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Epileptogenic networks in seizures arising from motor systems

Francesca Bonini[a,b], Aileen McGonigal[a,b], Fabrice Wendling[d], Jean Régis[e], Didier Scavarda[f], Romain Carron[e], Patrick Chauvel[a,b], Fabrice Bartolomei[a,b,c,*]

[a] *CHU Timone, Service de Neurophysiologie Clinique, Assistance Publique des Hôpitaux de Marseille, Marseille F-13005, France*
[b] *Institut de Neurosciences des Systèmes, INSERM UMR 1106 Aix Marseille Université, France*
[c] *Hôpital Henri Gastaut/Centre Saint-Paul, CINAPSE, 300 Bd Sainte-Marguerite, 13009 Marseille, France*
[d] *INSERM, U642, Université Rennes 1, Rennes, France*
[e] *Functional Neurosurgery Department, Assistance Publique des Hôpitaux de Marseille, Marseille F-13005, France*
[f] *Pediatric Neurosurgery Department, Assistance Publique des Hôpitaux de Marseille, Marseille F-13005, France*

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Summary Classification of seizures arising from the cortical motor system classically distinguishes between primary motor seizures and supplementary motor area (SMA) seizures. With the aim of better characterizing the underlying networks of motor seizures, we quantitatively studied the ''epileptogenicity'' of brain structures in 28 patients investigated by intracerebral recordings (stereoelectroencephalography, SEEG). Epileptogenicity of various motor regions (rolandic, SMA, pre-SMA, cingulate motor area (CMA), lateral area 6) as well as prefrontal and parietal areas, was calculated according to the ''epileptogenicity index'' (EI), a technique that allows mathematical quantification of rapid discharges at seizure onset. According to the maximal value of EI five groups of patients were identified: precentral, premotor/precentral, mesial premotor, lateral premotor and mesio-lateral premotor groups. Most patients disclosed a complex pattern of motor/premotor involvement, while pure mesial premotor seizures (''SMA seizures'') were rare. A positive correlation between the number of structures exhibiting high EI and epilepsy duration was found, as well as a relationship between high EI values in rolandic cortex and poorer surgical outcome. Seizures arising from the motor system appear to be organized in complex electrophysiological patterns that often involve both lateral and mesial aspects of premotor areas together with precentral cortex.

Introduction

Seizures arising from the cortical motor system are usually classified into two main patterns: motor seizures and supplementary motor seizures (Commission, 1989; Morris et al.,

* Corresponding author at: Service de Neurophysiologie Clinique, CHU Timone-264 Rue st Pierre, Marseille F-13005, France.
E-mail address: fabrice.bartolomei@ap-hm.fr (F. Bartolomei).

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1988). Clinical aspects of pre-central seizures, together with their underlying anatomo-physiological organization, have been extensively studied from the end of the nineteenth century by Sherrington and notably by J.H. Jackson, who, beside the Jacksonian march, also described a wider range of semiological phenomena (Jackson, 1931). Seizures arising from premotor regions have been long recognized, following identification of the frontal adversive fields (Foerster, 1931) and the supplementary motor area (SMA) (Penfield and Welch, 1951). The concept of SMA seizures stemmed from these last observations, further elucidated by several stimulation studies (Bancaud and Talairach, 1967; Chauvel et al., 1996; Fried, 1996; Penfield and Welch, 1951). In anatomical terms, besides the antero-posterior separation of premotor from precentral seizures, a mesial/lateral (or dorso-lateral) division of frontal seizures has also been proposed (Beleza and Pinho, 2011; Chauvel et al., 1995; Quesney et al., 1992; So, 1998). However the utility of such antero-posterior and mesio-lateral separation can be questioned to some degree, given the existence of electroclinical patterns of motor seizures that do not appear to clearly fit these subdivisions. The notion of pre-central seizures has been elaborated by the observation of more complex and bilateral features (Ajmone-Marsan and Goldhammer, 1973; Chauvel et al., 1992a) and, in a similar manner so-called supplementary motor seizures have been demonstrated to possibly involve rolandic cortex, the lateral pre-motor cortex (Baumgartner et al., 1996; Chauvel et al., 1992b) as well as cingulate gyrus/area 24 (Munari et al., 1996).

Recent advances in functional neuroimaging have provided better knowledge of the functional organization of the human motor system, clarifying the roles of different motor areas and revealing a functional gradient within human non-primary motor cortex similar to that found in primate brain (Geyer et al., 2000; Picard and Strick, 1996). This information, together with human stimulation studies, could help to better characterize motor seizures including their semiological features and preferential ictal propagation patterns. In this study we aimed to better delineate the organization of seizures arising from the motor system using SEEG recordings. We used a quantification of the epileptogenic zone (EZ) by the estimation of a mathematical quantity called ''epileptogenicity index'' (EI) in brain structures involved (or not) by the ictal discharge (Bartolomei et al., 2008). Computation of the EI was performed to quantify the degree of involvement of various cortical structures, in order to identify possible network subtypes of motor and pre-motor seizures and to correlate these with clinical data including ictal semiology, epilepsy duration, etiology and surgical outcome.

Patients and methods

Patient selection and SEEG recording

Twenty-eight consecutive patients undergoing presurgical evaluation for drug-resistant frontal lobe epilepsy were selected out of a total of 60 patients with frontal lobe epilepsy explored with intracerebral electrodes between 2000 and 2010 (Timone Hospital, Marseille, France). Selection was based on the results of SEEG recordings showing involvement of primary motor cortex or premotor cortex in ictal onset. Prior to selection for SEEG all patients underwent non-invasive assessment for drug resistant partial epilepsy including detailed clinical history, neurological examination, neuropsychological evaluation, long-term video-EEG recording and structural magnetic resonance imaging (MRI). SEEG recording was carried out during long term video-EEG monitoring in order to record several of the patient's habitual seizures, following complete or partial withdrawal of antiepileptic drugs. SEEG exploration was performed using intracerebral multiple contacts electrodes (Dixi Medical (France) or Alcis (France); 10—15 contacts, length: 2 mm, diameter: 0.8 mm, 1.5 mm apart) placed intracranially according to Talairach stereotactic method (Talairach et al., 1992) (Supplemental Fig. 1). Anatomic positioning of electrodes was established in each patient based upon available non-invasive data and hypotheses of localization of the epileptogenic zone. Post-operative computerized scan (CT) was performed in order to verify the absence of bleeding and the position of each recording lead. After intracerebral electrodes removal, following a recording period of 1—3 weeks, cerebral MRI was performed, permitting the visualization of the trajectory of each electrode. Subsequently CT scan/MRI data fusion was performed in order to accurately identify and locate each contact along the electrode trajectory. All patients had spatial sampling of primary motor (namely Rolandic cortex, Rol) and pre-motor structures both in mesial (Supplementary Motor Area, SMA; pre Supplementary Motor Area, preSMA; cingulate motor area, CMA) and lateral aspects (lateral Brodmann area 6, BA 6 lat; Brodmann area 8, BA 8) (Rizzolatti et al., 1998). In many cases extra-motor structures were also sampled (including pre-frontal cortex, PreF; parietal cortex, Par). The anatomical definition and the boundaries of the pre-SMA and SMA were chosen according to previous studies (Chassagnon et al., 2008; Picard and Strick, 1996). The pre-SMA was defined as the region located above the cingulate sulcus, anterior to the VAC (vertical line passing through the anterior commissure), extending anteriorly to the VAC up to 17% of the total anteroposterior length of the brain. The SMA corresponded to the area between the VAC and the VPC (vertical line passing through the posterior commissure) and superior to the cingulate sulcus. In the present study, we did not differentiate between anterior and posterior portions of the CMA. We defined the CMA as the region lying on the banks (ventral or dorsal) of the cingulate sulcus and inferior to the SMA region. Signals were recorded on a 128 channel system (Natus/Deltamed^{TM}) sampled at 512 Hz and recorded on a hard disk (16 bits/sample) using no digital filter. A high-pass filter (cut-off frequency equal to 0.16 Hz at −3 dB) was used to remove very slow variations that sometimes contaminate the baseline.

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.eplepsyres.2013.04.011.

Signal analysis: definition and computation of the epileptogenic index (EI)

The EI is a normalized quantity, ranging from 0 to 1, computed from SEEG recorded signals with the aim of objectively