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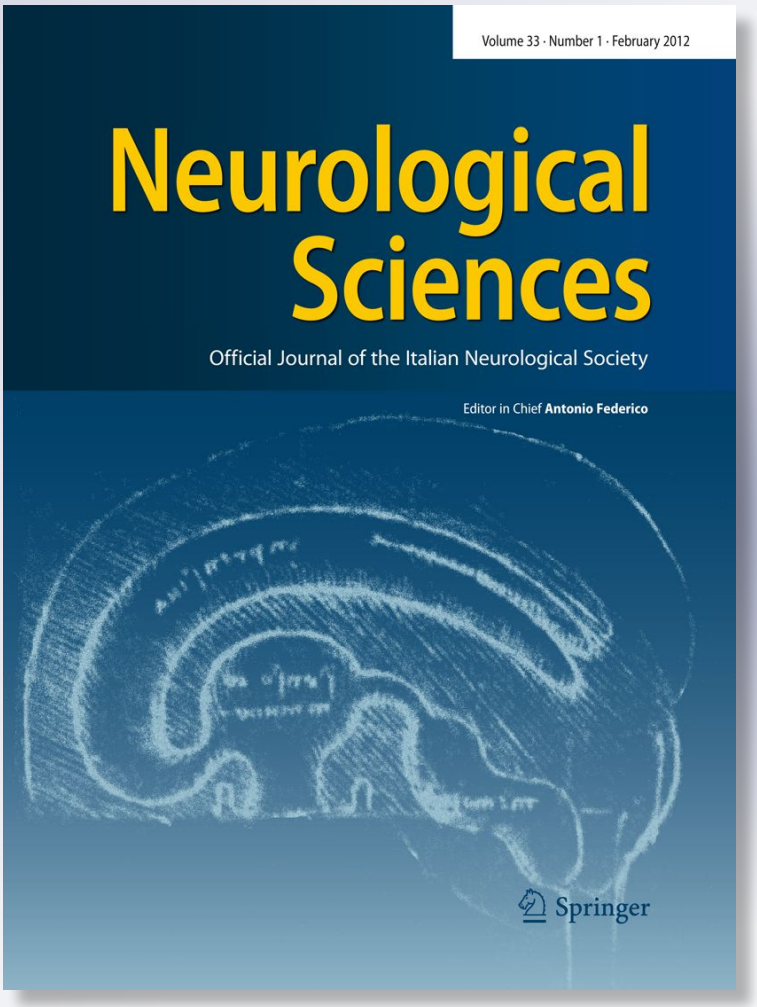

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NEWS AND VIEWS

From migralepsy to ictal epileptic headache: the story so far

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Abstract In the last few years several cases of headache as sole manifestation of an epileptic seizure have been reported and the term "ictal epileptic headache" has been recently proposed to identify an EEG-recorded epileptic seizure with migraine/headache-like features. Among the potential practical implications arising from these clinical observations, there is the urgent need for a revision of both International Classifications of Epilepsy and Headache disorders. We discuss these topics and provide additional comments about the physiopathological links between epilepsy and migraine.

Keywords Ictal epileptic headache · Migralepsy · Migraine with aura · EEG

The historical context

Epilepsy and migraine are two frequent chronic neurological disorders, characterized by recurrent epileptic or migrainous attacks, that sometimes are intermingled and their clinical symptoms may overlap (*I have seen cases intermediate in type between migraine, epileptiform seizures and epilepsy proper (JH Jackson, 1888)*). In 1907, Gowers [1] stated that "migraine is given a place in the borderland of epilepsy, but the position is justified by many relations, and among them by the fact that the two maladies are sometimes mistaken, and more often their distinction is difficult. The next step was the introduction of the term *migralepsy*, coined by Dr. Douglas Davidson but mainly attributed to Lennox and Lennox, to define a condition wherein "ophthalmic migraine with perhaps nausea and vomiting (was) followed by symptoms characteristic of epilepsy" [2]. However, after the first three reported migralepsy-patients by Lennox and Lennox [2], this term was largely ignored for more than 20 years until 1993 when the term was re-introduced by Marks and Ehrenberg [3]. However, despite the scepticism surrounding the concept of migralepsy, as a migraine-epilepsy sequence, the term has been included in the recent ICHD-II as a complication of migraine (1.5.5) [4]. Over the last 10 years, several cases of headache as sole manifestation of an epileptic seizure have been well documented and the term "ictal epileptic headache" has been recently proposed in order to categorize, with EEG recording, an epileptic seizure with migraine/headache-like features [5–8].

The clinical context

The distinction between migraine visual auras and occipital lobe seizures must be kept in mind when evaluating attacks suggestive of migralepsy [9]. Recently, Sances et al. [10] underscore the high prevalence of purely epileptic disorders among cases reported as migralepsy. In particular, among the about 50 potential migralepsy cases identified in

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the literature, only two meet the current ICHD-II criteria supporting a diagnosis of migralepsy [10].

Ictal headache is associated with other seizure symptomatology emanating from the affected epileptogenic zone. It may be exceptional to have headache as a sole manifestation of a seizure and this is more unlikely to be consistent in all seizures of the same patient [9]. Ictal headache is unlikely to be confused with migraine though this may be the case in some exceptional patients and circumstances referred to as hemicrania epileptica and status epilepticus migrainosus [8].

In this issue of the journal, Labate et al. [11] illustrate the EEG recording of an usual episode of migraine attack, lasting several minutes, followed by a tonic–clonic seizure in a 23-years-old woman patient who suffered from migraine and epilepsy. The authors raise the key question: is this a case of migralepsy or ictal epileptic headache? According to the few well-documented case in literature, the term "ictal epileptic headache" should be used to classify the events in which headache represents the only ictal epileptic feature (i.e., recognizable by EEG recording) with a complete remission of headache/migraine after intravenous administration of an antiepileptic drug [8]. Unlike ictal epileptic headache, according to the current ICHD-II classification, the clinical picture and the ictal EEG recording reported by Labate et al. fell into classification criteria for migralepsy. Moreover, Labate et al. [11] highlight an additional important topic: visual aura precipitating or preceding an epileptic seizure? In this sense, the concept of migralepsy should be revised keeping in the mind that headache or visual symptoms can be the epileptic "aura" of a seizure, as it has been shown in the case description of a patient with a partial status epilepticus in occipital lobe epilepsy [7]. Notably, visual symptoms of migraine origin, with a score of 6 in the visual aura rating scale, associated with a de′ja'-vu sensation, a smell of fresh laundry, and nausea, lasting about 10 min, which then developed into a generalized tonic–clonic seizure, has recently reported in a case of migralepsy [10].

The pathophysiological context

Cortical spreading depression (CSD) is known as an intrinsic electrophysiological property of central nervous systems [12]. Although evidences support a causal relationship between CSD, and migraine aura and headache, CSD may also be involved in migraine attacks without a "perceived" aura [12]. This ictal phenomenon shares some pathogenic mechanisms with epilepsy, involving ionic channels and many neurotransmitter systems. Alterations at these levels could create a condition of abnormal excitability, which could increase susceptibility to CSD [13].

In this issue of the journal, Dainese et al. [14] illustrate the clinical evolution from visual aura to visual seizures in a patient with a glioblastoma multiforme involving the occipital lobe. The authors show the EEG features during a typical aura with initial evidence of slow waves in the left posterior derivation which evolved in bursts of epileptiform activity when the patient complained a different visual pattern (i.e., a round-shaped image) long-lasting 10–20 s, suggestive of a seizure of occipital origin. Dainese et al. [14] suggest the existence of a possible increasing CSD threshold mechanism to explain the continuum of expression of related pathology from visual aura to occipital seizure. Regarding neuronal excitability, the most convincing evidence of a possible continuum is observed for migraine aura, in particular FHM, and epilepsy with three known mutations associated with enhanced extracellular glutamate concentration resulting in both cortical spreading depression and seizure [13]. However, there seems to be more differences than similarities between the disturbances in neuronal excitability observed in migraine and epilepsy, both during and between attacks. One ictal difference is the propagation speed of cortical spreading depression as compared to that of epileptic discharge (3 mm/min vs. 70–200 mm/s) [13]. Moreover, during the inter-ictal period, epileptiform discharges appear to reflect neuronal hyperexcitability, while the disturbance underlying the abnormal brain function observed in migraine is not so clear. Nonetheless, in epilepsy hyperexcitation occurs certainly, while in migraine, sequentially, hypoexcitation and hyperexcitation, as rebound phenomenon; in other words, a disexcitability (hyper- and hypoexcitation in the same migraine patient at different points in time) condition has even been demonstrated [15].

Conclusions

Over the last two decades, the medical literature has been flooded with single case report and epidemiological study suggesting a possible comorbidity of epilepsy and migraine; however, two key points have been raised: (1) ictal headache and visual seizures are often misdiagnosed as migraine, and (2) "epilepsy-migraine sequence" is much more common and well documented than a "migraine-epilepsy sequence" (i.e., migralepsy). We are aware that the current ICHD-II criteria for migralepsy have been made before publication of nearly all of the currently reported and the previously reviewed cases, achieving clarity and consensus in this area may be challenging but with the ICHD-III on the horizon, now is the time for this to happen. Finally, further studies are warranted to better delineate the complex link between epilepsy and migraine.

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