Review article

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Evolution and management of Lennox-Gastaut syndrome through adolescence and into adulthood: are seizures always the primary issue?

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ABSTRACT – Although Lennox-Gastaut syndrome (LGS) typically begins during childhood, it frequently persists through adolescence and on into adulthood. It may also, rarely, have late onset during adolescence or adulthood. Longitudinal studies have highlighted that the "typical" features of LGS observed during childhood evolve and change over time, so that by adulthood it might be difficult to recognise LGS in previously undiagnosed patients. Approaches to treatment must therefore adapt to the changes in a patient's condition as they progress through life. Effective management of LGS requires a global approach to care that not only encompasses seizure control, but also the management of co-morbidities associated with the condition, such as cognitive and behavioural problems, sleep disturbances and physical disability, together with the specific educational and psychosocial needs of the individual. This is particularly relevant during adolescence, when patients have to cope with a host of additional issues alongside those relating to their epilepsy. During all stages of life, management of LGS must carefully balance the need for treatment against its side effects, with the patient's overall quality of life always being the primary focus. The transition of care from paediatric to adult services presents important challenges for patients, their families and healthcare providers, and requires particular consideration to ensure that it is as smooth as possible. It also presents an important opportunity to review and reappraise a patient's condition, treatment and other longer-term needs as they journey into adulthood.

Key words: adolescence, adulthood, Lennox-Gastaut syndrome, co-morbidity, quality of life

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As with other types of difficult-to-treat childhood-onset epilepsy, Lennox-Gastaut syndrome (LGS) frequently persists through adolescence and into adulthood. In addition (albeit rarely), LGS may have a late onset, either in adolescence or in adulthood (Lipinski, 1977; Bauer *et al.*, 1983). Management of LGS in adolescence and adulthood is problematic: seizures are often intractable, there are complex problems associated with intellectual development, and the combination of intellectual disability and frequent behavioural difficulties can have serious social consequences (Paolicchi, 2002). By necessity, management is therefore multilayered and cannot simply focus on seizure reduction alone. The domains of care include: the control of seizures, management of behavioural and cognitive co-morbidities associated with LGS, minimisation of antiepileptic drug (AED)-associated side effects, and the provision of support for the social and developmental needs of the patient.

As discussed elsewhere in this supplement (see the chapter "All children who experience epileptic falls do not necessarily have Lennox-Gastaut syndrome... but many do"), the diagnosis of LGS is hampered by the fact that the seizure types and other features by which it is defined and characterised evolve and change over time. Consequently, subjects diagnosed with LGS during childhood may display very different clinical and electroencephalographic features by the time they reach adulthood. The recognition and diagnosis of LGS in later life is particularly challenging: the way it presents may not be consistent with the typical features associated with early-onset LGS; details of medical history and care during childhood may be lacking when a patient presents at a later stage; investigation may be hampered by complex behavioural problems associated with patients' intellectual disability; and clinicians may not consider LGS as a diagnostic option in older patients, and therefore overlook it.

In focusing on the management of LGS during adolescence and on into adulthood, this paper will describe how the features of LGS evolve over time, and outline and discuss issues relating to the management of LGS-associated co-morbidities and the need for a global approach to care, within the context of the specific problems faced by patients as they progress through adolescence into adulthood. It will also discuss the issues faced by LGS patients as they transition from school to work, and from paediatric to adult care environments.

Evolution of LGS through adolescence and into adulthood

Several longitudinal and retrospective studies have documented the progress into adulthood of patients diagnosed with LGS in childhood, in terms of clinical/EEG features and outcomes *(table 1)* (Ohtsuka *et al.*, 1990; Oguni *et al.*, 1996; Yagi, 1996; Ferlazzo *et al.*, 2010). Although the inclusion criteria and duration of follow-up vary between the studies, several important features emerge. Most notably, the studies illustrate that, by adulthood, approximately 50-75% of patients diagnosed with LGS during childhood no longer display all of the clinical and EEG features typically used to diagnose the syndrome. Due to treatment and/or the natural history of the syndrome, the number and variety of seizure types usually decrease over time, although tonic seizures tend to persist, particularly during sleep. The presence of slow spike-wave (SSW) complexes on EEG (commonly used as a diagnostic criterion during childhood) appears to be transitory in a high proportion of patients, with only a minority displaying SSW complexes in adulthood. However, the presence of diffuse fast rhythms during sleep, usually associated with tonic seizures, appears to be relatively consistent among adult LGS patients. Another common feature of the studies is that the majority of patients ($> 90\%$) have moderate to severe cognitive impairment by adulthood, often associated with behavioural problems, which affects their social independence and occupational status (Ohtsuka *et al.*, 1990; Oguni *et al.*, 1996; Yagi, 1996; Ferlazzo *et al.*, 2010). Although it is possible that these longitudinal studies are limited by selection bias, since patients with "milder" symptoms of LGS in adulthood may drop out of the system and go unrecognised, they highlight some important features of patients whose symptoms persist into adulthood and continue to require treatment, and illustrate that LGS is a condition that can and does affect patients throughout their lives. Even when seizures are fully controlled (which is rare), the adverse effects of treatment, and cognitive and behavioural disturbances, continue to affect patients' quality of life. These studies also highlight that, unless an adult is known to already have LGS, it may be difficult to recognise and make a definitive diagnosis of the condition in patients in whom it has evolved over an extended period of time into adulthood. For example, given the evolving nature of the condition, the overall value of using EEG to aid diagnosis of LGS appears to be very much reduced in the adult patient. An added challenge is that there is often a lack of accurate and detailed medical records for a patient presenting in adulthood (depending on the nature and extent of the medical care they received during childhood/adolescence) and the adult neurologist may need to rely on the family or caregiver for recollection of the patient's medical history.

It is also important to bear in mind that LGS can occur with late onset during adolescence or adulthood, although this is rare (Lipinski, 1977; Bauer *et al.*,

1983; Unterberger *et al.,* 2010). The seizure types and EEG features of late-onset LGS may be similar to those of childhood-onset LGS, but it may be difficult to recognise if it develops gradually from another pre-existing epileptic condition. In addition, the presence or development of cognitive impairment, which is very characteristic of LGS in childhood, may be less pronounced when LGS develops in adults, further hampering ready recognition of the syndrome (Bauer *et al.,* 1983). This may be because, with later onset, the brain has already progressed beyond certain critical developmental stages, so that seizures have a less damaging effect on cognitive development.

Regardless of whether it has persisted from childhood or developed later in life, the recognition and diagnosis of LGS in adults is often overlooked, since clinicians are not necessarily expecting to encounter it in adulthood. This underlines the crucial importance of re-assessing and re-evaluating patients' symptoms and features, and being prepared to amend diagnoses – and the appropriate approach to management – accordingly.

LGS-associated co-morbidities

In addition to, and often associated with, seizure-related pathology, epilepsy frequently involves serious co-morbidities that also require careful management. This is particularly true for LGS, since patients are not only impaired in their daily lives by a variety of seizure types – which are often frequent and physically damaging (*e.g.* drop attacks) – but also by impairments in cognition and behavioural problems, these being a characteristic feature of the syndrome (Arzimanoglou *et al.,* 2009). It is therefore important to recognise – particularly during adolescence, when individuals are undergoing great physical, mental, emotional and social changes – that seizure control is not necessarily the only concern in successfully managing LGS.

Cognition and behaviour

Patients with secondary or symptomatic LGS usually have delayed development at the onset of the condition. A small proportion of LGS patients may have intellectual ability within the accepted range of "normality", but even these individuals often have difficulties in daily life that appear to be related to a slowing of mental processing. Overall, the proportion of LGS patients with cognitive impairment increases to 75-95% by 5 years from syndrome onset, with significant decreases in IQ scores after 10 years (Ferrie and Patel, 2009; Arzimanoglou *et al.,* 2009). Cognitive impairment in LGS is frequently associated with behavioural problems, with approximately 50% of patients exhibiting symptoms such as hyperactivity, insecurity, aggressiveness and autistic traits (Besag, 2004; Arzimanoglou *et al.,* 2004; van Rijckevorsel, 2008).

The overall disability resulting from LGS-associated cognitive impairment interferes with normal school attendance and learning and results in feelings of social insecurity, even when the cognitive impairment is relatively mild (Arzimanoglou *et al.,* 2004). Adolescents with epilepsy are at considerable risk of developing psychopathology, such as depression (Dunn *et al.,* 1999; Turky *et al.,* 2008). In a survey of 56 children and adolescents with epilepsy, aged 5-17 years (mean age 12 years), 61.5% were found to have chronic distress and social impairment (Turky *et al.,* 2008). Cognitive impairment was significantly associated with behavioural issues – specifically conduct problems, hyperactivity/inattention and peer problems – and cognitive impairment and seizure frequency were significantly associated with diminished quality of life (Turky *et al.,* 2008). Adolescents' attitudes towards their epilepsy and satisfaction with family relationships appear to be related to depression (Dunn *et al.,* 1999). Unfortunately, recognition of depression in children and adolescents can be particularly problematic, especially when intellectual disability is present (Kanner and Dunn, 2004), and rates of underdetection and undertreatment of mental health problems in this age group are high (Dunn *et al.,* 1999; Ott *et al.,* 2003).

Similarly, during adulthood, problems with cognition and behaviour affect patients' ability to live independently and their employment prospects. Since intellectual disability is common (and seizure freedom rare), driving is not an option for most patients, which further affects both their independence and their employment choices. Many adults with LGS are unable to work and require institutional care (Yagi, 1996).

Sleep

Another co-morbidity associated with LGS is sleep-cycle disruption arising from seizure activity during the night. The occurrence of tonic seizures during sleep is particularly characteristic of LGS and often considered an essential diagnostic feature (Dulac and N'Guyen, 1993; Arzimanoglou *et al.,* 2009). Since epileptic activity during sleep is known to interfere with nocturnal long-term potentiation, which is responsible for establishing and strengthening memory and learning patterns (Parisi *et al.,* 2010), it may feed into the cognitive impairment resulting from the encephalopathy. Sleep disruption can also have many other detrimental effects, including behavioural impairment and psychological problems, such as hyperactivity, anxiety and depression (Neckelmann *et al.,* 2007; O'Brien, 2009).

Table 1

Table 1. Summary of longitudinal and retrospective studies assessing the evolution of LGS from childhood into adulthood.

Author(s)	Population	Follow-up	Key findings
Ohtsuka *et al.*, 1990	89 patients; 55M/34F Age at final follow-up: 10-15 years (n = 33), 15-20 years (n = 38), 20-25 years (n = 14), > 25 years (n = 4)	5.3-21.4 years	*At final follow-up*: - 21/89 (23.6%) patients were seizure-free for >1 year; 66/89 (74.2%) continued to have "minor seizures characteristic of LGS" (tonic spasms, atypical absences, atonic seizures, myoclonic seizures); 2/89 (2.2%) only had generalised tonic-clonic seizures. Predominant seizure type was tonic seizures (62/89 [69.7%] patients) - Only 8/89 (9.0%) patients had normal mental ability (IQ/DQ > 75); 48/89 (53.9%) were severely retarded (IQ/DQ < 25); mental prognosis was significantly worse in symptomatic *vs* cryptogenic patients and particularly poor in patients with a history of West syndrome - Diffuse SSW were observed in only 31/89 (34.8%) patients; focal discharges were observed in 26/89 (29.2%) patients - Only 31/89 (34.8%) patients continued to have minor seizures and diffuse SSW (*i.e.* LGS characteristics) - Age of disappearance of diffuse SSW: < 5 years (n = 17), 5-10 years (n= 9), 10-15 years (n = 14), 15-20 years (n = 7), > 20 years (n = 1) - In 27/89 (30.3%) patients, LGS developed into "severe epilepsy with multiple independent spike foci"; these patients were found to have the worst seizure and mental prognoses
Oguni *et al.*, 1996	72 patients; 46M/26F; 51 symptomatic, 21 cryptogenic. Mean age at LGS onset was 6 ± 3 years. Mean age at final follow-up was 23 ± 5 years in symptomatic patients and 21 ± 5 years in cryptogenic patients	Mean: 17 ± 5 years in symptomatic patients and 17 ± 4 years in cryptogenic patients (all >10 years)	*At final follow-up*: - 6/72 (8.3%) patients were either seizure-free or only had a few seizures annually; more than two-thirds had daily or weekly seizures, of which generalised tonic seizures were the most common; there were no differences in seizure outcomes between symptomatic and cryptogenic patients - IQ levels were below "moderate" in 96% and 86% of symptomatic and cryptogenic patients, respectively; severe/profound mental retardation was diagnosed in 76% and 43% of symptomatic and cryptogenic patients, respectively Epilepsy classifications were re-evaluated: - Symptomatic patients (n = 51): LGS (n = 23; 45.0%), non-specific symptomatic generalised epilepsy (n = 14; 27.5%), severe epilepsy with multiple independent spike foci (n = 8; 15.7%) and localisation-related epilepsy (n = 4; 7.8%); 2 patients (3.9%) had no seizures - Cryptogenic patients (n = 21): LGS (n = 14; 66.7%), non-specific symptomatic generalised epilepsy (n = 5; 23.8%) and localisation-related epilepsy (n = 1; 4.8%); 1 patient (4.8%) had no seizures

Table 1. (*Continued*)

Author(s)	Population	Follow-up	Key findings
Yagi, 1996	102 patients. Mean age at epilepsy onset was 4.3 years (range 0.2-18 years). Mean age at time of survey was 28.6 years (range 15-60 years)	Mean: 16.3 years (range 10-20 years)	*At time of survey*: - 8/102 (7.8%) patients were seizure-free for >1 year; 94/102 (92.2%) continued to have seizures, which were mainly tonic seizures (89.2% of patients) and which occurred more frequently during sleep than wakefulness - EEG: 33/102 (32.4%) patients had SSW complexes, fast rhythms and burst or repetition of multiple spike-and-wave complexes; 39/102 (38.2%) had fast rhythms and burst or repetition of multiple spike-and-wave complexes; 9/102 (8.8%) had burst or repetition of multiple spike-and-wave complexes; 8/102 (7.8%) had solitary multiple SSW complexes; 3/102 (2.9%) had SSW complexes; 1 (1.0%) had SSW complexes and multiple spike-and wave complexes; 4 (3.9%) had fast rhythms or SSW complexes or both, with focal spikes; 5 (4.9%) had no epileptic discharges - Overall, characteristic clinical and EEG symptoms of LGS were present in only 33/102 (32.4%) patients - Occupational status: 12/102 (11.8%) patients worked normally; 36/102 (35.3%) worked part-time or at a sheltered workplace; one (1.0%) was a housewife; most of remaining 53/102 (52.0%) were under home care or institutionalised
Ferlazzo *et al.*, 2010	27 patients; 15F/12M; 8 symptomatic, 19 cryptogenic. Mean age at LGS onset was 3.6 years (range 1.5-8 years). Mean age at final follow-up was 45.2 years (range 40-59 years)	Mean: 35.7 years (range 22-47 years)	*At final follow-up*: - All subjects still had tonic seizures during sleep; 11/27 (40.7%) had tonic seizures during wakefulness ($p < 0.0001$ *vs* onset); 6/27 (22.2%) had atypical absences ($p < 0.0001$ *vs* onset); 4/27 (14.8%) had atonic seizures ($p=0.035$ *vs* onset); absence or tonic status epilepticus were not reported in any patient ($p < 0.0001$ *vs* onset) - EEG: 7/27 (25.9%) patients had diffuse SSW complexes during wakefulness ($p < 0.0001$ *vs* onset); 15/27 (55.5%) had slow background activity; all patients still had diffuse fast rhythms during sleep - 26/27(96.3%) patients had moderate to severe cognitive impairment; 1/27 (3.7%) had mild cognitive impairment and was married with a child (she presented with only rare tonic seizures during sleep); 12/27 (44.4%) had behavioural disorders (mostly hyperactivity and aggressiveness); 15/27 (55.6%) were institutionalised

DQ: developmental quotient; EEG: electroencephalogram; IQ: intelligence quotient; LGS: Lennox-Gastaut syndrome; SSW: slow spike-wave.

Physical impact

LGS has a profound physical impact on patients. The mobility of LGS patients is often severely affected by the frequent occurrence of seizures (particularly drop attacks), which are physically demanding and often result in injury. For example, akinetic seizures cause frequent face and mouth injuries and in some patients
11 the use of protective clothing (*e.g.* a helmet with face-mask) is required in order to minimise the extent of injury (Camfield and Camfield, 2002). Variable degrees of gait disturbances, both pre-existing and acquired, can be present in a substantial proportion of patients, with some individuals becoming wheelchair-bound (Oguni *et al.*, 1996). In addition, severe motor and intellectual disability in patients with LGS is associated with dysphagia, the early development of which is strongly linked to poor long-term seizure prognosis (Ogawa *et al.*, 2001). This can affect patients' ability to eat and take medication, requiring the use of a percutaneous endoscopic gastronomy tube for feeding and/or non-oral drug administration in some patients. Such physical co-morbidities add further burden to patients already having to cope with cognitive and behavioural difficulties.

Issues relating to treatment of LGS

The aim of treatment of LGS in adolescence and adulthood will not be specifically focused on an attempt to achieve complete freedom from seizures but, rather, to suppress or reduce the frequency of the more disabling seizure types (such as drop attacks), as these may be having a profound impact on physical well-being and social integration. Furthermore, it is often a
12 concern for carers that an individual's quality of life can be impaired by the side effects of treatment in addition to the epilepsy itself (Arzimanoglou *et al.*, 2009). AEDs are commonly used in a variety of combinations in order to try and control the multiple seizure types associated with LGS, but the use of polytherapy increases the risk of adverse effects, and may aggravate seizures and/or existing co-morbidities (Arzimanoglou *et al.*, 2009; Mula and Trimble, 2009). Since the risk of AED-induced seizure aggravation is also increased by the presence of epileptic encephalopathy, a high frequency of seizures and cognitive impairment (Gayatri and Livingston, 2006), the use of polytherapy in LGS should be minimised wherever possible. Medications commonly used to treat co-morbid sleep problems may themselves cause or aggravate seizures; for example, several reports have correlated the use of benzodiazepines with the precipitation of tonic status epilepticus in patients with LGS (Guerrini *et al.*, 1998; Perucca *et al.*, 1998). There are also important considerations regarding AED treatment in female LGS patients of childbearing age. Whether used for contraception or menstrual management, the effectiveness of oral contraceptives can be impaired by concomitant treatment with AEDs, due to pharmacokinetic interactions (Reddy, 2010; Perucca *et al.*, 2008). The complex issues of sexuality in epilepsy, including the impact of AED treatment on sexual function (Luef, 2008), should also be considered in the treatment of LGS patients.

Other issues relating to the management of LGS during adolescence and adulthood

Adolescence is associated with particular issues that have a direct bearing on how epilepsy is treated and managed. Since the pharmacokinetic properties of AEDs differ between children and adults, and since the pubertal growth spurt results in rapid increases in body weight that can lower the effective serum concentration of AEDs, there is a risk of suboptimal dosing during adolescence (Nordli, 2001; Paolicchi, 2002). Changes in weight are also often experienced as side effects of AED treatment (Sheth, 2002; Ben-Menachem, 2007), and for adolescents who are vulnerable to peer pressure and likely to be image-conscious, such side effects can have an adverse effect on self-esteem, and/or encourage poor compliance. Poor compliance is common among adolescents, par-
13 ticularly those with epilepsy (Sheth and Gidal, 2006), though it is less clear whether this is still the case in those with cognitive impairment and LGS. It is nevertheless good practice to take a holistic view of the adolescent with LGS being subject to the same influences as one from the general epilepsy population. In this context, many factors can contribute to poor compliance; for example, adolescents may rebel against parental involvement in the management of their epilepsy (Smith and Wallace, 2003), or find the taking of regular medications an unwelcome reminder of their condition, and a source of embarrassment among their peers (Anderson *et al.*, 2000; Sheth and Gidal, 2006). Cognitive, behavioural and cosmetic side effects also contribute to non-compliance (Sheth and Gidal, 2006). Indeed, alongside severity of epilepsy, side effects of medication are the main factors affecting the quality of life of adolescents with epilepsy (Benavente-Aguilar *et al.*, 2004). Education about their condition, medication and the likely side effects of treatment, together with practical advice on how to cope with and minimise these side effects, is of central importance in encouraging compliance in adolescents. However, since adolescents generally do not like being told what to do, physicians should try to avoid

"giving advice" but, rather, try to encourage questioning and provide information, whilst emphasising that the individual is in control of their own life (Besag, 1996).

Due to the intellectual impairment and behavioural difficulties associated with the syndrome, many children with LGS require intensive supervision and care, usually provided by specialist schools, residential centres and/or their parents or guardians at home. As they mature into adolescence and on into adulthood, patients spend increasing amounts of time
14 outside these closely supervised environments, eventually leaving the school system to enter work/skills programmes or to take up jobs. This has important implications for their medical welfare, since on-site nursing care is less likely to be available in such settings. In the event of a seizure (or other medical) emergency, delaying therapy until a patient is admitted to a hospital emergency department can result in increased morbidity and unnecessary patient distress (Ramsay *et al.,* 2007). Therefore, emergency plans and clear guidelines need to be put in place, so that individuals receive out-of-hospital treatment (*e.g.* in the form of rescue medication [Alldredge *et al.,* 1995; Alldredge *et al.,* 2001]) and in-hospital treatment, as appropriate (Ramsay *et al.,* 2007). As patients mature further into adulthood and their parents/guardians become older, responsibility for their care often transfers to someone else (*e.g.* a residential facility), or to the adult patients themselves. Transition out of family care and between care providers is an inevitable aspect of management of individuals with LGS patients, as it is with other individuals with intellectual disability.

The risk and fear of seizures and other medical emergencies severely restricts the social participation and physical activities of LGS patients, and may lead to social isolation, with associated complications (*e.g.* depression). As with other types of epilepsy, lifestyle choices, such as the use of alcohol, can have a great impact on the occurrence of seizures (Samokhvalov *et al.,* 2010; Brust, 2008).

Sudden unexpected death in epilepsy (SUDEP) is the most common cause of death directly related to epilepsy (Tomson *et al.,* 2005; Bell and Sander, 2006; Surges *et al.,* 2009). Since key risk factors for SUDEP include intractable epilepsy, high seizure frequency (particularly generalised tonic-clonic seizures), use of
15 polytherapy, onset of epilepsy at an early age, and long epilepsy duration (Tomson *et al.,* 2005; Bell and Sander, 2006; Surges *et al.,* 2009), patients with LGS are particularly at risk of SUDEP. As such, a pragmatic approach to treatment is required, whereby treatment decisions may need to be based on establishing which seizure type is most dangerous or distressing to the patient, on an individual basis.

Impact of LGS on health-related quality of life (HRQOL)

Throughout their lives, the HRQOL of LGS patients is impaired on many levels – physically, mentally and socially *(figure 1A)* (Gallop *et al.,* 2009; Gallop *et al.,* 2010). Seizures, which are often both frequent and severe, affect patients' mobility not only through injury, but also via attempts to reduce such injury (*e.g.* a non-ambulatory child is less likely to be injured by seizures than an ambulatory child), severely restricting patients' participation in everyday activities and often affecting school attendance (Gallop *et al.,* 2010). The occurrence of night-time seizures disrupts patients' sleep (Batista and Nunes, 2007), which is known to significantly affect HRQOL (Katz and McHorney, 2002). Cognitive and behavioural problems affect relationships with peers and family, limit recreational activity and result in specific educational and care needs that may prevent mainstream 16
school attendance, all of which can have a profound impact on HRQOL (Gallop *et al.,* 2010). The types of co-morbidities associated with LGS, particularly cognitive and behavioural impairments, become of critical importance during adolescence and have a major impact on HRQOL, since the individual's developing independence is impeded, education is at a critical stage, and issues such as employment, relationships and the ability to drive become increasingly relevant (Smith and Wallace, 2003). Moreover, since feelings of "not fitting in" and deviating from the norm are very important to adolescents, epilepsy and its associated co-morbidities can have disastrous effects on self-esteem and self-identity – issues which, once acquired during childhood and adolescence, may persist even after the condition itself has been adequately controlled (Smith and Wallace, 2003). Other aspects of the condition – its effects on independence, ability to work, social participation and personal relationships – continue to severely impair patients' HRQOL in adulthood.

It is important to highlight that LGS also impacts the HRQOL of carers and families. Caring for a patient with LGS can lead to a restricted social life and relationship problems between partners and other family members, and may lead to feelings of isolation, which 17
may in turn result in depression (Gallop *et al.,* 2010). Childcare can be problematic, since many people do not want the responsibility of looking after someone who has frequent seizures; this can further restrict social participation and limit opportunities to take a break from the challenges of caring (Gallop *et al.,* 2010). Caregiving is physically demanding and sleep is often disrupted, and carers and families also have to deal with the emotional impact of looking after and living

Fig 1

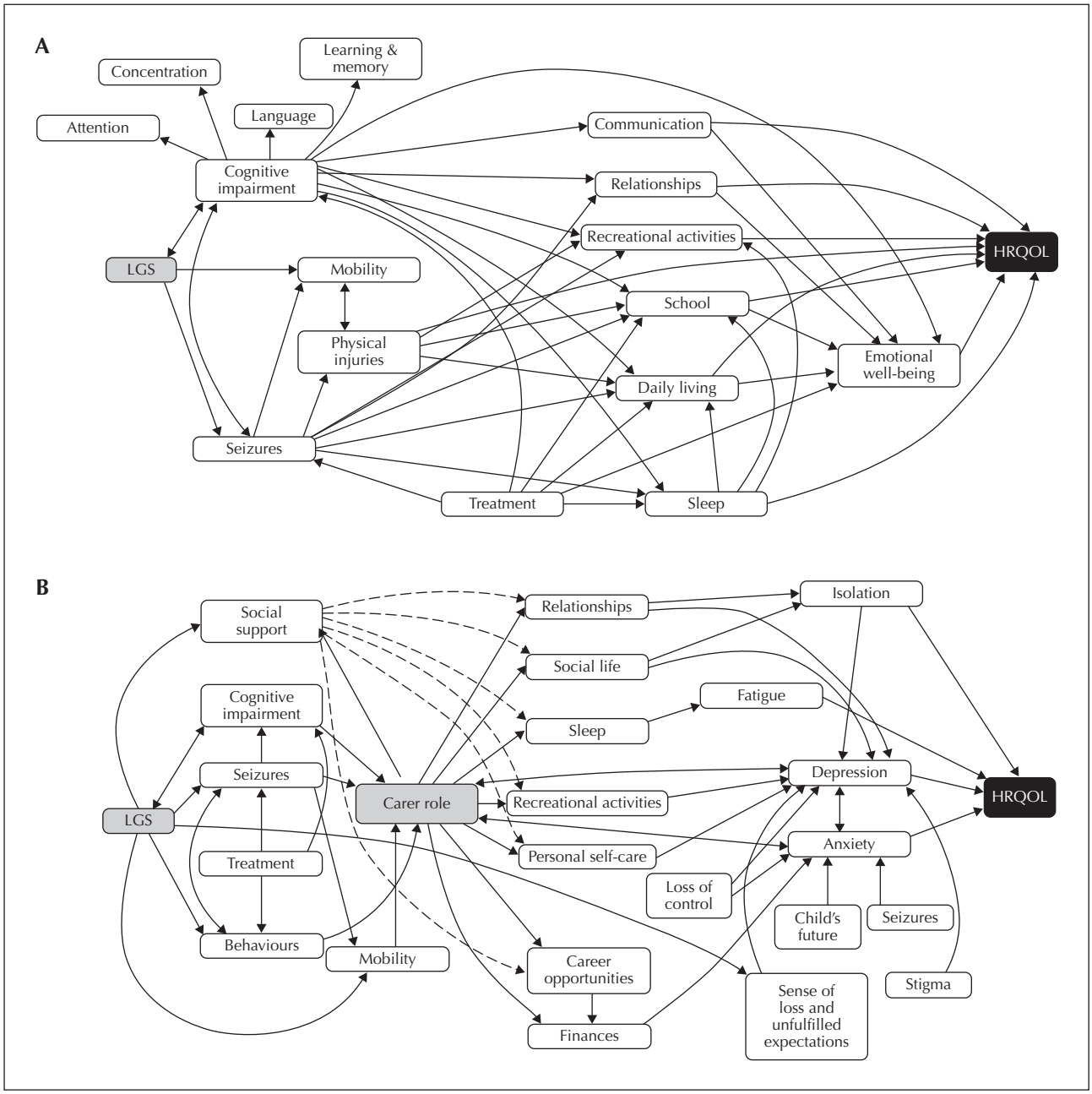


Figure 1. Summary of ways in which LGS may impact the HRQOL of **(A)** patients and **(B)** parents/carers (reprinted from Gallop *et al.,* 2010 with permission from Elsevier).
HRQOL: health-related quality of life; LGS: Lennox–Gastaut syndrome.

with someone with LGS, anxieties about when seizures might next occur and about the future of the individual with LGS, and the social stigma associated with the condition (Gallop *et al.,* 2010). In addition, carers may experience financial hardship through having to forgo job opportunities and career development in order to look after their charge (Gallop *et al.,* 2010). Such factors interlink and feed into each other, resulting in impairments in HRQOL that may affect all areas of life *(figure 1B)*.

Transition of care into adulthood

Given the complexity of LGS and the effects of its associated cognitive and behavioural co-morbidities, patients' medical, educational, psychological and social needs require a multidisciplinary approach to management, involving cooperation between physicians, psychologists, social workers and specialised agencies (Arzimanoglou *et al.,* 2004). Such a global model of care should already be in place by

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adolescence, when the main focus is the transitioning of the patient from paediatric to adult care, which can be particularly challenging. On the one hand, developing teenagers may find paediatric clinics embarrassing or inappropriate (Smith and Wallace, 2003). On the other hand, the transition from relatively easy-access paediatric services to adult neurology and learning disability clinics may be equally problematic, particularly since the provision of care becomes increasingly dispersed *(figure 2)*. This transition can be very painful for patients, who commonly experience sadness over the ending of close relationships, together with fear and uncertainty about the future (Warnell, 1998). These considerations have led to recommendations for transitional arrangements to put in place, in the form of specialist "teenager clinics" (Smith and Wallace, 2003), which have proven to be of benefit (Appleton *et al.*, 1997; Lossius and Nakken, 1999; Appleton, 2001; Smith *et al.*, 2002; Jurasek *et al.*, 2010). Such clinics are able to address the concerns expressed by adolescents and their parents/carers about transitioning from paediatric to adult care (such as fear of the unknown and loss of established relationships), as well as those expressed by healthcare providers about ensuring that adolescents develop a good working knowledge of issues that would prepare them for their transfer to adult epilepsy services (such as how their particular condition and its management interact with typical adolescent developmental challenges) (Jurasek *et al.*, 2010). Most adolescents with LGS require continuing treatment in a specialised epilepsy service.

A key aspect of the transition from paediatric to adult care is that it provides an important opportunity to carefully re-assess all aspects of patient care. Aetiology should be re-evaluated, making use of MRI and other types of investigation, in order to exclude or detect specific aetiologies that might affect treatment decisions, such as tuberous sclerosis complex (Krueger and Franz, 2008), or causal treatable epilepsies, such as pyridoxine dependency (Gospe, 2006). Treatment should also be re-evaluated to determine whether all

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Fig 2

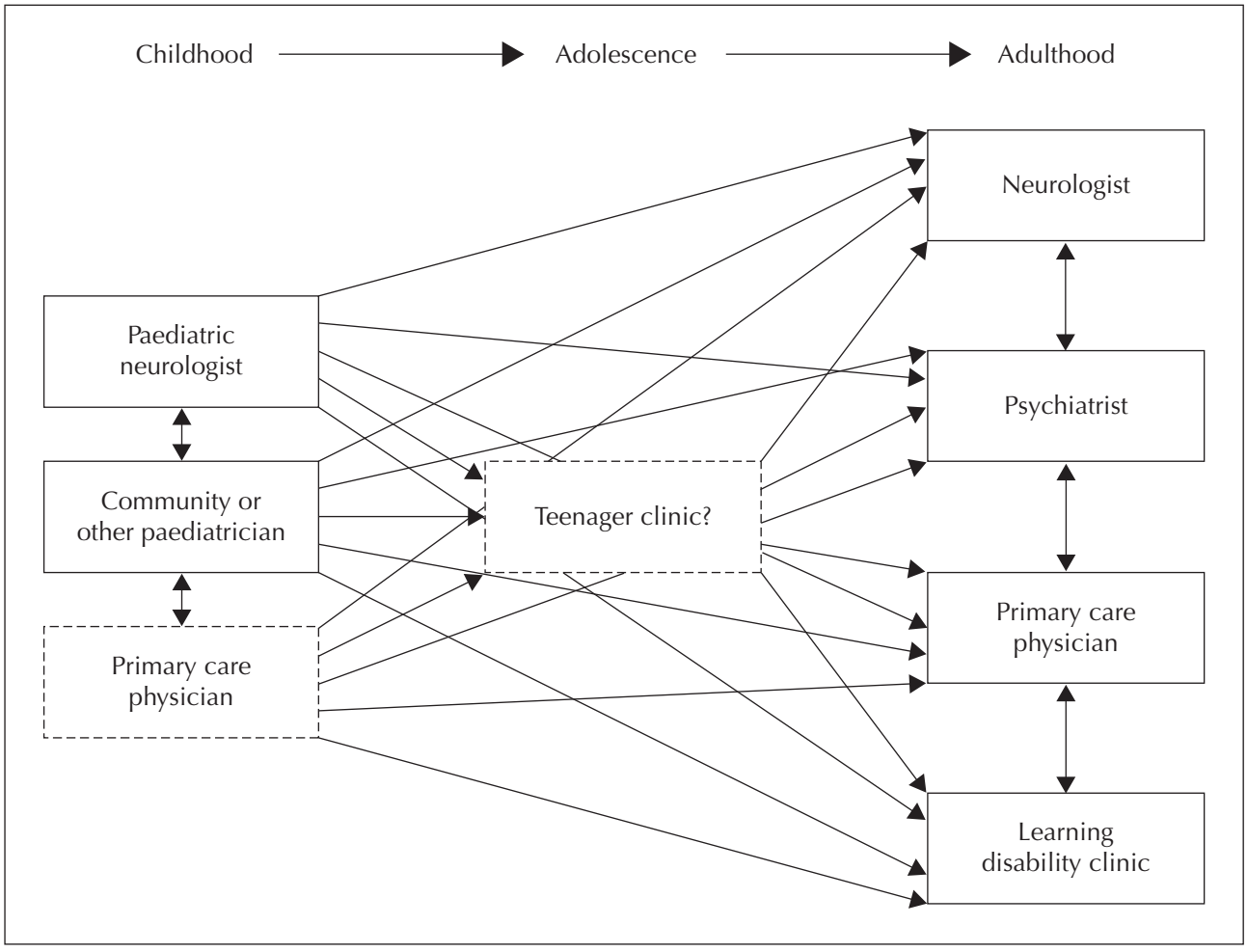


Figure 2. Management of care for LGS patients becomes increasingly dispersed as patients transition from childhood into adulthood.

appropriate AEDs have been tried; whether they are being used at the correct dose; and whether any agents could be removed to minimise polytherapy, as a means of reducing drug interactions and side effects. Some AEDs may need to be re-introduced, and/or new agents introduced, and it is important to note that conventional definitions of first- and second-line AEDs may not apply for the treatment of non-*de novo* adult patients, since they are likely to have been treated with several AEDs by that age.

In addition to AED therapy, patients should be re-assessed to determine whether surgery is indicated and/or whether other types of therapy should be considered. Importantly, the long-term needs of patients must be assessed, since they and their families will need enthusiasm and support for decades. This will involve long-term social care, perhaps requiring the support of psychiatric services and the provision of community or residential care. Above all, it is important that deterioration of the patient's condition is anticipated and managed effectively. It has recently been suggested that the International Classification of Function, Health and Disability (ICF) (WHO, 2001), which is widely used in rehabilitation outcome research, might be used as a global assessment tool in LGS, not only as an aid to plan interventions on an individual patient basis, but also as an outcome assessment in research studies (Arzimanoglou *et al.*, 2009). However, this is likely to pose a challenge, since the ICF model was developed for the assessment of stable disorders (psychomotor disabilities); therefore, its use in epilepsy will need thorough investigation (Arzimanoglou *et al.*, 2009).

Transition into adult care is a difficult time for both patients and families, since educational provision ends and there are generally less resources available for adult compared with paediatric patients. Patients and their families should therefore ideally receive counselling, covering issues such as management of co-morbidities, lifestyle advice and life expectancy – not only to ensure as smooth a transition as possible, but also to provide information to help cope with LGS over the long term.

Conclusion

The management of LGS through adolescence and into adulthood requires a global approach to care that takes careful account of the specific issues arising during adolescence and tries to ensure the smoothest possible transition from paediatric to adult care. It is important to recognise that, particularly during adolescence, complete and total control of seizures is not necessarily the primary issue, since the management of co-morbidities, especially cognitive and behavioural difficulties, is often a higher priority. Furthermore, educational and psychosocial requirements must be coordinated in conjunction with medical care, which must take account of treatment-associated side effects and the need for patients to be able to integrate with their peers and participate in social activities, in order to ensure an optimal outcome and quality of life. Similarly, the management of LGS in adulthood presents unique challenges, particularly in terms of its recognition and diagnosis. Outside of the relatively supervised and secure environment of paediatric care, patients and their families require other resources and sources of support to ensure that their needs are met. In addition to these challenges, LGS management during the transition into adulthood presents an important opportunity for re-assessment of the patient's condition, treatment and long-term needs. □

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