finally, it was found out that he was taking cannabis. After he stopped taking cannabis, the seizures were controlled with valproic acid, but reflex seizures persisted so he could not perform any intellectual work. The seizures were triggered by playing chess, doing sums or subtracting, or playing any other game that required mental concentration. These seizures consisted of a stereotyped pattern: left forearm flexion posture, and a dystonic posturing of the left hand.

Monitoring with 24-hour video-EEG was performed showing generalized 3-Hz spike–and–wave discharges. In order to exclude any kind of focal pathology, a 3-T magnetic resonance imaging (MRI) (General Electric Medical Systems, Milwaukee, WI, USA) with epilepsy protocol including sagittal T1 fluid-attenuated inversion recovery, and axial T2 fast spin echo was recorded; both sets of images were normal. The brain PET-FDG study was also normal.

A neuropsychological evaluation was performed, including direct and reverse digits test, Corsi cube test, Rey figure, texts memory
subtests, FAS verbal fluency test, arithmetic and similarity tests, trail making test, STROOP, and Wisconsin cards classification test. The neuropsychological evaluation showed a deficit consistent with bilateral dysfunction of the dorsolateral.

All data were analyzed anonymously and ethical approval was granted by the Local Ethics Committee of the Hospital.

3. Methods

3.1. MEG registration

Magnetencephalography data were acquired during a single 30-min session (sampling rate: 1 kHz, online band-pass: filter 0.10–330 Hz).

Fig. 1. Intermittent electroencephalogram (EEG) (amplitude: 15 μV/mm; filter: 30 Hz): A) bipolar montage, showing high-amplitude, widespread, bilaterally synchronous 3-Hz epileptiform discharges; B) average reference montage, showing negative epileptiform discharges with frontocentral maxima.

Fig. 2. A) Ictal event recorded by magnetoencephalography (MEG) right frontal and parietal sensors. B) Simultaneous electroencephalography (EEG) recordings from some representative channels. Bilateral parietal and predominantly right frontal activation at seizure onset (t0, red cursor). C) MEG source reconstruction at the seizure onset time (t0), showing bilateral parietal predominantly right frontal activation in the course of the seizure spread. D) MEG and EEG sensor topography at t0. E) Source activation overlapped with the subject MRI (axial, coronal and sagittal view). Cursor located at the point of maximum activity at seizure onset time, t0. MRI coordinates (169, 136, 172), SCS (36.5, -43.5, 68.0), and MNI (45.8, 8.3, 31.4).
using a 306-channel whole head ElektaNeuromag® MEG system (Elekta Oy, Helsinki, Finland), comprising 102 magnetometers and 204 planar gradiometers in a helmet-shaped array covering the entire scalp, while the subject was seated inside a magnetically shielded room (Vacuumschmelze GmbH, Hanau, Germany). A 64-channel EEG (included in the Elekta system) was also recorded simultaneously. Eye movements were monitored by simultaneously recording the electrooculogram (EOG) with three Ag/Cl electrodes, two above and below the right eye and one at the right earlobe (ground reference), following guidelines of good MEG practice [12]. Four head position indicator (HPI) coils, whose data were used to correct head movement during the session, were placed on the scalp, appropriately spaced in the region covered by the MEG helmet. The locations of the nasion, two preauricular points, and the four HPI coils were digitized prior to MEG study using a 3D-digitizer (Fastrak; Polhemus, Colchester, VT, USA) to define the subject-specific Cartesian head coordinate system. One hundred to two hundred additional anatomical points were digitized on the head surface to provide a more accurate shape of the subject’s head together with the EEG electrode positions. Once the subject was comfortably positioned in the MEG machine, short electrical signals were sent to the HPI coils to localize them with respect to the MEG sensor array. The session consisted of 20 min of resting state; 10 min with eyes open fixating vision on a cross on the screen, followed by 10 min with eyes closed. The patient also performed mathematical mental activity consisting of a series of sums, subtractions, multiplications, and square roots of increasing difficulty during another 10 min, as a mechanism to trigger ictal events.

3.2. MEG source reconstruction

External noise on MEG signals was removed using the temporal extension of Signal-Space Separation (tSSS) [13] as implemented with the MaxFilter® software (version 2.0 ElektaNeuromag®, sliding window of 10 s, subspace correlation limit of 0.98) [14]. The individual scalp and cortical surfaces of the patient were extracted from the MRI volume data using Freesurfer [15], with default parameter settings. Head position indicator (HPI) information was used to complete the registration of the MEG channel array with the subject’s head surface envelopes obtained from MRI, thereby defining a subject-centered coordinate system. Magnetoencephalography forward and inverse modeling steps for source reconstruction [16] were subsequently completed using Brainstorm [17], using a multisphere analytical approximation for the head model [18] and weighted-minimum norm estimate (wMNE) with unconstrained source orientation. [19].

4. Results

A myoclonic seizure beginning as left forearm flexion, followed by dystonic posturing of the left hand, was triggered by mental calculation. The EEG showed paroxysmal discharges consisting of 3-Hz synchronous, symmetric spike–wave activity including all MEG derivations. Source reconstruction corresponding to the first spike and wave complex localized the origin of the discharge to the right frontal region (Fig. 2). Through seizure propagation, a frontal predominating generalized activation of sources was observed (see the video provided in the Supplementary Material).

5. Discussion

A patient with well-defined JME was studied; he usually had myoclonic seizures on awakening with onset in adolescence; the patient’s EEG at diagnosis showed typical generalized spike–wave paroxysms at 3 Hz. The patient also presented with reflex myoclonus triggered by different. One of these seizures could be recorded using MEG. The subsequent seizure source reconstruction constrained to the patient’s anatomical MRI surface located anatomically the beginning of the seizure to the right frontal lobe. These results correlate well with the patient’s symptoms: the asymmetric myoclonus predominantly on the left side, the left forearm bending, and sometimes the dystonic attitude of the ipsilateral hand. Thus, the data correspond to the semiology of foci in the frontal premotor area. Rarely, asymmetrical myoclonic jerks have been described in patients with JME [19,20–21]. Additionally, neuropsychological results also supported the existence of dysfunction attributable to the frontal lobes; specifically, concept formation, mental flexibility, information speed processing, planning and complex behavior organization, tendency to persevere, and impulsivity.

Although a genetic basis of JME is presumed, the specific pathogenetic mechanism is not entirely known [20]. Several studies have demonstrated subtle structural changes in the frontal cortex in patients with JME as well as predominantly dysexecutive cognitive dysfunction [22–24]. Consistent with these results, the work presented by Vollmar et al demonstrates coactivation between the primary motor cortex and supplementary motor area as well as an increase in functional connectivity between the motor and cognitive frontal networks [25]. Recent studies confirm such findings and demonstrate the existence of globally dysfunctional neuronal networks with functional connectivity abnormally increased in the premotor area and prefrontal cognitive cortex [25–28].

The presence of reflex seizures in these patients constitutes an important opportunity to study the pathophysiology underlying ictogenesis. In particular, for reflex seizures induced by praxis, the crucial element for precipitating seizures lies in the transformation process that proceeds from the mental conception of a movement (motor idea) or sequential planning of complex spatial tasks the voluntary motor movements that completes the intended action [29]. Glenn et al. hypothesize that in the beginning of the praxis-induced seizures, a proprioceptive stimulus and a local excitatory area are involved [30]. A myoclonic jerk is generated once the neural hyperarousal is able to activate a “critical mass” of the cortical area with synchronization and subsequent spread to the motor cortex through transcortical tracts [30].

In conclusion, reflex seizures triggered by activities involving frontal structure activation in patients with JME confirm the existence of a seizure triggering mechanism in these hemispheric regions. This observation suggests that seizure onset localizes to the frontal lobes in such reflex epilepsies. In this sense, studies using MEG can provide additional information on the location of the epileptogenic area extend our knowledge of ictogenesis in JME.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ebcr.2015.10.002.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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