

All children who experience epileptic falls do not necessarily have Lennox-Gastaut syndrome... but many do

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ABSTRACT – Lennox-Gastaut syndrome (LGS) is a severe, chronic, epileptic encephalopathy, primarily with childhood onset, which is characterised by a triad of features: multiple seizure types, including tonic seizures that may appear late in the course of the disorder; abnormal EEG features with slow spike-wave discharges; and cognitive impairment. Recognition of LGS is problematic, since the seizure types and EEG features that characterise it are not pathognomonic and often change over time. Furthermore, although seizures associated with LGS may occur *de novo*, the appearance of core LGS seizures may be preceded by prolonged periods of other seizure types, including myoclonic seizures, partial seizures, or infantile spasms. This has led some authors to postulate that a continuum between LGS and other types of childhood epilepsy may exist. Accurate diagnosis requires careful assessment of both clinical and EEG features, in order to distinguish LGS from other childhood epilepsy syndromes, such as atypical benign partial epilepsy of childhood, Dravet syndrome or epilepsies with predominantly myoclonic-astatic seizures. Since there is no biological marker that can be used to confirm diagnosis of LGS and because of the multiple aetiologies that could lead to its development, early referral to a specialist team may prove to be crucial for facilitating both diagnosis and management. Such an approach ensures that patients receive the appropriate treatment at the correct time, providing the best opportunity for the clinical course and overall prognosis to be improved. Effective management of LGS requires regular reappraisal of the evolving symptoms and features, and adjustment of the treatment accordingly.

Key words: differential diagnosis, Dravet syndrome, Lennox-Gastaut syndrome, myoclonic-astatic seizures, Doose syndrome, atypical benign partial epilepsy

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Although the term “Lennox-Gastaut syndrome” (LGS) is sometimes used loosely to describe severe epilepsy syndromes of childhood that feature several types of intractable seizures, including falls (drop attacks) and tonic seizures, such a broad definition is both misleading and unhelpful, since it encompasses several epilepsy disorders, including those featuring predominantly myoclonic-astatic seizures, for which the appropriate therapy – and outcome – can differ markedly from that of LGS. The accurate and early diagnosis of LGS is key to its effective treatment and management. However, this is often difficult to achieve, since the aetiology, seizure types and electroencephalographic features that characterise LGS are not pathognomonic, and no biological marker for the disorder is yet available. Moreover, the seizure types and other features associated with LGS are not static, but evolve over time, further complicating the diagnostic picture. Importantly, LGS is often confused with other syndromes, particularly during its early stages, when appropriate treatment may have the potential to alter the patient’s clinical course and overall prognosis.

As the onset of LGS is usually during early to mid childhood, this paper will focus on its management in children; in particular, on the issues associated with recognising and accurately differentiating it from other childhood epilepsy syndromes. A detailed discussion of antiepileptic medication and the role of surgery are beyond the scope of this paper.

Characteristics of LGS

Occurring more frequently in males than females, the age of onset of LGS is typically between 1 and 7 years, most commonly between 3 and 5 years (Arzimanoglou *et al.*, 2004a). In approximately one-fifth of cases, age of onset is <2 years (Arzimanoglou *et al.*, 2004a). Although onset after 8 years of age is rare (Roger *et al.*, 1989), LGS may also be diagnosed in adolescence and adulthood (Lipinski, 1977; Bauer *et al.*, 1983; Kerr *et al.* 2011). The incidence of LGS is low – estimated at 0.1 per 100,000 inhabitants per year (Campos-Castelló, 2004), but prevalence is high due to its intractability, with reported rates in the range of 3-10% in children with epilepsy (Cavazzuti, 1980; Sidenvall *et al.*, 1996; Trevathan *et al.*, 1997; Markand, 2003). The majority of cases of LGS (~67-75%) have a symptomatic aetiology, usually occurring as a secondary result of a brain abnormality (e.g. developmental malformation, brain insult, infection, tumour) (Arzimanoglou *et al.*, 2004a; Markand, 2003). Genetic factors may also be involved, but are thought to be less important aetiologically than brain injury. Approximately 25-33% of LGS cases are cryptogenic, developing *de novo* in previously healthy

subjects (Arzimanoglou *et al.*, 2004a). LGS has a poor prognosis, with reported mortality rates in the range of 3% (mean follow-up period 8.5 years) to 7% (mean follow-up period 9.7 years), often related to seizure-associated accidents (Glauser *et al.*, 2010).

Diagnostic criteria

A precise definition of LGS remains elusive, since there is still considerable debate concerning the specific limits, cause(s) and diagnosis of the syndrome. Currently, the most widely accepted diagnostic criteria comprise a triad of features (*figure 1*) (ILAE, 1989; van Rijkevorsel, 2008; Arzimanoglou *et al.*, 2009; Ferrie and Patel, 2009):

- *multiple seizure types (table 1)*: these are mainly generalised and typically include tonic and atonic seizures – which often cause falls (drop attacks/astatic seizures) – and atypical absences. Between 50% and 75% of patients have episodes of nonconvulsive status epilepticus; myoclonic, generalised tonic-clonic and focal seizures may also occur. The occurrence of tonic seizures, particularly during sleep, is particularly characteristic of LGS, and is often considered a prerequisite for diagnosis (Dulac and N’Guyen, 1993; Arzimanoglou *et al.*, 2009). The vast majority of patients continue to have seizures (Roger *et al.*, 1989; Guerrini, 2006) – reported remission rates in the range of 0-7% (Arzimanoglou *et al.*, 2004a) – although the types of seizure usually evolve over time (Glauser, 2004b);

- *abnormal EEG (figure 2)*: this consists primarily of an interictal pattern of diffuse, slow spike-wave (SSW) complexes at <3 Hz, occurring during wakefulness. Several authors consider the presence of paroxysmal fast rhythms (10-20 Hz), appearing mainly during non-REM sleep, to be an additional necessary criterion (Beaumanoir, 1985; Genton *et al.*, 2000). Given the semiological importance of seizures occurring during sleep, the use of sleep EEG recording is considered mandatory for the diagnosis of LGS (Arzimanoglou *et al.*, 2009). EEG abnormalities generally persist, although the characteristic SSW pattern may disappear over time, often developing into focal discharges, and diffuse and focal slow waves (Ohtsuka *et al.*, 1990; Hughes and Patil, 2002);

- *cognitive impairment*: this involves mental retardation and is often accompanied by behavioural problems. Cognitive impairment may exist prior to the onset of seizures when LGS results from an underlying brain abnormality (e.g. tuberous sclerosis), or following infantile spasms. However, since LGS is an epileptic encephalopathy, cognitive impairment of variable degree is considered by most epileptologists to be an essential diagnostic feature of the condition

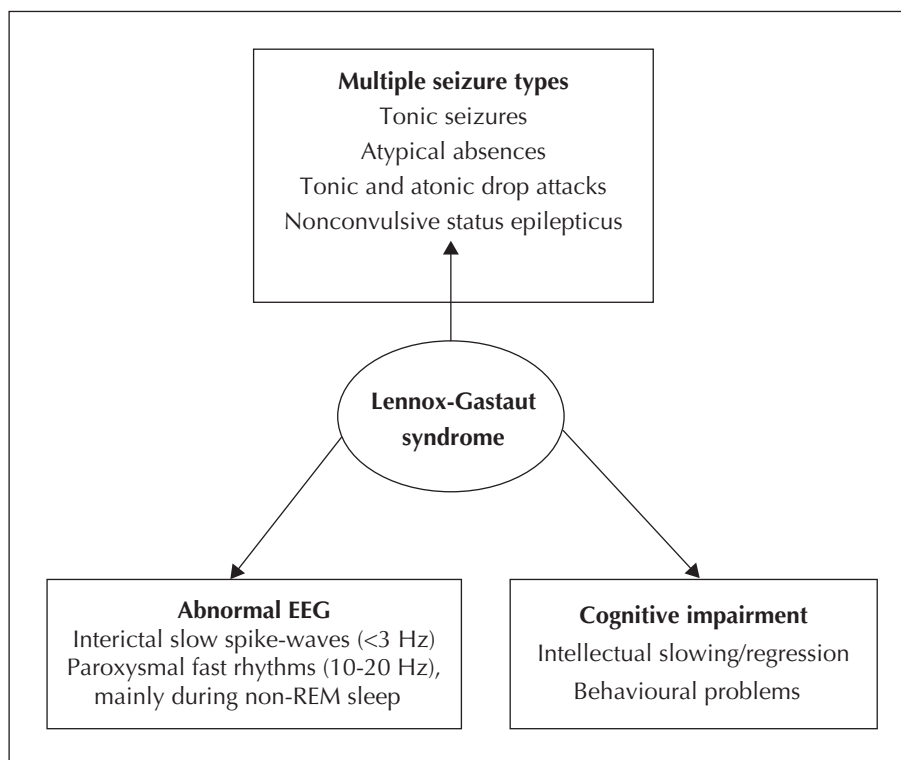


Figure 1. Characteristic triad of features associated with Lennox-Gastaut syndrome.

(van Rijckevorsel, 2008; Arzimanoglou *et al.*, 2009; Ferrie and Patel, 2009). Following seizure onset, there is a progressive slowing or arrest of cognitive development (IQ tending to decrease over time [Glauser, 2004b]), with behavioural problems in approximately 50% of cases, including hyperactivity, aggressiveness and autistic traits (van Rijckevorsel, 2008). In later stages of LGS, it may be difficult to differentiate problems relating to the syndrome from those occurring as a result of numerous drop attacks or frequent status epilepticus, or as adverse effects of antiepileptic drug (AED) treatment. Disability resulting from cognitive and behavioural problems often interferes with normal school attendance and social participation, even when the cognitive deficit is relatively mild.

Diagnosis of LGS is thus dependent on the interaction between these clinical and EEG features, and the differentiation of defining (as opposed to associative) features helps to distinguish LGS from other epileptic disorders.

Differential diagnosis of LGS

Problems associated with diagnosis

Relatively broad definitions have sometimes been used to denote LGS, but these can themselves be

unhelpful, since they encompass other epilepsy syndromes that may require alternative approaches to treatment and management. For example, LGS has been defined on the basis of a diffuse spike-and-wave EEG pattern, mental retardation and multiple seizure types, without reference to age or night-time tonic seizures (French *et al.*, 2004), and such a definition could encompass Dravet syndrome, myoclonic-astatic epilepsy (Doose syndrome) and focal cryptogenic epilepsies (van Rijckevorsel, 2008).

Even if the stricter characteristic triad of features outlined above (*figure 1*) is accepted, the diagnosis of LGS can still be problematic for a variety of reasons, not least because there is currently no biological marker for the syndrome, hampering differential diagnosis at onset, particularly for cryptogenic cases. Crucially, the limits of the syndrome are difficult to define precisely and the clinical presentation of LGS may be highly heterogeneous.

Not all patients with LGS display the characteristic triad of features, particularly at onset. For example, although the occurrence of tonic seizures is often considered a prerequisite for diagnosis of LGS (Arzimanoglou *et al.*, 2009), they are not necessarily evident at its onset, their presence being reported to vary between as much as 17% and 95% (Arzimanoglou *et al.*, 2004a). Similarly, fast rhythms during slow sleep are only seen in approximately 50% of LGS patients for whom whole-night EEGs

Table 1. Seizure types associated with Lennox-Gastaut syndrome.

Core seizure types	
Tonic seizures	- Most characteristic seizure type in LGS, particularly when occurring during sleep - Variable rate of occurrence: more commonly reported when polysomnography is used - Not always present at onset of LGS - Characterised by “a sustained increase in muscle contraction lasting a few seconds to minutes” (Blume <i>et al.</i>, 2001) - Usually brief, lasting from a few seconds to 1 minute (average: 10 s) - Muscle contraction may be limited to a flexor movement of the head and trunk (axial subtype), abduction and elevation of the arms (axorhizomelic seizures), or affect most muscles (global tonic attack) - Seizures may be subtle (e.g. a slow rolling upward of the eyes); polygraphy, including surface electromyography recording, is therefore particularly useful for recognition
Atypical absences	- Second most common type of seizure in LGS, observed in 13-100% of patients (Aicardi and Gomes, 1992; Gastaut <i>et al.</i>, 1973) - Frequency is difficult to evaluate due to gradual onset/offset, particularly in patients whose responsiveness is already diminished due to cognitive impairment - Seizures with a different underlying pathophysiology can manifest clinically as a “pseudo absence”, further hampering correct identification (e.g. focal seizures with alteration of consciousness, episodes of nonconvulsive status)
Sudden tonic or atonic falls (drop attacks)	- Particularly hazardous source of injury to patients - Occur in approximately 50% patients who have SSWs (Chevrie and Aicardi, 1972) - Not diagnostic for LGS, since also observed in other epilepsy syndromes (e.g. those with predominately myoclonic-astatic seizures)
Non-convulsive status epilepticus	- Occurs in 50-75% of LGS patients - Usually consists of subcontinuous atypical absences with varying degrees of altered consciousness, periodically interrupted by recurring brief tonic seizures
Myoclonic seizures	- Occur in 11-28% of patients (Beaumanoir and Dravet, 1992; Geoffroy <i>et al.</i>, 1983; Dravet <i>et al.</i>, 1982; Gastaut <i>et al.</i>, 1973; Chevrie and Aicardi, 1972) - Shorter than tonic seizures (<100 ms) (Blume <i>et al.</i>, 2001), but may also lead to falls - Occur in many generalised epilepsy syndromes and should therefore be regarded as associated (rather than defining) features of LGS
Other seizure types	
- Focal seizures ± secondary generalisation - Generalised tonic-clonic seizures - Unilateral clonic seizures	- Commonly occur in addition to the core seizures of LGS (outlined above) - Usually occur in later stages of LGS, but may sometimes precede core attacks, further complicating differential diagnosis

EEG: electroencephalogram; LGS: Lennox-Gastaut syndrome; SSW: slow spike-wave.

are performed. In one study, 37% of a total of 103 LGS patients presented with only some of the characteristic features of the syndrome, exhibiting a variety of other seizure types, including focal seizures and, in a few cases, generalised tonic-clonic seizures or absences suggestive of primary generalised epilepsy (Beaumanoir and Dravet, 1992).

Seizures associated with LGS may occur *de novo*, but the appearance of core LGS seizures may be preceded

by prolonged periods of other seizure types. Indeed, the gradual progression of infantile spasms and hypsarrhythmia into LGS with SSW complexes may account for around 20% of all cases of LGS (Genton *et al.*, 2000). This illustrates an important factor affecting LGS diagnosis: that seizure types and other features associated with the condition do not remain static, but evolve over time. For example, patients aged 2-5 years may present with mainly myoclonic

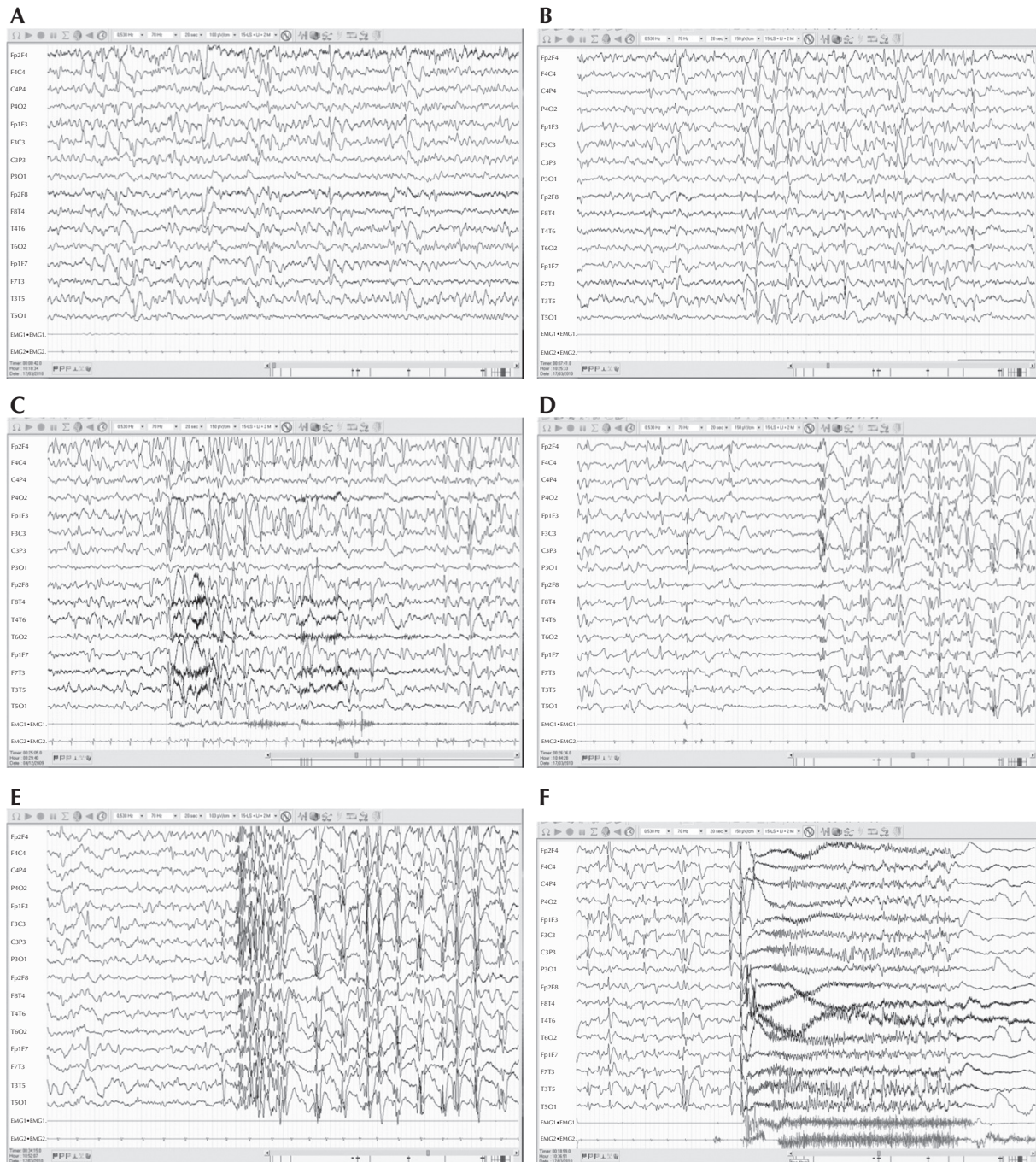


Figure 2. Polygraphic EEG recording of a 9-year-old boy with Lennox-Gastaut syndrome (Courtesy Dr. Julitta de Bellescize; IDEE, Lyon). While awake (A-C): slow background activity; multifocal paroxysmal abnormalities with anterior predominance of slow spike-wave complexes; also note (B, C) the presence of rather rhythmic and diffuse bursts of polyspikes (Gain on B and C at 150 microV/cm). Sleep recording (D-F): note the generalised polyspikes discharge (E; Gain 100 microV/cm) and the tonic seizure (F; Gain reduced to 100 microV/cm) with the tonic contraction of both deltoids (EMG1 and EMG2 derivations).

or myoclonic-astatic seizures, episodes of nonconvulsive status epilepticus and EEGs variably featuring fast spike-wave and SSW complexes (suggestive of myoclonic-astatic epilepsy); but some may subsequently develop tonic seizures and fulfil the main criteria for LGS. The pattern of SSW complexes that characterise LGS may be transient; for example, a study of long-term changes in EEG patterns in 64 LGS patients followed up over a period of 42 years found that the mean duration of classic SSW complexes was 8.2 years (range 1-35 years; median 5.5 years) (Hughes and Patil, 2002). In addition, learning difficulties and behavioural problems develop over time and may not be present or evident at presentation (e.g. in cases that do not have symptomatic aetiology involving brain damage). Encephalopathic features may appear very gradually and mental difficulties may be wrongly attributed to adverse effects of medications used to control seizures.

Another important factor that can complicate the diagnosis of LGS is that none of its features are pathognomonic. Drop attacks, although commonly present at onset, easily identified and readily counted, are not unique to LGS. For example, they are also associated with myoclonic-astatic seizures. Seizure semiology can also be misleading. Some secondarily generalised seizures with a very brief partial phase may be mistaken for the primary generalised seizures of LGS (Stafstrom, 2009), and it can be difficult to differentiate between tonic and atonic drop attacks. Video and sleep EEG recording may be required to detect difficult-to-distinguish tonic seizures and surface electromyography recording may be needed in order to identify subtle tonic seizures. Accurate identification and quantification of atypical absences can be problematic (Stafstrom, 2009), particularly in patients whose responsiveness is already compromised by cognitive impairment. However, typical and atypical absences can easily be differentiated when assessed alongside their EEG correlates, which differ greatly from each other.

There is a risk of underdiagnosing LGS, since some types of seizures might occur many months before the onset of SSW complexes, and EEG recordings during sleep are not always available. There is also a risk of overdiagnosis, if diagnosis is made solely on the basis of the presence of SSW complexes on the EEG; also, patients with only tonic seizures or drop attacks do not necessarily meet the criteria for LGS. These issues underline the fundamental importance of the conjunctive use of clinical and EEG assessments when diagnosing childhood epilepsy syndromes.

Although LGS diagnosis can be problematic, the clinical and EEG criteria used to define the syndrome have been successfully used to identify patients, both in

clinical practice and for participation in trials assessing the efficacy and safety of AEDs for the treatment of LGS (Motte *et al.*, 1997; Sachdeo *et al.*, 1999; Felbamate Study Group in Lennox-Gastaut Syndrome, 1993; Glauser *et al.*, 2008; Conry *et al.*, 2009).

Differentiation of LGS from other childhood epilepsies

Careful attention to both clinical and EEG features should allow the discrimination of LGS from other epilepsy syndromes in the majority of cases, but there are certain types of epilepsy with which it may be confused. For example, atypical benign partial epilepsy of childhood, also known as “pseudo-Lennox syndrome”, is characterised by the presence of generalised seizures (including atonic-astatic seizures, atypical absences and myoclonic seizures), multiple partial and secondarily generalised seizure types, and focal sharp waves on EEG with generalisation during slow sleep (Hahn, 2000). It is important to distinguish this type of epilepsy from LGS (and myoclonic-astatic epilepsy), because of differences in prognosis – atypical benign partial epilepsy of childhood typically remitting by adolescence – and the possible need for different AED therapies (Hahn, 2000). The main source of confusion is that the EEG features of atypical benign partial epilepsy of childhood can mimic those of LGS (*figures 3, 4*) (Arzimanoglou *et al.*, 2009). However, the absence of tonic drop attacks and nocturnal tonic seizures, together with a lack of fast (>10/s) spike discharges and the presence of a normal or slightly slow background activity, enable atypical benign partial epilepsy to be distinguished from LGS (Hahn, 2000).

Another common source of misunderstanding is the differentiation of LGS from myoclonic-astatic epilepsy and Dravet syndrome, since all three conditions involve multiple seizure types. Differential diagnosis of these syndromes is of considerable prognostic, therapeutic and genetic importance, since (a) at least half of children with myoclonic-astatic epilepsy have a good prognosis, (b) drug treatments that are effective for LGS can exacerbate myoclonic seizures in patients with Dravet syndrome (e.g. lamotrigine) (Guerrini *et al.*, 1998), and (c) the risk of familial recurrence is higher for Dravet syndrome and myoclonic-astatic epilepsy than it is for LGS (Arzimanoglou *et al.*, 2004b). However, accurate history-taking and the use of appropriate electroencephalography (including sleep recording) and simultaneous electromyography – ideally accompanied by video recording – makes differential diagnosis feasible in the majority of cases.

Differentiation between LGS and myoclonic-astatic epilepsy is normally straightforward, since the core types of seizures associated with LGS are tonic attacks,

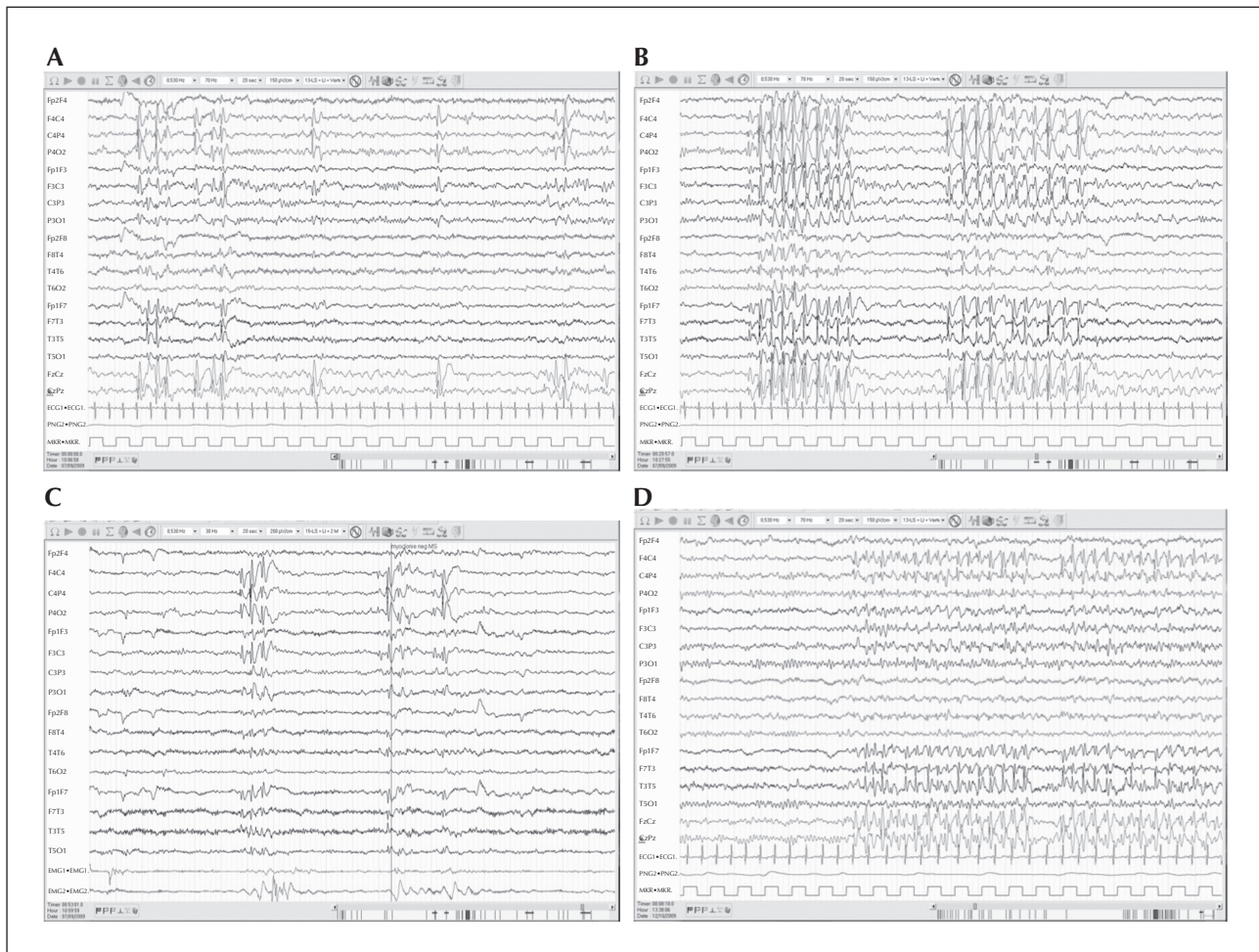


Figure 3. Polygraphic EEG recording of a 3-year-old boy consulting for “absence” episodes and falls. Atypical partial epilepsy of childhood (also reported as pseudo-Lennox syndrome) (Courtesy Dr. Julitta de Bellescize; IDEE, Lyon). **A)** Normal background activity; right centro-temporal pseudo-rhythmic biphasic spikes and slow waves with diffusion to the left derivations. **B)** Bursts of bi-synchronous, rather diffuse and ample biphasic spikes. During the second bout the child stopped sucking his thumb. **C)** Child recorded with arms stretched; note loss of tone on polygraphic recording, concomitant to the central slow wave. **D)** Clear activation of the right central focus during sleep with sequences of rhythmic spikes, lasting several seconds each. In this case, activation did not reach the stage of continuous spike-waves during slow sleep; tonic seizures were not recorded.

atypical absences and atonic seizures, and the EEG features of LGS are usually distinctive. Myoclonic seizures are, however, sometimes present in LGS. Moreover, although rare at the onset of myoclonic-astatic epilepsy, tonic seizures may occur later in the course of the disorder, leading to confusion with LGS; several authors have reported a high proportion of such cases (Kaminska *et al.*, 1999; Oguni *et al.*, 2001; Dravet *et al.*, 2002). Indeed, there have been reports of a myoclonic variant of LGS (Giovannardi-Rossi *et al.*, 1988; Dravet *et al.*, 1982; Aicardi and Chevrie, 1971), characterised by prominent myoclonic or myoclonic-astatic seizures and, less commonly, tonic seizures (usually late-onset and almost always nocturnal) and absence status, with EEGs variably featuring fast spike-wave and SSW complexes. Onset is generally later,

and outcome less unfavourable, than “typical” LGS. Distinction between the myoclonic variant of LGS and myoclonic-astatic epilepsy is particularly difficult (Markand, 2003), although specific diagnostic criteria for the latter have been published (Doose, 1992). Cases of epilepsy with myoclonic astatic seizures as the only type of seizures at onset may evolve to LGS (Hoffmann-Riem *et al.*, 2000). Differential diagnosis at an early stage is often very difficult and large-spectrum AEDs should be used to avoid an aggravating effect.

Similar to LGS, Dravet syndrome is characterised by brief seizures with falls and cognitive deterioration. However, the early history of patients with Dravet syndrome differs from that of LGS patients. The onset of Dravet syndrome is characterised by the occurrence of prolonged generalised or unilateral clonic

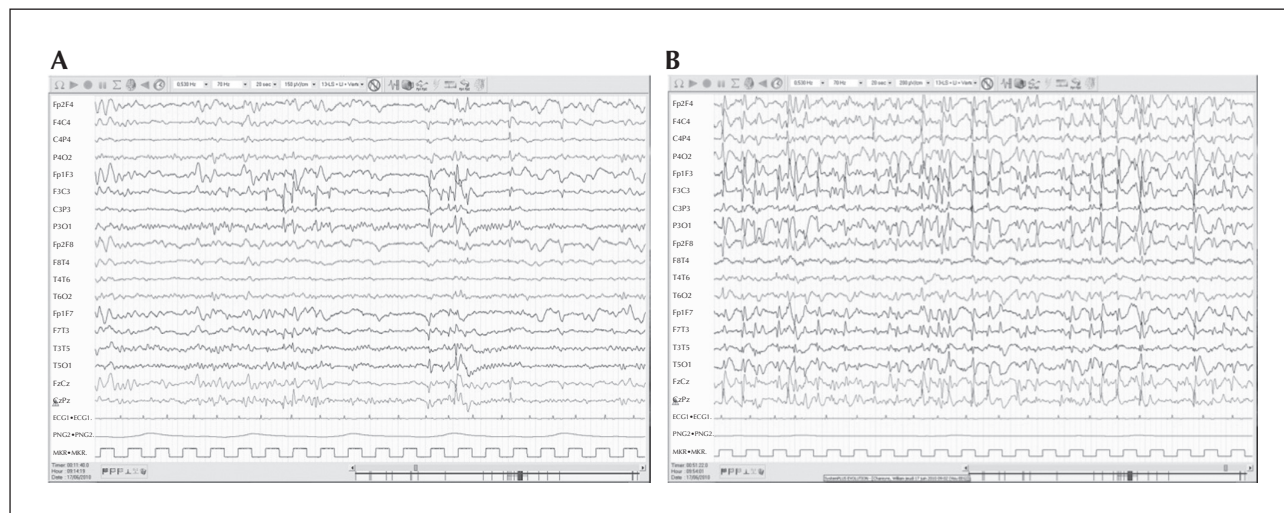


Figure 4. Polygraphic EEG recording of a 12-year-old boy. Atypical partial epilepsy of childhood (also reported as pseudo-Lennox syndrome) (Courtesy Dr. Julitta de Bellescize; IDEE, Lyon). Focal diphasic slow-spike-slow-wave complexes with left fronto-central-temporal predominance (A), evolving to continuous spike-waves during slow sleep (B).

febrile seizures, typically between the ages of 2 and 12 months (Dravet *et al.*, 1992). During the second and third years of life, brief attacks of different seizure types start to emerge, including myoclonic seizures, atypical absences, convulsive generalised tonic-clonic or clonic seizures, uni- or bilateral seizures, focal seizures, nonconvulsive status epilepticus and – only exceptionally – tonic seizures. Interictal EEG recordings are usually normal during the first few months of the disease, but subsequently change, with the progressive appearance of generalised, focal and multifocal abnormalities, and, from the second year of life, generalised discharges of fast spike-wave or polyspike-wave complexes and, often, focal or multifocal spikes (Dravet *et al.*, 1992; Arzimanoglou, 2009). Although children with Dravet syndrome appear to develop normally at first, developmental progression deteriorates substantially during the second or third year of life, resulting in psychomotor and neuropsychological disturbances (often accompanied by behavioural problems), which appear to be related to the severity of the epilepsy during the first 2 years of life (Wolff *et al.*, 2006). Most importantly for the differential diagnosis of LGS, EEGs of patients with Dravet syndrome never feature SSWs, and tonic seizures – if present at all – occur late and are few in number. Dravet syndrome can be differentiated from myoclonic-astatic epilepsy, since the overall history of patients with Dravet syndrome is dominated by repeated and prolonged convulsive seizures, which are not seen in myoclonic-astatic epilepsy.

The clinical and EEG features of the Dravet syndrome (Dravet, 1978), together with more recent supporting diagnostic evidence identifying an association with

SCN1A mutations (Claes *et al.*, 2001), makes feasible the early diagnosis and treatment of the condition. Clinical trials have demonstrated that adjunctive therapy with the novel AED stiripentol not only significantly reduces seizure frequency in children with Dravet syndrome (Chiron *et al.*, 2000; Thanh *et al.*, 2002; Chiron *et al.*, 2006; Chiron, 2007; Inoue *et al.*, 2009) but also reduces the duration of seizures and the occurrence of status epilepticus (Thanh *et al.*, 2002; Inoue *et al.*, 2009). Importantly, these effects have been shown to be greatest in the youngest patients, particularly those aged <2 years (Thanh *et al.*, 2002). Improvements in cognition and behaviour following stiripentol treatment have also been reported (Inoue *et al.*, 2009). Since patients with Dravet syndrome who are treated earlier appear to have a better prognosis than those treated later, it might reasonably be inferred that the same could be true of patients with LGS. This is of considerable importance, since it raises the possibility that early treatment might be able to alter the course of disease – for example, by helping to minimise mental deterioration resulting from epileptic encephalopathy or drop attack injury. Indeed, early, aggressive intervention is recommended for disorders that involve cognitive decline, psychomotor regression or intractability, such as LGS (Arts and Geerts, 2009). Although results from class I or II studies are not available for AED treatment of LGS at onset or early in the course of the disorder, it has been recommended that patients should be treated with a broad-range AED early on, when drop attacks are most prevalent, particularly since such agents might also be effective in treating atypical absences (Arzimanoglou *et al.*, 2009). Early use of a ketogenic diet, immunother-

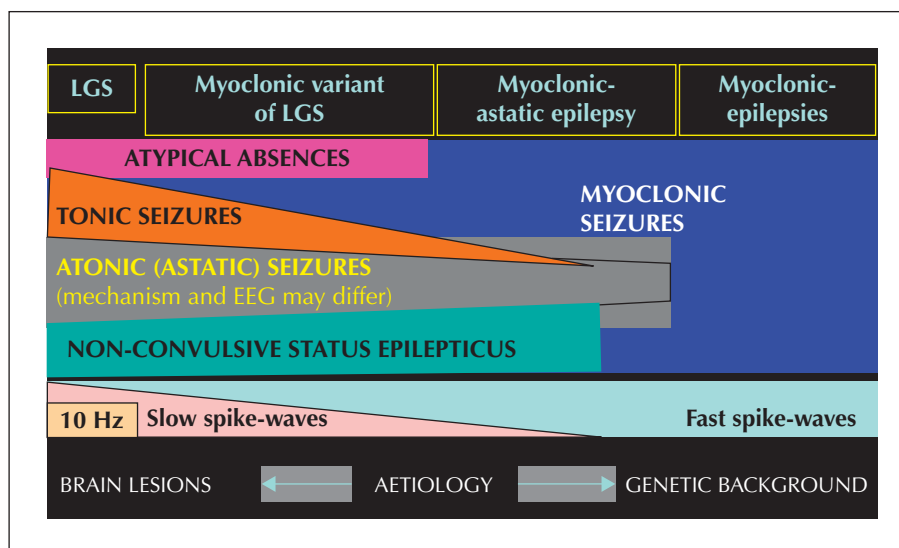


Figure 5. Potential overlap between LGS, myoclonic-astatic epilepsy and syndromes with predominantly myoclonic seizures (modified from Arzimanoglou *et al.*, 2004b).

rapy and vagus nerve stimulation, and early referral for epilepsy surgery, have also been suggested as important considerations in the management of LGS (Arts and Geerts, 2009; Arzimanoglou *et al.*, 2009; Ferrie and Patel, 2009; Liu *et al.*, 2007). The role of surgery in the treatment of LGS is beyond the scope of this paper.

As a result of the multiple aetiologies that could lead to the development of LGS, the lack of biological markers that could facilitate diagnosis and the complexity of the electroclinical picture, all children suspected to be at risk should be referred early to specialist epilepsy teams. Clinical experience may prove to be the only effective means of identifying LGS early. Appropriate diagnostic workup, including ≥ 24 -h video-EEG monitoring, will help early detection of tonic seizures. Appropriately chosen broad-spectrum AEDs will then be used early in the course of the disorder and heavy polytherapy will be avoided.

LGS is defined as a catastrophic epilepsy, since it typically involves seizures that are intractable and physically damaging, stagnation or regression of intellectual development, and serious, far-reaching social consequences (Camfield and Camfield, 2002). Early diagnosis is therefore central to the successful management of LGS (and other childhood epilepsy syndromes), since it not only dictates the appropriate choice of treatment, which could potentially alter the course and overall outcome of the condition, but also affects the expectations of patients and their families. Furthermore, early diagnosis enables the necessary support systems to be put in place to ensure that those affected receive the help that they will need throughout the course of the condition.

The progressive evolution of LGS features, the fact that it may precede or follow other epilepsy syndromes, and the degree of overlap between some syndromes have led some authors to postulate that there may be a continuum between LGS and other types of childhood epilepsy, such as those with predominantly myoclonic-astatic seizures at onset (*figure 5*) (Arzimanoglou *et al.*, 2004b; Shields, 2004; Camfield and Camfield, 2002). This concept highlights the need for and importance of continual reappraisal of patients' clinical and EEG features, re-evaluation of diagnoses, and willingness to change or adapt therapeutic approaches accordingly. In particular, the difference in AED response of the various syndromes that may mimic LGS should be taken into consideration.

Conclusions

LGS is characterised by a triad of symptoms: multiple seizure types, abnormal EEG features with SSW discharges, and cognitive impairment. The seizure types and EEG features that characterise LGS are not pathognomonic and may change over time, hampering diagnosis. Accurate diagnosis requires careful assessment by an experienced epilepsy team of both the clinical and EEG features, in order to distinguish early in the course of the disorder LGS from other childhood epilepsy syndromes. Early diagnosis of LGS is necessary to ensure that patients receive beneficial interventions at the appropriate time – early enough to allow the possibility of improving prognosis – and also to ensure that psychosocial support systems are initiated so that patients and families receive the assistance they need.

Physicians need to be aware that LGS features can evolve over time, and be alert to the possibility that a child may have LGS without presenting with all the features of the syndrome. They should also be prepared to review diagnostic criteria regularly, revise diagnoses, and change their approach to treatment/management accordingly, in order to ensure that patients receive the appropriate treatment at the correct time and thereby have the best chance of a favourable outcome. □

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