

Epilepsia partialis continua and cortical motor control: insights into physiology

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ABSTRACT – Motor epilepsy partialis continua is a widely described variant of simple focal motor status epilepticus. However, few studies have addressed associated pathophysiological anomalies that may help us understand the cortical organization, basic functioning and control of voluntary movement. We describe the clinical, video-EEG and neuroimaging findings from two cases of motor epilepsy partialis continua that support the hypothesis of the coexistence of both classic body and complex motor map models in the cortical organization of voluntary movement in humans. [Published with video sequence]

Key words: epilepsy partialis continua, video-EEG, motor control

Motor epilepsy partialis continua (EPC) is a variant of simple focal motor status epilepticus in which frequent repetitive muscle twitches or jerks, occurring at intervals below 10 seconds, continue for more than one hour (Mameniskiene and Wolf, 2017). In recent years, many reports have described the clinical features and neurophysiological findings. It is well-known that clonic movements may sometimes be very limited and may be restricted to parts of one muscle group, whereas in other instances, the involvement is more global,

affecting entire muscle groups (e.g. groups of agonists). Typically, there is a predilection for face muscles and distal portions of the limbs but the trunk or the diaphragm may be involved (Fernández-Torre *et al.*, 2004). Few attempts have been made to draw conclusions regarding motor cortical organization and basic functioning, as well as control of the voluntary movement. Currently, there is controversy over the structure and nature of the motor map and debate about whether this map represents individual muscles (*i.e.* Penfield's



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classic homunculus) or is a map of movements and motor intentions (*i.e.* as suggested by microstimulation techniques).

The aim of this article is to describe two cases of motor EPC in which the clinical manifestations, video-electroencephalography (vEEG) and neuroimaging features might support the coexistence of both proposed physiological models.

Clinical cases

Case 1

An 83-year-old-man was admitted to our emergency unit because of continuous twitches in the right thigh. He had a past history of hypertensive heart disease. Neurological examination was completely normal except for continuous rhythmic muscle movements in the right thigh (*see video sequence*). An urgent vEEG and electromyogram (EMG) were requested. The EMG of the right quadriceps revealed rhythmic bursts of polymorphic motor potentials, at a constant frequency of 3 Hz. This muscle activity was absent in the rest of the muscles of the right lower limb. Somatosensory evoked potentials (SEPs) of both tibial nerves showed responses of normal morphology

and amplitude with increased latencies of the cortical components. Back-averaging techniques failed to reveal a spike on the scalp preceding the EMG discharge, and the presence of transcortical long-loop reflexes such as c-reflex were also negative. The vEEG was within normal limits and frank epileptiform discharges were absent. A computed tomography (CT) scan of the brain was normal. Head magnetic resonance imaging (MRI) revealed a cortical-subcortical area of increased T2/FLAIR signal and restricted diffusion localized in the left superior frontal convolution suggestive of acute ischaemic infarction (*figure 1*). Muscle contractions stopped after intravenous administration of 10 mg of diazepam. Finally, the patient was discharged with complete recovery on treatment with levetiracetam (1,000 mg/24 h).

Case 2

A 63-year-old-man with a history of pulmonary tuberculosis, chronic alcoholism and past surgery and radiotherapy due to an oropharyngeal epidermoid carcinoma was admitted to our emergency unit because of involuntary movements of the right leg. The movements persisted for more than one hour and prevented him from walking. Neurological examination was

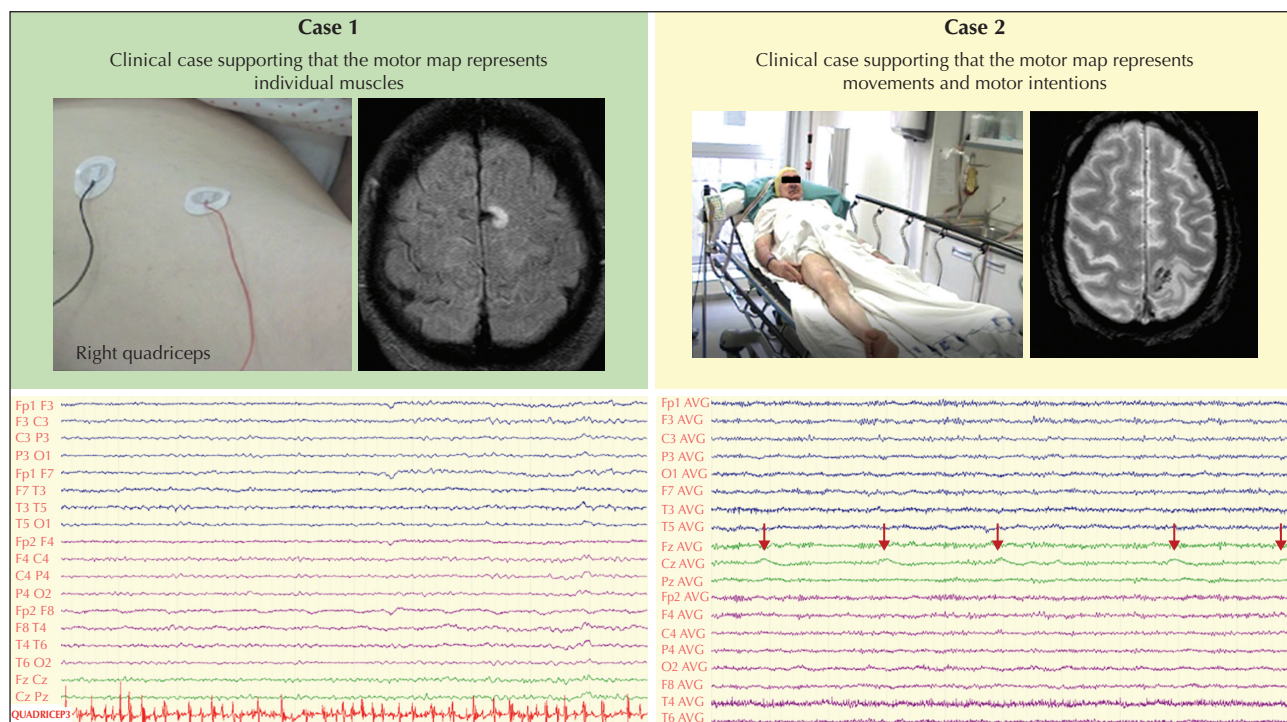


Figure 1. Case 1. Surface electrodes on the right quadriceps during the polygraphic v-EEG; despite the normality of the electrophysiological studies, brain MRI revealed a small left frontal paramedial cortical lesion that was hyperintense on FLAIR. Case 2. Image of the patient while experiencing the rotation movements of the right leg; head MRI showed subcortical hyperintensity with discrete oedema localized in the left posterior parietal convexity.

Low filter: 0.53 Hz; high filter: 70 Hz; notch filter: 50 Hz; sensitivity: 10 μ V/mm; speed: 30 mm/second.

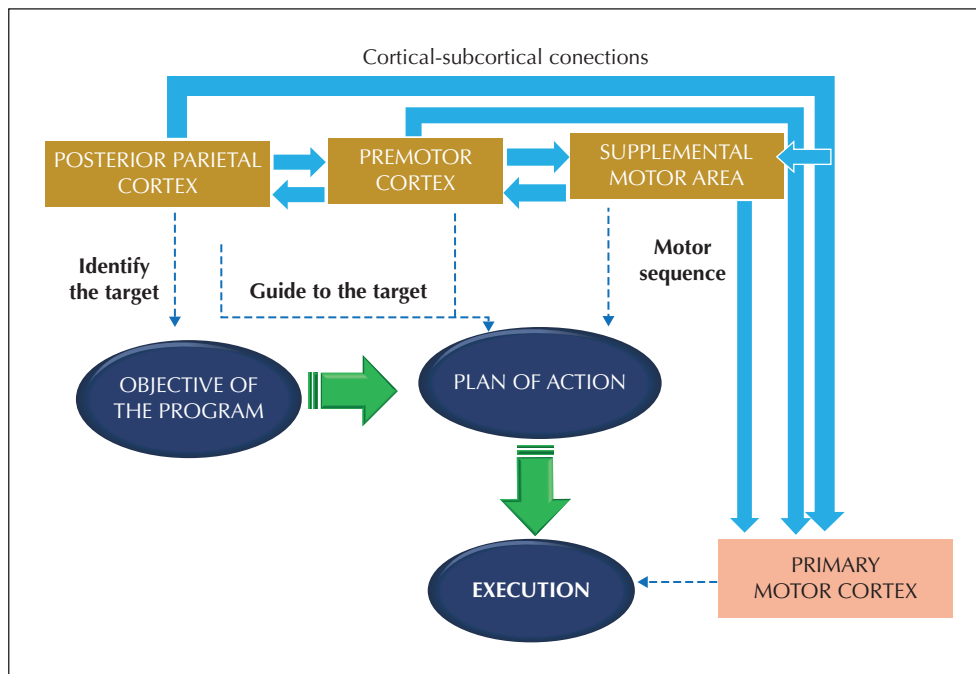


Figure 2. The central motor plan, showing areas, functions and reciprocal connections involved.

normal except for involuntary movements of the right leg. The movements consisted of internal rotation of the leg and foot without clonic jerks (see *video sequence*). An urgent vEEG revealed a normal background and slow periodic waves in the central parasagittal region (Cz). However, frank epileptiform discharges were absent. A CT scan of the brain was normal. Head MRI revealed a subcortical hyperintensity with discrete oedema localized in the left posterior parietal convexity (*figure 1*). The presence of several centres of enhancement at the bottom of the affected sulci was suggestive of meningeal infiltration from an inflammatory or tumoral cause. A cerebral biopsy demonstrated an inflammatory reaction with astrocyte reaction, oedema and lymphocyte infiltrate. Several days later, the patient was discharged with control of his seizures and he had a normal neurological examination following treatment with levetiracetam (1,000 mg/24 h) and lacosamide (400 mg/24 h). Clinical-radiological follow-up was recommended as an outpatient. A few months later, the patient was finally diagnosed with tuberculous meningitis with good response to the antituberculous therapy.

Discussion

Cortical governance of voluntary movement is not completely understood (*figure 2*). The motor map is

widely known to be disproportionate since muscles used for precise movements (of the face and hands) are controlled by a larger number of cortical neurons relative to other muscles. In addition, there is a radial columnar organization. Withal, there is debate on whether each column is related to the control of organized movements or of individual muscles. These clinical cases may support the two hypotheses regarding coexisting but different physiological models for the organization of cortical motor control. The first case involves a single muscle activation, suggesting muscle-by-muscle control in the cortex. The second case involves activation of a set of muscles, suggesting a more complex, integrated control of movement in the cortex.

In Case 1, clonic twitches remained localized to the right quadriceps. During the clinical examination and EMG, no other muscles were affected. This is, therefore, an example of cortical activity controlling the motor function of a single limb muscle. It may be argued that the muscle activation was not directly caused by the motor cortex damage, but by subjacent or underlying white matter damage resulting in excessive neural activation that was more muscle-specific than that following a cortical map.

By contrast, in Case 2, the patient presented with a repetitive, and continuous movement of internal rotation of the right leg. This motor activity was complex and stereotyped and might represent a complex motor primitive and ethological behaviour (Graziano *et al.*,

2002a). This case is an unusual clinical presentation for EPC and provides clinical evidence that cortical motor organization in humans can also represent complex multijoint movements and represent motor intentions. Hence, a particular movement or motor behaviour might be elicited by stimulation of widely separated sites, supporting the argument that neurons in nearby regions are linked by local circuits in the cortex and spinal cord to produce specific movements (Graziano *et al.*, 2002a, 2002b; Purves *et al.*, 2019). However, it could be argued that in this case the motor cortex is still organized on an individual muscle basis, but the damage is extensive enough to affect more than one muscle group. Alternative mechanisms for global epileptic movements might involve activation of regions in the supplementary motor area. However, clinical semiology (vocalizations, asymmetric tonic posturing, head deviation, speech arrest, *etc.*) and EEG alterations are somewhat inconsistent (Fernández-Torre and Leno, 2008).

Scalp vEEG failed to demonstrate electrical changes in the first patient but revealed slow periodic waves in the central parasagittal region in the second. It could be argued that the activation of a single muscle requires the synchronization of a smaller population of neurons and cortical surface than that for complex motor behaviours or complex postures. This interpretation might explain the v-EEG changes. A combination of functional MRI (fMRI) and EEG recordings might support this hypothesis.

Complex motor postures and ethological behaviours

Ethologically relevant behaviours may give rise to the existence of coordinated complex motor responses. Graziano and colleagues (Graziano *et al.*, 2002a, 2002b) found that a half second of electrical microstimulation in the motor cortex of monkeys can result in complex, multijoint movements and postures, and suggested that the precentral gyrus contains a representation of complex behaviourally meaningful postures (Graziano *et al.*, 2002a, 2002b). Of note, Ferrier in 1873 had already described that long stimulation of the motor cortex evoked coordinated and apparently purposeful movements (Ferrier, 1873; Graziano *et al.*, 2002b). Interestingly, Desmurget *et al.* (2014) have recently established the presence of complex motor responses with ethological value in humans. Thus, hand/mouth movements, a typical ethologically relevant human behaviour, are represented as integrated synergies within the human precentral gyrus.

Most recently, Graziano (2016) reviewed the current state of research on action maps in the motor cortex and reassessed some of the original claims and

controversies. This investigator explains that the motor cortex contains functional zones each of which subserves a complex, ethologically meaningful category of behaviour. This basic research concept is consistent with Case 2 described here. However, the described movement could simply represent a complex motor pattern without purposive significance. Much of the evidence so far is based on laboratory experiments with animals such as primates and rodents. However, our two clinical cases provide evidence of both physiological models in humans.

Most recently, Insola *et al.* (2019) evaluated the thalamo-cortical network in patients with motor EPC based on analysis of low-frequency (LF) and high-frequency (HF) SEPs, and found a significant suppression of post-synaptic HF-SEP burst and an amplitude reduction of the P24 wave of the LF-SEPs. Both findings support an important pathophysiological role for GABAergic interneurons in the cortical sensory-motor network where they reside.

In summary, we describe two cases of motor EPC of which the clinical and neurophysiological features support the coexistence of both classic body and complex motor map models for the cortical organization of voluntary movement in humans. □

Supplementary data.

Summary didactic slides are available on the www.epilepticdisorders.com website.

Disclosures.

None of the authors have any conflict of interest to declare.

Legend for video sequence

Video showing twitches in the right thigh (Case 1) and recurrent rotation movements of the right leg (Case 2).

Key words for video research on www.epilepticdisorders.com

Phenomenology: twitching/rotation of the right leg
Localisation: not applicable
Syndrome: epilepsy partialis continua
Aetiology: not applicable

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TEST YOURSELF



- (1) How long should muscle jerks last for in order to establish a diagnosis of epilepsia partialis continua (EPC)?
- (2) Is the columnar radial organization of the motor map related to individual muscles or organized movements?
- (3) What is the map that represents motor behaviour called?

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com, under the section "The EpiCentre".