Despite several studies there are still some issues concerning the correct diagnosis of epilepsy that should be distinguished from many other critical symptoms and diseases. Moreover, the assessment of a specific epileptic syndrome can have some degree of uncertainty. In this research highlight we discussed the findings of our recent study that demonstrated that at the onset of seizures an initial diagnosis is possible in the majority of cases; epilepsy syndromes can be identified at the time of the initial diagnosis and, at follow up, this diagnosis has not to be revised in 90% of the cases. Moreover, we analysed the main data form literature concerning the difficulties of the epilepsy syndromes diagnosis.

**Keywords:** Epilepsy; Classification; Follow-up

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**Introduction**

The most important purpose for a clinician is to identify a correct diagnosis of epilepsy. In fact, at initial presentation it may be difficult also for an experienced epileptologist or neurologist. In some cases, misdiagnosis is inevitable because of many reasons such as overlapping clinical features with other conditions, inadequate available history and limitations of investigations. The consequences can be an inappropriate treatment despite of a correct management [1], adverse reactions with antiepileptic drugs (AED) [2] and the psychological impact related to the diagnosis of epilepsy. Tics, staring, syncope, dystonia, psychogenic non epileptic-seizures and behavioural disturbances are the most common clinical conditions misdiagnosed with epilepsy. Moreover, some studies [3, 4] showed that tongue biting, urinary incontinence and post-ictal confusion, can occur not only in seizures but also in syncope and non-epileptic attack disorder. Thus, anamnesis is crucial for a good diagnosis even if patients are unable to explain what happened both due to a loss of consciousness and, in some cases, due to a lack of witness during the episode. In most cases, interictal electroencephalographic (EEG) evaluation gives an important contribute to the classification and identification of seizures but it has some limitations because EEG abnormalities can be observed in epilepsy and also in non-epileptic patients. [5]

Furthermore, it is important that, in the majority of cases in epilepsy, the diagnosis can be identified at onset although there are additional informations, (such as subsequent EEGs, imaging data and new clinical symptoms, assessed during a follow-up period), which can allow to clarify the etiology of seizures and classify patients in a specific syndrome [6].

**Analysis of literature**

The aim of this review is to investigate the possibility to diagnose epilepsy after a first unprovoked seizure, on
the basis of clinical and EEG characteristics, and to confirm it after a follow-up period. We based on a recently published study of Gaggero et al. [7], which evaluated the possibility of early syndrome classification of idiopathic partial epilepsies in children after the first seizure. The study involved 107 children with a first unprovoked focal seizure. A specific syndrome diagnosis was possible in 74.7% of patients; at the end of follow-up (mean period 6.9 years), the initial diagnosis was confirmed in 90% of patients and, among the unclassified cases, the diagnosis was confirmed in 40.7%, whereas, in 59.3%, it changed into other syndromes or atypical forms. The conclusion was that, at the onset of seizures, the diagnosis is possible in the majority of cases. Starting from these findings, we researched previous studies that have addressed the subject in its various aspects.

Initial results were very conflicting; in 1997, Arts et al [8] concluded that classification of epilepsy at the time of diagnosis may lead to errors, especially in children with mental retardation and that International League Against Epilepsy (ILAE) classification is not always useful for clinical epidemiologic studies because some epileptic syndromes are not frequent. In contrast, Loiseau et al. [9] found that 28% of patients could be diagnosed with epilepsy after a first event, on the basis of symptoms and electroencephalographic results. Another study published in 1999 [10] concluded that, after 2 seizures from the onset of these, childhood-onset epilepsy can be classified according to the ILAE guidelines, but such classification may change with long-term follow-up because epileptic syndrome can evolve. Other 2 studies reached the same conclusions of Gaggero et al [7]. Berg et al. [8] compared the initial classification of epileptic syndromes with the classification made after a follow-up of 2 years. This study involved a cohort of 613 children with newly diagnosed epilepsy and classified according to ILAE guidelines; after 2 years, classification did not change in 86.3% of cases. Conclusions were that epileptic syndromes can be diagnosed after the first presentation in the majority of cases and that changes were made, in particular, for those syndromes that were non completely defined at initial diagnosis. In agreement, Sarisjulis et al. [11] demonstrated that for over 75% of children with cryptogenic epilepsy, the diagnosis of an epileptic syndrome can be made during the first month of observation, based on clinical and EEG characteristics.

Some years before, in 1998, Stroink et al. [12] tried to assess the accuracy of diagnosis of a first unprovoked seizure in children, the recurrence rate after a follow-up period, the risk factors associated and their long term outcome. The overall recurrence rate after 2 years was 54%; risk factors were pathological EEG (recurrence rate 71%) and symptomatic aetiology or mental retardation (recurrence rate 74%). For children with recurrences, terminal remission 2 years later was > 12 months in about 59%. Considering both groups with recurrence and no recurrence of seizures, a terminal remission of 12 months was present in 78% of cases. In conclusion, a first critical event can be precisely diagnosed only using strict diagnostic criteria, that may also help to determine the high risk of recurrence, and the overall prognosis after a first seizure is excellent, even without treatment. These results were confirmed by other studies: in particular, Ramos-Lizana et al. [13] found a recurrence risk of 87% after a first unprovoked seizure in children. In contrast with Stroink et al. [12] but in agreement with 2 other studies [14, 15] abnormal EEG was not a risk factor for recurrence in symptomatic seizures. A more recent study [16] analysed a group of 200 children with a first unprovoked seizure after a 15 years follow-up and found that significant variables for the development of epilepsy were partial seizure type and EEG with epileptic abnormalities, and that epilepsy group had a 2.6 greater risk of psychiatric and academic comorbidities compared to the group without epilepsy.

Studies published later focused on another aspect: the misdiagnosis of epilepsy, due to different reasons, which often leads to mistreatment. In particular, Leach et al. [17] evaluated 275 adult patients with a previous diagnosis of epilepsy and receiving anti-epileptic drug therapy. The purpose was to identify patients previously evaluated by a neurologist, in whom diagnosis of epilepsy was uncertain, withdrawal of anticonvulsant therapy could be considered and seizure control could be improved. They concluded that 55% of adult population receiving AED has never seen a specialist and that reassessment of these patients revealed diagnostic uncertainty, failure to classify, which caused inadequate therapy, and lack of information about all aspects of epilepsy.

Epilepsy must be differentiated from non-epileptic events but misdiagnosis of epilepsy can be frequent as suggested by the study of Beach et al. [18] They described a group of children with new presentation of paroxysmal disorders classified at first evaluation and after a period of 6-30 months. Their conclusion was that non-epileptic events are twice as common as epilepsy and that diagnosis is uncertain in above 20% of cases after a first event. Acknowledging uncertainty is clinically useful and may reduce the rate of misdiagnosis and the pressure to make an unclear diagnosis of epilepsy. Such conclusions were supported by the study of Uldall et al. [19] on a cohort of children with a previous diagnosis of epilepsy, who were admitted to a tertiary epilepsy centre in Denmark. On discharge, 39% of these patients were found not to have epilepsy; the most frequent diagnosis was staring episodes in mentally retarded children and
psychogenic non-epileptic seizures. Almost half of these children received antiepileptic therapy at the time of admission; thus, at discharge, therapy was tapered off. The Authors underlined the necessity of caution in diagnosis, especially of staring episodes, and the opportunity of a diagnostic re-evaluation in difficult cases, in order to avoid unnecessary therapy and restrictions of the child’s lifestyle.

Moreover, Chowdhury et al. explored the causes of misdiagnosis of epilepsy and imputed them to: overlapping clinical features, inadequate witnessed history, limitations of investigations, particularly EEG, and insufficient experience of clinicians in distinguishing epileptic from non-epileptic events. They assessed the necessity of a gold standard to improve diagnostic accuracy, but this is not available in epilepsy. Thus, they proposed that management of a patient with a probable but not definite diagnosis of epilepsy should be based on reassessment and re-evaluation of the patient over the time, in order to review, when possible, the initial diagnosis.

As mentioned above, although EEG may be helpful in classifying epilepsy, often patients with epilepsy can have normal interictal EEG and patients without epilepsy may present abnormal electroencephalogram. Its value in childhood onset epilepsy was better described in the study of Shahar et al. The purpose was to demonstrate whether sleep deprivation evoked epileptic discharges in children with new onset of seizures and an initial normal awake record. Sleep deprivation of 6 hours provoked epileptic discharges in 27.2% of children, especially in whom with focal seizures. This result was in agreement with previous pediatric studies. Therefore, they recommended performing a sleep-deprived EEG in all children with new onset of epilepsy and normal standard EEG and underlined the value of sleep-deprived EEG in sleep-dependant epileptic syndromes, such as frontal lobe epilepsy. The conclusion was also supported by the study of Gaggero et al.

The importance of making diagnosis of epileptic syndrome after a first seizure is also associated to the possibility of predicts the outcome of the syndrome itself. The study of Gaggero et al. demonstrated that an initial prognosis is possible in the majority of patients with idiopathic partial epilepsy at the onset; in particular, children with idiopathic childhood occipital epilepsy of Gastaut had more frequently a prolonged non remitting course, whereas those affected by childhood epilepsy with centro-temporal spikes and Panayiotopoulos syndrome presented a good prognosis. These results are in agreement with the study of Geerts et al. which better described the course and outcome of childhood epilepsy during 15-year follow-up. Conclusions were that in most children with newly diagnosed epilepsy, the long-term course was good, and, in particular, those with idiopathic aetiology reached remission.

Conclusions

The diagnosis of epilepsy can be sometimes difficult because many paroxysmal events may be mistaken for epilepsy (e.g. syncope, dystonia, psychogenic seizures); moreover, the syndromic diagnosis of epilepsy can be uncertain and it is possible that changes may occur in the assessment of the epileptic syndrome some years after initial diagnosis, although at the onset of seizures a correct diagnosis is possible in the majority of cases and in particular in idiopathic partial epilepsies.

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