EDITORIAL

# "Here, There, Everywhere", or is it Truly Partial Epilepsy?

Can. J. Neurol. Sci. 2010; 37: 721-722

Asymmetrical epileptiform activity and the question of secondary bilateral synchrony versus primary generalized discharges in electroencephalography (EEG) are sometimes challenging. The traditional classification of partial versus generalized epilepsies relies on the evidence of focal clinical (ictal) and/ or EEG findings as well as the presence or absence of focal structural or functional imaging. There are several studies in the literature reporting the asymmetrical or focal EEG abnormalities in idiopathic generalized epilepsies (IGE)[1-5].

Autopsy studies of small group of patients with IGE have documented focal microdysgenesis[6]. Whether these pathological findings represent etiological substrate of generalized epilepsies have been debated[7]. A histopathological study however, discovered that 37% of a large epilepsy cohort had micro-dysgenesis compared to only 4% in normal population[8]. In addition, Woermann et al (1998) found widespread focal brain abnormalities on volumetric MRI studies in patients with IGE compared to controls[9]. In a quantitative analysis in patients with juvenile myoclonic epilepsy (JME) he found an increase in cortical gray matter in the mesial frontal lobes[10]. Savic et al (2000) drew similar conclusions from MRI spectroscopy study in this population of patients[11]. Animal studies have also suggested temporal lobe abnormality may play a role in the pathophysiology of IGE[12].

Some imaging studies have also reported that generalized epileptiform discharges in IGE are generated or at least appear earlier in the frontal cortex than in the other parts of the brain[13,14]. This idea has contradicted the centrencephalic hypothesis first introduced by Penfield and Jasper in 1954, suggesting rostral brain stem structures and thalamic nuclei as the source[15].

Juvenile myoclonic epilepsy is the most common form of idiopathic generalized epilepsies and comprises 4-7% of all epilepsies. It usually begins in adolescence. Myoclonic seizures are hallmark of this syndrome and are present in all cases. They occur predominantly but not invariably in the early morning hours after awakening. The myoclonic jerks are often aggravated by sleep deprivation and fatigue. More than 90% of patients will also develop generalized convulsive seizures in the course of the disease often two to three years after the onset of the myoclonic seizures. Absence seizures occur in about 35% of patients with JME[16].

Juvenile myoclonic epilepsy has genetic background and several studies have reported linkage to chromosome 6p[17]. Others have disputed this finding[18]. No single causative gene has been reported and polygenic factors are likely involved.

The EEG background is often normal with well developed alpha rhythm. The most common abnormality is the paroxysm of generalized bisynchronous spike or polyspike activity with or without a slow wave[19]. The frequency is 3.5-6 Hz. In one fourth of the cases, the frequency is lower and in the range of 2.5-3 Hz. Spikes have the highest voltage in the frontal and central regions[20]. Increased amounts of theta slowing may also be present.

The typical EEG abnormalities have been reported as 73-100% in different studies. The variability could be related to the different recording method, awake or sleep studies, and the length of EEG. The probability of detecting epileptiform activity was also 100% in untreated compared to 63% in JME patients on treatment[21].

Several studies have reported focal EEG abnormalities in 16% to 54% of JME patients[22,23]. Most studies do not define asymmetry or focal abnormality very clearly. These findings are sometimes described as asymmetrical spike-waves, focal or unilateral spikes-waves and/ or slowing. The question is whether the asymmetrical EEG change represents a true focal source for the generalized discharge. These abnormalities often demonstrate alternating laterality and the asymmetry is not consistent as it was found in the present study published in this issue. The majority of these so called "focal discharges" in fact represent fragments of the generalized spikes.

Lancman et al (1994)[23] reported both clinical and EEG asymmetries in 30.6% of 85 patients with JME. The unilateral predominance of spikes or voltage asymmetries in EEG was not consistent in subsequent records and they did not find definite focal EEG abnormalities. The clinical characteristics in these patients were not statistically different from those who had symmetrical epileptiform discharges.

Clear asymmetry of clinical myoclonic jerks was identified in four of five patients with JME in a video-Polygraphic analysis of myoclonic seizures[24]. The same study reported that ictal EEG findings were very similar to interictal EEG abnormalities that do not accompany clinical jerks. The frequency of the ictal spikes is often higher and in the range of 10-16 Hz[25]. Many patients with JME do not report myoclonic seizures. In addition, misinterpretation of myoclonic jerks as simple partial seizures and asymmetrical EEG were important factors in missed or delayed diagnosis of JME[26]. Panayiotopoulos et al (1991) also found that in 33% of 70 patients with JME the correct diagnosis was established after a mean of 8.3 ± 5.5 years from the disease onset. Other than misclassification of seizures, the factors that delayed the correct diagnosis of JME were normal EEG or the presence of focal EEG abnormalities[3].

The literature also describes unusual response to treatment with known first choice medication for JME. Although the excellent response to Valproic acid is almost diagnostic[27], there are subgroup of patients with JME that do not respond well to this drug.[28]

The authors in the present study, published in this issue,[29] examined the characteristics of JME patients with focal or asymmetrical epileptiform abnormalities and specifically in terms of response to treatment. The proportion of EEG asymmetries between medication sensitive group (52.9%) and treatment resistant group (63.5%) did not reach statistical significance. Patients with or without asymmetries showed no statistically significant difference in all clinical characteristics.
In this study, similar to the report by Lancman et al, the

asymmetrical EEG features were not consistent suggesting that they were fragments of generalized spikes rather than true focal discharges[23]. In addition, the start of treatment before EEG in majority of patients in the current study could have changed the generalized and asymmetrical spikes differently. The impact of the inter-interpreter variability was also addressed.

Correct diagnosis of JME avoids delay in treatment with proper anti seizure drugs and also appropriate genetic counselling. History is most important in diagnosis and EEG is an ancillary tool. The question about myoclonic jerks and absence and family history of seizures should be asked in patients presenting with seizures.

There have been reports of benign variants misinterpreted as focal epileptiform discharge. Therefore the diagnosis of partial epilepsy will be premature if it is based on a single focal interictal abnormality and isolated clinical signs. This could result in the wrong treatment and aggravation of seizures[30]. Serial EEGs and with sleep deprivation, photic stimulation and hyperventilation could be helpful in revealing the typical generalized discharges.

The asymmetrical spikes are more likely to be "focal" if the slow wave of the discharge does not mirror the generalized spike-wave; the maximum voltage is not in the frontal or central regions and if there is associated focal slowing of the background. Asymmetrical EEG findings and focal abnormalities are not primary in making the diagnosis when the patient has EEG evidence of absence, ictal myoclonus and photoconvulsive response. However, in JME patients with so called "focal EEG abnormalities", ictal video/EEG recording could improve the diagnostic yield.

Other helpful diagnostic features include the presence of absence and generalized tonic/clonic seizures in sequence and in the appropriate age group, circadian distribution, typical seizure provoking factors, normal neurological examination and neuroimaging, and excellent response to treatment with Valproic acid.

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https://doi.org/10.1017/S0317167100051374 Published online by Cambridge University Press