

Epilepsia partialis continua: semiology and differential diagnoses

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ABSTRACT – Epilepsia partialis continua (EPC) is a rare form of focal status epilepticus. It may have vascular, immune-mediated, neoplastic or metabolic-toxic causes. The origin of EPC has been linked with the motor cortex. This has been solidly supported by sophisticated electrophysiological studies. Here, a series of video sequences from patients with EPC (due to Rasmussen encephalitis, early-stage multiple sclerosis, and steroid responsive encephalopathy with autoimmune thyroiditis), and other cases with repetitive myoclonic jerks or movement disorders (myoclonic epilepsy associated with ragged-red fibers, Jacksonian march, myoclonic seizures in other types of frontal lobe or idiopathic generalized epilepsies, and different types of tremor) is presented. *[Published with video sequences]*.

Key words: epilepsia partialis continua, semiology, diagnosis

In 1894-1895, Koževnikov (or Koshewnikow) reported in Russian and in German on four patients who suffered from mild to moderate hemiparesis and from what he called “epilepsia corticalis sive partialis continua” in the paretic parts of the body (Koževnikov 1894, Koshewnikow 1895). Today, only the term epilepsia partialis continua (EPC) is still in use. The Russian neurologist conceptualized EPC as a particular form of epilepsy and distinguished it from “common epilepsy” because it did not have the tendency to spread and was often not self-limiting. It was clear to Koževnikov that in the four patients he described, the EPC originated in the hemisphere contralateral to the affected side of the body, close to the primary motor area. He was, however, unable to clarify the nature of the organic brain lesion, which in his opinion was underlying the continuous myoclonic jerks. Based on the slowly progressive

nature of the disease in his patients, he hypothesized that a chronic encephalitic process was at work. He was probably right because it can be assumed that the majority of his patients suffered from tick-borne, viral Russian spring summer meningoencephalitis, which was detected only some decades later (Omorokow 1927, Smorodintsev 1958).

In contrast to Koževnikov’s terminology, EPC is today conceptualized as a seizure type rather than a form of epilepsy, and is subsumed under the group of focal status epilepticus (Engel 2001).

Following Koževnikov’s publications, subsequent research on EPC has mainly dealt with three – in part interrelated – questions: how should EPC be defined? Which pathological processes cause EPC? Where in the nervous system does this phenomenon arise?

The current, broadly accepted answers to these questions are very briefly



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summarized in the following paragraphs. Thereafter, a description of the semiological features of EPC and possible differential diagnoses are given, with a video sequence illustrating them (*see video sequence*).

Definition of EPC

Basically, two types of definitions have been suggested: some authors have confined themselves to defining EPC only on clinical (semiological) grounds, whereas others have demanded additional electrophysiological evidence regarding the cortical origin of the phenomena to be considered. Combining the two most frequently used clinical definitions (Thomas *et al.* 1977, Obeso *et al.* 1985) results in the following: “EPC is defined as spontaneous regular or irregular clonic muscular twitching affecting a limited part of the body, sometimes aggravated by action or sensory stimuli, occurring for a minimum of one hour, and recurring at intervals of no more than ten seconds”.

The neurophysiological conceptualization of EPC is complicated – or rather: enriched – by the fact that it has been studied from the viewpoint of both epilepsy and movement disorder research. Depending on their main field of interest, authors may – in addition to the aforementioned clinical features – require the demonstration of epileptiform EEG abnormalities (ideally in a fixed temporal coupling to the muscle jerks), or abnormalities as shown by other electrophysiological studies such as giant somatosensory-evoked potentials [SSEPs]) in order to demonstrate the cortical origin of the muscle jerks (Cockerell *et al.* 1996).

Pathological processes underlying EPC

The three largest EPC series available – 32 patients (Thomas *et al.* 1977), 40 patients (Cockerell *et al.* 1996), and 76 patients (Sinha and Satishchandra 2007) – came to surprisingly homogenous results regarding the causes of EPC: *vascular disorders* (stroke, intracranial bleeding, cerebral venous thrombosis, vasculitis: 24-28%), *encephalitides* (Rasmussen encephalitis [the most common cause of EPC in childhood], or infectious encephalitides: 15-19%), *neoplasms* (glioma, haemangioblastoma, meningioma, lymphoma: 5-16%), and *metabolic disorders* (diabetic non-ketotic hyperosmolar coma, mitochondrialopathy, Alpers syndrome, intoxications: 6-14%). In 19-28% of cases, the authors could not determine the cause of the EPC.

A painstaking compilation of case reports and small case series ($n = 162$) in an excellent review article from the 1970s resulted in the following figures: inflammatory disorders 32%, neoplastic disorders 19%, head trauma 16%, vascular disorders 14%, others 3%, unknown 16% (Löhler and Peters 1974).

The site of origin of EPC

Virtually all authors today agree that a contribution from the primary motor area is indispensable for the generation of EPC, not to say that the cortex is its main or even single generator. (Some decades ago, an influential publication had suggested that subcortical structures play the main role in generation of EPC [Juul-Jensen and Denny-Brown, 1966]). Evidence for a cortical dysfunction underlying EPC comes from studies showing epileptiform EEG potentials recorded by surface or even subdural electrodes time-locked to the muscle jerks, giant SSEP over the suspicious cortex, or enhanced C reflexes. Further corroborating evidence comes from neuroradiological or neuropathological studies (Thomas *et al.* 1977, Wieser *et al.* 1978, Obeso *et al.* 1985, Cockerell *et al.* 1996). The duration of the muscle twitches, as documented by EMG, has been reported to be brief in cortically-generated myoclonic jerks including EPC (< 100 ms) compared to subcortically-arising jerks (> 100 ms). The muscle jerks affect agonistic and antagonistic muscles simultaneously (Obeso *et al.* 1985, Cockerell *et al.* 1996).

Semiology of EPC

Typical clinical signs of EPC are: combination of the repetitive myoclonic jerks with hemiparesis or – less frequently – with other cortically-generated deficits; monomorphic, simple, brief excursions of the affected limb; regular or irregular occurrence of the jerks; involvement of distal rather than proximal muscle groups; physical exercise, sensitive stimulation or psychic exertion may increase the amplitude and frequency of the myoclonic jerks; more frequent involvement of the upper than the lower half of the body (in 151 patients, the distribution was as follows: head: 16%; head and upper extremity: 14%; upper extremity: 40%; trunk: 5%; lower extremity: 14%; whole side of body: 11% - the sum is larger than 100% because multiple sites may have been affected during the disease course [Löhler and Peters 1974]); EPC more often continues during sleep – sometimes in a milder form – rather than stops (25 *versus* 5 patients from the literature according to [Löhler and Peters 1974]). The same authors calculated a mean frequency of 90 jerks per minute (*i.e.* 1.5 Hz; range 3-360 per minute, equaling 0.06-6 Hz) from the literature. There is no preference for one side of the body or the other.

Differential diagnoses

In the second part of the video sequence and the accompanying table (*table 1*), differential diagnoses for EPC are presented. Tremor has a characteristic alternating agonist-antagonist innervation pattern (patients 13, 15). The cortical myoclonic jerks of patients with myoclonus epilepsies

affect the limbs diffusely (patient 14). Sometimes, even extensive investigations do not clarify the origin of the repetitive myoclonic jerks as in patient 12; the long duration of the bursts mitigates against a typical cortical origin. The Jacksonian march (patient 16) is clearly distinguishable because of the sequential involvement of unilateral body parts.

Summary

EPC is a rare type of focal status epilepticus. Characteristic semiological features enable it to be diagnosed and distinguished from other movement disorders or myoclonic symptoms. Additional electrophysiological studies can contribute to an enhanced degree of certainty regarding the cortical origin of the myoclonic jerks. In childhood, the most frequent cause of EPC is Rasmussen encephalitis (Schomer 1993). At older ages, vascular and neoplastic diseases are the most frequent causes. Metabolic, toxic and other immune-mediated causes account for most of the remaining cases. The prognosis depends on the underlying cause and its appropriate treatment. The search for the underlying disease is therefore of paramount importance. □

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Legend for video sequence

In the attached video sequence, we present video EEG recordings of patients with repetitive involuntary jerks:

Eleven patients with EPC, defined according to clinical criteria (all patients with the diagnosis of EPC and an adequate video EEG recording from this center during the period September 2000 until March 2007), and 5 patients with other types of myoclonia or movement disorders are included.

Ten of the EPC patients have been diagnosed with immune-mediated disorders; one patient's EPC was of unknown cause.

In some patients, additional electrophysiological studies were performed. For details, see *table 1*.

The apparently long duration of the EMG jerks on our recordings are probably best explained by the peculiarities of recordings with an EEG system with a lower sampling rate (here: 200 Hz), and filter settings different from those usually applied in pure EMG recordings.

SSEPs on stimulation of the median nerves were considered as giant potentials if the amplitude of P25-N33 was > 12 μ V (Obeso *et al.* 1985). The overrepresentation of inflammatory conditions and the lack of vascular diseases in this series is due to the patient population from this tertiary center, with its particular interest in immune-mediated syndromes and a (surprisingly) low number of referrals of elderly patients. For recording montages, see *figures 1* and *2*; in the split-screen videos, red curves represent left hemispheric leads, and blue curves represent right hemisphere leads. EEG channels with epileptiform activity, and EMG channels are marked by red colour.

Figure 1. 23 EEG channels.

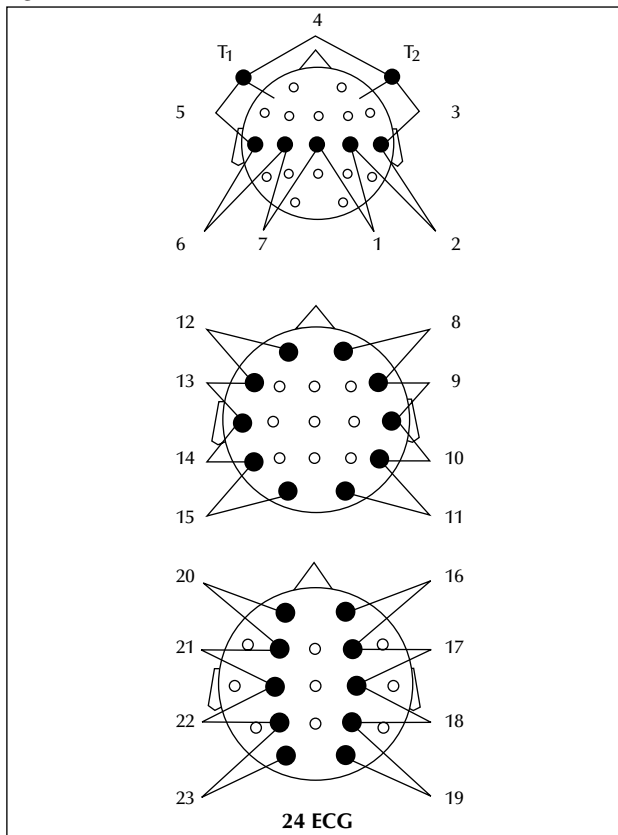
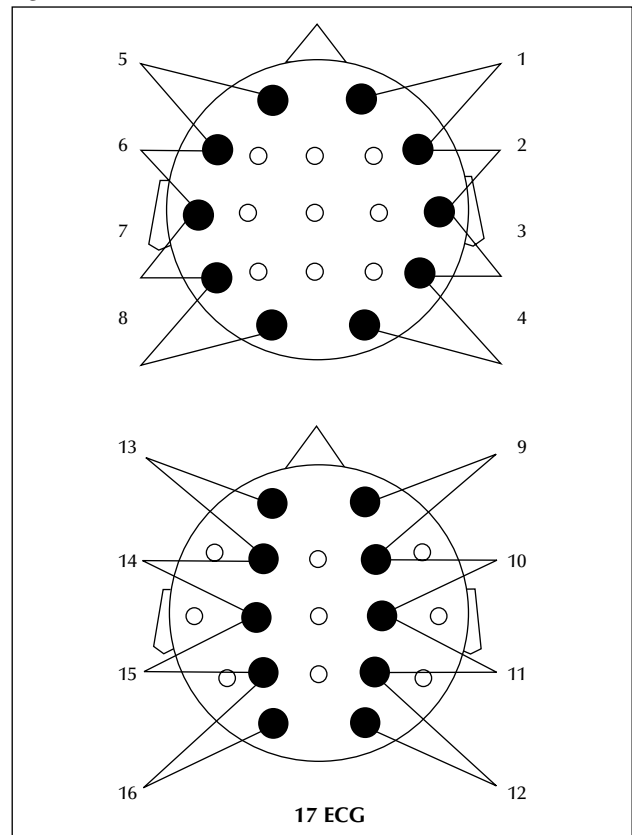


Figure 2. 16 EEG channels.



ADM: musculus abductor digiti minimi
 AH: musculus abductor hallucis (foot)
 APB: musculus abductor pollicis brevis (hand)
 centr: central
 EPC: epilepsia partialis continua
 F: female
 FCU: musculus flexor carpi ulnaris
 FLE: frontal lobe epilepsy
 fr: frontal
 hem: hemisphere
 Hypoth: hypothalamus
 IGE: idiopathic generalized epilepsy
 L: left
 LTG: lamotrigine
 M. add. long.: musculus adductor longus
 M. grac.: musculus gracilis
 M. orb. oc.: musculus orbicularis oculi
 M. vast. lat.: musculus vastus lateralis
 M: male
 MERRF: myoclonic epilepsy-associated with ragged-red fibers
 mo: months
 MS: multiple sclerosis
 Nd: not done
 R: right
 RE: Rasmussen encephalitis
 SREAT: steroid responsive encephalopathy with autoimmune thyroiditis (formerly Hashimoto's encephalopathy)
 SSEPs: somatosensory-evoked potentials
 sync: synchronous jerks in the recorded muscles
 temp: temporal
 VPA: valproic acid
 wks: weeks
 yrs: years

Table 1. Patients shown in video with epilepsy partialis continua and with other conditions.

Patient no. gender	Age (yrs)	Diagnosis	Time since onset	Body region affected	Epileptiform potentials on EEG	EMG bursts: apparent duration and synchronicity	Amplitude of SSEPs on stimulation of median nerve P25-N33 (μ V Ipsilateral-contralateral)	Additional neurological deficit
Epilepsia Partialis Continua								
1, M	11.3	RE, R hem	3.0 yrs	L face	Yes	Nd	Nd	L hemiparesis
2, F	11.4	RE, L hem	13 mo	R tongue	Yes	Nd	Normal	R hemiparesis
3, M	13.2	RE, L hem	4.0 yrs	R face	No (artifacts)	< 200 ms (only one muscle)	30-5	R hemiparesis
	Same patient, 1.8 yrs later			R face	Yes	Nd	Nd	R hemiparesis
4, M	18.6	Unclear	3 yrs	Face, pectoral muscle, L arm	No	< 150 ms, sync	12.5-1.8	None
5, M	10.5	RE, L hem	2.2 yrs	R hand	Yes	Nd	Nd	R hemiparesis
	Same patient, 8 mo later			R hand	Yes	< 200 ms, sync	87-7	R hemiparesis
6, F	23.8	Early-stage MS	Days	L hand	No	< 250 ms, sync	Normal	None
7, F	62.8	SREAT (Hashimoto's)	3 wks	L hand	No	Nd	Nd	Dystonia L hand
8, F	42.1	RE, L hem	26 mo	R hand	No	Nd	Normal	R hemiparesis
	Same patient, 1.8 yrs later			R leg	Yes	Nd	Nd	R hemiparesis
9, M	6.3	RE, L hem	1 mo	R foot and leg	Yes	Nd	Nd	R hemiparesis
10, F	5.1	RE, L hem	10 mo	R hand and foot	Yes	< 150 ms, sync	Normal	R hemiparesis
11, F	16.6	RE, R hem	3.3 yrs	L hand and foot	No	< 150 ms, sync	Normal	L hemiparesis
Differential diagnoses								
12, F	18.9	Myoclonia of unknown origin. FLE or IGE	5.9 yrs	L leg	No	< 600 ms, sync	Nd	None
13, F	2.8	Tremor ataxia teleangiectasia	2 mo	L arm	No	Nd	Nd	Ataxia
14, M	23.3	Cortical myoclonia MERRF	14 yrs	Diffuse	No	Nd	Nd	Ataxia, paraparesis
15, M	26.8	Tremor VPA-LTG overdose	Weeks	Upper extremities	No	Nd	Nd	None
16, M	21	Jacksonian march. FLE	9 yrs	L hand, spread to rest of hemibody	Late in seizure	Nd	Nd	None