Epilepsia partialis continua: past and present
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ABSTRACT

Introduction. The concept of epilepsia partialis continua (EPC) originated in Moscow in 1894, with the first description by Yakovlevich Kozhevnikov. While more than a century has passed, we still lack a universally accepted definition. This article presents a historical review of the concept.

Development. Kozhevnikov described EPC as constant, high-frequency muscle spasms limited to one part of the body. He accurately proposed that the cause was chronic focal cortical encephalitis with motor pathway involvement. Russian spring-summer encephalitis (a tick-borne disease) was discovered in 1937; the disease was frequently associated with EPC. At the time, “Kozhevnikov epilepsy” was thought only to be a typical manifestation of this infectious disease. Perpetuating this idea, a 1958 study by a group of Canadian scientists described persistent focal epilepsy secondary to chronic encephalitis in children, which was considered a new disease: Rasmussen encephalitis. Subsequently, numerous descriptions of patients led to the concept of EPC being redefined: it was differentiated from Rasmussen syndrome and all association with Kozhevnikov was eliminated. In more recent publications, a European multicentre study group for status epilepticus proposed that the concept should be expanded and subdivided according to the stage of progression. In contrast, the International League Against Epilepsy opted to simplify the concept, treating it as a type of continuous seizure.

Conclusions. Unlike the definition proposed by Kozhevnikov, EPC is now considered to be a type of focal epileptic seizure, rather than a type of epilepsy. This may be an overly simplistic view of such a complex disease with an equally complicated history.

KEYWORDS
Chronic encephalitis, cortical myoclonus, epilepsia partialis continua, focal motor status epilepticus, Kozhevnikov, Rasmussen

Introduction

Epilepsia partialis continua (EPC) is a type of focal status epilepticus first described in 1894 by the Russian neuroscientist Aleksei Yakovlevich Kozhevnikov. EPC was initially defined as a specific clinical syndrome consisting of uninterrupted, rhythmic movements limited to a single part of the body, and attributed to a process of chronic encephalitis. It subsequently came to be known among Russian neurologists as “Kozhevnikov epilepsy,” and has been the subject of numerous controversies that resulted in changes in its definition and the eponyms attributed. Later, the reference to Kozhevnikov was removed from official publications.

Besides the considerations on eponyms, in the early years after it was first described, and later in the 20th century, the concept underwent numerous modifications; it
has even been suggested that the definition should be expanded to include other forms of focal status epilepticus. However, there is currently no universally accepted definition.

The objective of this study is to give a historical overview of the term from its origins in Russian neuroscience, still largely overlooked, up to today’s clinical practice. Under the premise that “to understand the present we must know the past,” we aim to clarify this imprecise concept.

Development

Origins in Russian neuroscience

The concept of EPC was first defined in 1894 by the Russian neuropsychiatrist Aleksei Yakovlevich Kozhevnikov in his article “a special type of cortical epilepsy.” Kozhevnikov, considered the founder of Russian neurology, described four patients who presented constant, high-frequency muscle spasms limited to one part of the body, with preserved awareness; they were typically treatment-resistant. He recognised that this type of epilepsy may have many different causes, and accurately proposed (without having performed any post mortem study) that they all resulted in chronic focal encephalitis involving the motor pathway.

In a letter to the editor of the journal Epilepsia in 2002, addressing the eponym attributed to EPC, Panayiotopoulos translated and synthesised Kozhevnikov’s original description as follows:

In recent years, I happened to observe several cases of cortical epilepsy […] that it may be called epilepsy partialis corticalis sive partialis continua, in that here the convulsive manifestations were continuous […] The question of the nature of the disease process is much more difficult […] in all cases the illness developed little by little and once it had developed persisted for a very long time, so that we can postulate only chronic processes here […] Thus, of the chronic processes, encephalitis with transition to secondary hardening of the brain, or sclerosis cerebri, is almost the only possibility […] Thus, not knowing precisely what we are dealing with, and proposing the presence of chronic encephalitis.

The definition of EPC and its aetiology remained largely unchanged among various Russian authors, including Orlovsky (1896) and Khoroshko (1908). In 1927, Omorokov reviewed 42 cases from the literature and described 52 patients from his own centre with this form of epilepsy. He found that all cases occurred in the context of acute infectious processes, and decided to group them under the term “Kozhevnikov epilepsy.” Years later, this entity was associated with Russian spring-summer encephalitis, a tick-borne disease.

Some authors, particularly Dr Alla Vein, a Dutch neurologist with extensive knowledge of Russian neurology, having trained at the University of Moscow and specialised at the Moscow Clinic for Nervous Diseases, founded by Kozhevnikov, considers this study to have given rise to the confusion about the term. Thus, Omorokov associated EPC with acute infection of the central nervous system; this differs considerably from
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and in 1956 he and Hecaen published a study of 99 patients, reporting that EPC was associated with chronic inflammatory processes in the brain in a high percentage of patients. Following the same line of research, a 1958 study by the Canadian neurologist, neurosurgeon, and neuropathologist Theodore Rasmussen (Figure 2) described three cases of persistent focal epilepsy secondary to chronic focal encephalitis in children. His publication makes an isolated reference to Kozhevnikov’s original description, noting that it was a distinct entity to that of his own patients, only related to Russian spring-summer encephalitis. The disease described by Rasmussen was acknowledged then as a new entity, bearing his eponym: Rasmussen syndrome or Rasmussen encephalitis (RE).

According to Vein, this moment was probably the culmination of a series of historical misinterpretations, overlooking the work of Kozhevnikov and his contemporaries. This situation cannot be explained solely by the language barrier, but rather must be considered within the historical context of the 20th century, when there was little encouragement for the exchange of information between Western and Soviet scientists. In any case, it resulted in Kozhevnikov’s name frequently being mentioned erroneously, even in official documents, or worse still, being overlooked entirely.

Setting aside these possible misinterpretations, the historical development of EPC continued; after Rasmussen’s contribution, a series of other authors reviewed and updated the concept. In 1966, Juul-Jensen and Denny-Brown published a series of nine cases and a literature review, reaching the conclusion that the aetiology of EPC encompasses a broad range of lesions, which may involve both cortical and subcortical regions. They propose that the clinical syndrome be defined as “clonic muscular twitching repeated at fairly regular short intervals in one part of the body for a period of days or weeks.” They also suggest that the syndrome differs from most of the other focal epilepsies in that EPC lacks progression from the tonic to the clonic phase and the Jacksonian march from one region of the body to another.

In 1977, Thomas et al. proposed an even more precise definition of EPC, based on a review of the clinical characteristics of 32 patients. They describe EPC as a syndrome characterised by “regular or irregular clonic muscular twitches affecting a limited part of the body, occurring for a minimum of one hour, and recurring at

Kozhevnikov’s initial description, which mainly referred to chronic processes.

In 1957, S.N. Davidenkov, considered the father of Russian neurogenetics, published his manual on nervous diseases, describing a chronic form of EPC in children that was probably caused by various infectious agents that could not always be identified. Despite the probably distinct aetiology, the associated clinical syndrome was indistinguishable from that described a year later by T. Rasmussen.

Development in Western neurology

In parallel to Davidenkov’s publications, Western authors also began to become interested in this peculiar form of epilepsy. In 1955, Dereux reviewed 41 cases,
intervals of no more than ten seconds.” While they do not include it in their definition, they note in the description of their series that, as in previous studies, the majority of patients responded poorly to antiepileptic treatment.

Subdivision of the concept

The concept of EPC underwent a significant modification in 1982. Bancaud et al. defined two EPC syndromes: type 1, caused by generally identifiable Rolandic cortical lesions, and type 2, associated with a diffuse but unilateral encephalitic process of unknown aetiology, possibly due to a slowly progressive viral infection. Both entities begin with similar seizures, but type 2 is untreatable and progressive. These authors also divide the clinical course of type 2 EPC into three stages: in the first, patients only present focal motor seizures with or without preserved awareness; in the second, focal motor manifestations are associated with progressive neuropsychological deterioration; and in the third stage, patients are apparently clinically stable, with arrest of this deterioration or remission of seizures. Considering this classification in greater detail, we may infer that, in principle, type 2 EPC would correspond to the clinical entity defined 25 years earlier by Davidenkov, as well as the cases presented later by Rasmussen. The original publication by Kozhevnikov would include patients in both groups, although they were significantly older than the typical age of patients with type 2 EPC.

Subsequent anatomical clarifications

The article “The spectrum of cortical myoclonus,” published in 1985 by Obeso et al., acknowledges the difficulty of defining EPC. Nonetheless, based on a thorough description of 11 patients, they concur with previous authors that EPC is characterised by clonic muscle contractions limited to one part of the body, which may persist for a period of hours, days, or weeks. However, they clarify that these movements must be spontaneous, potentially exacerbated by action or sensory stimuli, that their presentation may be regular or irregular, and that they must originate in the cerebral cortex (Figure 3) and not in subcortical regions, as proposed by Juul-Jensen and Denny Brown in 1966.

In 1996, the British group led by Cockerell and Shorvon conducted further research into the anatomical origin of EPC, in the light of the existing controversy. They conducted neurophysiological studies of 16 members of

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Figure 3. Patient no. 9 described by Obeso et al. A 33-year-old woman with EPC affecting the right hand. A) Permanent posture that the patient’s hand had acquired. B) Excerpt from the electromyography recording, showing irregular, spontaneous jerks of the right hand. The muscles shown are the hypothenar (hypothen.), flexor pollicis longus (FPL), and forearm flexor and extensor muscles (FF and FE, respectively). C) Electroencephalography recording showing a contralateral positive cortical potential preceding the initiation of the spontaneous contraction of the right hypothenar muscle (22 ms later).
After the First London Colloquium on Status Epilepticus, held in 2007, a European research group was formed to study EPC. Based on several previous studies describing the concept of aura continua, this multicentre group proposed that the definition of EPC be expanded to encompass other forms of focal status epilepticus with preserved awareness, thereby including forms presenting with continuous symptoms with somatosensory, visual, olfactory, auditory, and cognitive involvement. They proposed the following definition of EPC: “a condition of continuously repeated fragments of epileptic seizures (motor or sensory), with preserved consciousness, lasting ≥ 1 hour, and representing locally restricted epileptic activity.” They also proposed a classification according to clinical progression (Table 1).

Under this classification, EPC may initially be assigned one clinical type but can transition between the different forms. For example, as it progresses, an isolated episode (type 1) may become the first episode of type 2 EPC; type 2, in turn, may also progress to type 3 EPC. They also established that in type 2a, episodes last less than 24 hours and occur more than once per month, whereas in type 2b, episodes last longer than one day and occur at intervals of several months. Type 4 corresponds to Rasmussen syndrome.

This classification is clearly broader and more dynamic than those proposed by other groups. It includes continuous non-motor symptoms and places special emphasis on clinical course, which is conditioned by the different possible aetiologies and defines therapeutic management in clinical practice.

2. ILAE proposal

In 1985, the ILAE Commission on Classification and Terminology recognised two types of Kozhevnikov syndrome under its “special syndromes” section:

— Kozhevnikov syndrome type 1. This term refers to EPC, and is defined as:

A particular form of Rolandi partial epilepsy, in both adults and children, and is related to a variable lesion of the motor cortex. Its principal features are motor partial seizures, always well localised; often late appearance of myoclonias in the same site where there are somato-motor seizures; an EEG with normal background activity and focal paroxysmal abnormalities (spikes and slow waves); occurrence at any age in childhood and

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<th>Type 1: Solitary episode of EPC</th>
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<td>a. In pre-existing epilepsies</td>
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<td>b. De novo symptomatic EPC in patients without pre-existing epilepsy</td>
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<th>Type 2: Chronic repetitive non-progressive EPC</th>
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<td>a. With frequent brief episodes (more than one episode per month)</td>
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<td>b. With rare long episodes (one episode or fewer per month)</td>
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<th>Type 3: Chronic persistent nonprogressive EPC</th>
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<tr>
<td>a. Evolving from type 2</td>
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<td>b. Primary persistent</td>
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<th>Type 4: Chronic progressive EPC</th>
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Table 1. Classification of EPC proposed by the European multicentre EPC study group.

EPC: epilepsia partialis continua.
adulthood; frequently demonstrable aetiology (tumoral, vascular); and no progressive evolution of the syndrome (clinical, electroencephalographic, or psychological), except the evolutive character of the causal lesion.

— Kozhevnikov syndrome type 2. This is the only form included among the childhood epileptic syndromes in this classification (chronic progressive EPC of childhood). It is described as follows:

The childhood disorder, suspected to be of viral aetiology, has onset between 2 and 10 years (peak, six years) with seizures that are motor partial seizures, but are often associated with other types. Fragmentary motor seizures appear early in the course of the illness and are initially localised, but later become erratic and diffuse, and persist during sleep. A progressive motor deficit follows, and mental deterioration occurs. The EEG background activity shows asymmetric and slow diffuse delta waves, with numerous ictal and interictal discharges that are not strictly limited to the Rolandic area.

The 1989 ILAE classification introduced the term Rasmussen syndrome as a synonym of Kozhevnikov syndrome type 2. In subsequent revisions of the terminology, published in 2001 and 2006, the ILAE working group opted for the name “Rasmussen syndrome” alone, removing Kozhevnikov’s name. As discussed above, this seems to be based on a misinterpretation of historical information, according to the opinions of distinguished authors. In line with this theory, Panayiotopoulos proposes the joint name Kozhevnikov-Rasmussen syndrome, asserting that this is the only term that equally acknowledges both authors who described this epileptic syndrome, half a century apart. The subsequent ILAE review of terminology, published in 2010, finally included Rasmussen syndrome in the category of “distinctive constellations.” The value of including the syndrome in a different group seems to reside in the diagnostic relevance attributed to this entity, which is important in the treatment of the condition, in which surgery must always be considered.

Therefore, successive classifications differentiated EPC from Rasmussen syndrome. While it was initially called Kozhevnikov syndrome type 1 (1989), subsequent classifications (2001 and 2006) further simplified the concept, describing it as a type of continuous focal epileptic seizure: epilepsy partialis continua of Kozhevnikov. However, the ILAE’s subsequent position paper, published in 2010, and more recent publications from 2017 on the classification of seizures and epilepsies do not mention this term.

The last official reference to the concept of EPC is in the ILAE’s 2015 review on the definition and classification of status epilepticus. In this document, EPC is included in the category of focal motor status epilepticus (Table 2). It should be noted that this article is the last to cite Kozhevnikov as the first to describe EPC.

Epilepsia partialis continua in today’s neurology

The epileptic syndrome described by Kozhevnikov is currently considered to be a rare type of focal status epilepticus. It is characterised by muscle twitches limited to one part or one side of the body, with the upper limbs being affected most frequently, followed by the head, lower limbs, and trunk. These involuntary movements may be regular or irregular, occurring at least every ten seconds for at least an hour, and consciousness is not affected. There is general consensus that these involuntary movements originate in the cerebral cortex, specifically in the peri-Rolandic region.

EPC is associated with focal, multifocal, or diffuse brain lesions, with multiple possible aetiologies. The most frequent cause in children is Rasmussen syndrome; the most frequently reported aetiologies in adult patients are cerebrovascular disease and tumours. Less frequent causes include infectious encephalitis (Russian spring-summer encephalitis, progressive multifocal leukoencephalopathy, herpes simplex virus encephalitis, neurocysticercosis, etc) or non-Rasmussen autoimmune encephalitis (Sjögren syndrome, anti-Hu paraneoplastic encephalitis), metabolic alterations (inborn errors of metabolism in children and hyperosmolal nonketotic hyperglycaemia in adults), toxic reactions (penicillin, cefotaxime), mitochondrial encephalopathies, cortical dysplasia, multiple sclerosis, and even such prion diseases as Creutzfeldt-Jackob disease.

EPC can present as a single episode, recurrent episodes, or a chronic progressive or non-progressive disorder. Prognosis is variable and depends to a great extent on the underlying cause; thus, seizures are more likely to resolve in cases of cerebrovascular disease or other acute insults than in patients with chronic encephalitis. It is typically resistant to antiepileptic drugs, and recent studies suggest that delayed management of the disease...
is probably associated with longer duration of status epilepticus and poorer prognosis.  

Conclusions

EPC is a rare disease, and the available information has historically been obtained from case series. Over the years, neuroscientists have proposed various explanations and interpretations; however, the heterogeneity of the disease, characterised by an extensive list of aetiologies, complex pathophysiology, variable treatment response, and unpredictable prognosis, has resulted in the lack of a universally accepted definition.

Unlike the definition proposed by Kozhevnikov, EPC is now considered to be a type of focal epileptic seizure, rather than a type of epilepsy. This may be an overly simplistic view of a complex concept, overlooking the intricate history it conceals.