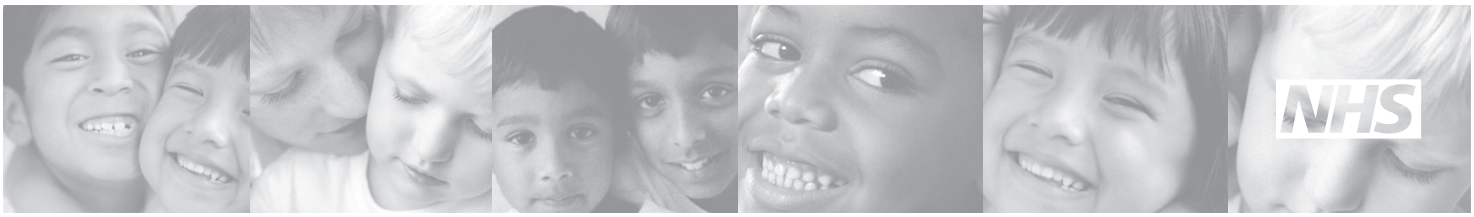


Great Ormond Street Hospital for Children NHS Foundation Trust: Information for Families

An introduction to Landau Kleffner syndrome

This information sheet gives an overview of Landau Kleffner syndrome and how it is managed at Great Ormond Street Hospital (GOSH). Further sheets in the series give more detailed information about specific aspects of Landau Kleffner syndrome including:

- **Language and communication**
- **Education**
- **Abilities and behaviour**

What is Landau Kleffner syndrome?

Landau Kleffner syndrome (LKS) is a rare epilepsy. It occurs in children usually between the ages of three and nine years and is characterised by loss of language skills and silent electrical seizures during sleep. It may be associated with convulsive seizures and additional difficulties with behaviour, social interaction, motor skills and learning. It is not usually life-threatening, but can impact greatly on quality of life unless it responds well to treatment. It occurs in approximately one child in a million. The disease is more common in boys and does not usually run in families.

LKS may also be referred to as:

- Acquired aphasia* of childhood with seizures
- Epileptic aphasia*
- Verbal auditory agnosia*

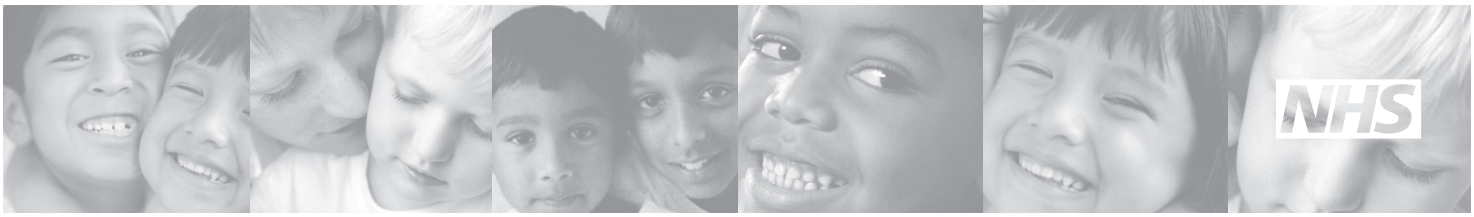
*Aphasia means disturbance in the ability to use language and agnosia means that a person is unaware of their failure to recognise or understand.

What causes LKS?

In LKS, there are abnormal electrical seizures in the language area of the brain, often occupying long periods when the child is sleeping. For a long time, we assumed that these seizures prevent normal brain function in these areas, so that the child loses language skills. However, this may be only part of the explanation.

We have now discovered that some types of epilepsy are due to a mistake in the genetic code. Often this mistake involves incorrect instructions for making proteins that regulate signal transmission in the brain, making children at risk of seizures and developmental problems.

Recently, a genetic mutation (GRIN2A) has been reported in up to 15 per cent of individuals with LKS. GRIN2A codes for part of a protein that is involved in transmitting signals that activate the brain. This protein is also thought to have a role in memory and learning. This is a major advance in our understanding of LKS, although the cause remains unknown for 85 per cent of LKS patients. We hope that research will explain how such gene defects cause disease and allow us to develop new treatments.



How is LKS diagnosed?

LKS is a clinical diagnosis, which means that it is made on the basis of the medical interview and examination. The core features are a history of normal early language development followed by loss of language skills, often in association with mild seizures and behavioural changes. Physical examination is usually normal, except for occasional difficulty with movement or coordination.

Brain imaging (MRI) is usually normal. Electroencephalograms (EEG) of brainwave activity show electrical discharges over the language areas of the brain and these often increase in frequency during sleep. Recently genetic abnormalities have been discovered in a minority of children with LKS.

As LKS is so rare, it is common for children to be investigated for deafness, autism, selective mutism, verbal dyspraxia or behavioural problems before the true diagnosis of LKS is made.

What are the main features of LKS?

In LKS, the child generally loses language understanding and then speech. This loss may be sudden (even overnight), or gradual over a period of months and is often mistaken for deafness initially. Many children compensate by using visual cues, gestures and by copying others and may initially hide their difficulty. The deterioration in skills is called a regression, as the child appears to have returned to an earlier stage in their development.

LKS was initially thought to be specific to language, but it is now clear that other abilities are also often affected. Behavioural changes are commonly reported and may include over-activity, reduced concentration span, irritability, tantrums and difficulties with social interaction. Non-verbal thinking (cognitive) skills are usually relatively unaffected, although there may be isolated difficulty, for example with thinking speed.

The child may also have problems with fine motor coordination and movement, such as dribbling, messy eating, loss of speech clarity, clumsiness and shakiness. These difficulties are thought to be a direct result of the disease process, rather than simply an emotional reaction to loss of language. It is hard to know what the child experiences, but some later have described being aware of muffled sounds but were unable to make out any words, or other unusual auditory experiences such as the sound of wind rushing or indistinct loud voices.

Most children have clinically obvious seizures and these often start before the initial regression. Seizures are generally short and do not show a close relationship to the language difficulties.

Variations and other diagnoses

Variations of LKS

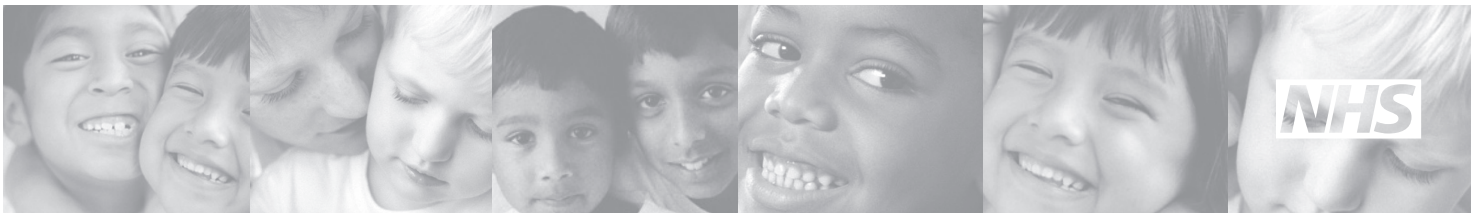
LKS may also occur in children who learn to speak late and who then have a language regression. This is LKS in the context of a developmental language disorder. Occasionally children with a classic LKS presentation are found to have an abnormality on brain scan and this may be amenable to direct treatment.

CSWS or ESES

Some children have the same sleep EEG abnormality as in LKS, but lose skills in many areas, rather than just language. This is referred to as Continuous Spike and Wave in Sleep (CSWS) or Electrical Status Epilepticus during Sleep (ESES). LKS can be regarded as a 'subgroup' of these.

Autism spectrum disorders

Children with an autism spectrum disorder can lose skills and have EEG findings similar to children with LKS. However, the regression is usually earlier, before the development of significant functional language. These children do not follow the pattern of illness seen in LKS and do not respond to treatments that help in LKS.



Developmental Language Disorder

Some children always have difficulty with language development and may also have an abnormal EEG, but have no history of loss of language. These children are less likely to respond to treatment, so any treatment needs careful evaluation of effectiveness before continuing.

How is LKS managed?

Management of LKS usually targets the electrical seizures that occur in sleep. However there is not always good correlation between EEG abnormalities and language skills, and so careful repeat neuropsychology and language assessments as well as EEG are an essential part of monitoring treatment.

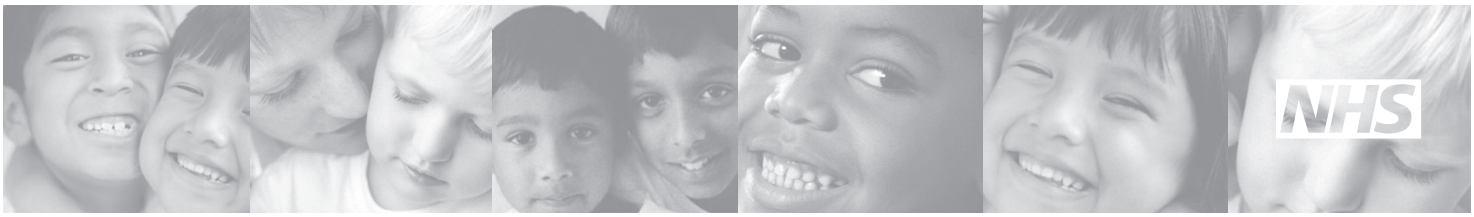
Steroids are often very effective treatment in LKS and sometimes lead to improvements within weeks. However they have dangerous side effects so it is important that their use is monitored (for example, checks on blood pressure, diabetes, growth and so on) and that there is evidence of their effectiveness (that is, by reassessing the child's language and learning profile) when deciding to continue using them. Daily steroids are usually restricted to a short period such as 6 to 12 weeks to minimise side effects. Experience shows that when steroids are stopped, children often lose their language again and seem more resistant to treatment after this. Therefore at the end of daily steroids, we commonly change to a twice weekly pulsed steroid regime as this appears to allow the medical benefit and reduces the side effects. Some children will require this specialised steroid regime for several years to cover the active phase of LKS.

Anti-convulsants are other medications that are commonly used in LKS. They are usually very effective for the visible (clinical) seizures, but less effective at stopping the invisible electrical activity during sleep. Commonly used anticonvulsants include ethosuximide, high dose benzodiazepines such as clobazam, sodium valproate and others. If the child has ESES (CSWS) on sleep EEG, it is important to avoid certain drugs (such as carbamazepine, phenytoin, phenobarbitone) that have the potential to make this worse.

Many parents worry about the effect that medication may have on learning. However it is the underlying disease process that is the main problem and medications that treat this usually mean that the child is more receptive to learning. Some parents express concerns about the possible behavioural effects of medications, such as drowsiness, over-activity, changed appetite, insomnia and bedwetting for instance. Behavioural changes can be a problem and children with LKS appear particularly vulnerable to some side effects, such as irritability with the medication sodium valproate, or sleep problems with lamotrigine. It is often hard to disentangle side effects from the behavioural changes commonly seen in children with LKS. For example, it is not unusual for parents to describe increased aggression and hyperactivity associated with the early phase of steroid treatment, although equally many parents report dramatic improvement in their child's behaviour during steroid treatment as the disease comes under control. Specific concerns about side effects should be discussed with your team.

There are also anecdotal reports of benefits from other treatments such as immunoglobulins or a ketogenic diet. Previously a special form of brain surgery called 'multiple subpial transection' was offered for children who had persisting profound language loss. However, careful review of outcomes from surgery has suggested that there is no significant additional benefit for most children, above the natural recovery that we know can take place over time. Therefore we no longer offer or recommend this surgery.

Assessment by a multidisciplinary team including medical, speech and language and clinical psychology services, is an integral part of management. It enables your child's full profile to be used to judge disease activity and monitor response to treatment, as well as identifying appropriate therapy and educational interventions. Repeat sleep EEG records are also used to monitor treatment.



Course and prognosis

The course of LKS is very variable. It is not usually life-threatening, but it can greatly affect a child's abilities and opportunities for learning. The active phase can last some years, but typically 'burns out' by early adolescence. During the active phase, the child will be vulnerable to further regression and fluctuation but usually the first regression is the most severe and in many children, medication can help to recover skills and prevent further relapse.

Initially, the brain is not 'damaged' in the conventional sense of injury, but rather it is unable to carry out its usual function (language). Children may lose skills and then regain them. There is often extreme fluctuation in how a child can access their skills. Therefore a child's abilities may appear to change dramatically, for better or worse, over short periods of time, even within a day. This lack of predictability and extreme fluctuation makes adjustment for families and school very difficult.

The best treatment response appears to be seen in children whose regression is largely limited to the ability to understand speech, without additional difficulty with behaviour, social communication and general learning. It is also important that treatment is given early.

Once the active phase is over, there is often a period of natural recovery. The extreme fluctuation settles and the child's good skills and remaining areas of difficulty become clearer. It is then usually possible to withdraw all medication. In our experience, recovery continues for many years after the active phase and this is a particularly important time to provide support and enriched learning opportunities as the young people are then receptive to learning and often need explicit teaching of topics and concepts that they missed when they were unwell. It is common for their skill profile to change and we often see considerable gains in skills throughout this time. Because of this, it is helpful to continue to monitor them, particularly as they start secondary school or consider further education or employment and they may benefit from continuing education into their twenties. It is therefore vital that they continue to receive educational support during this recovery phase.

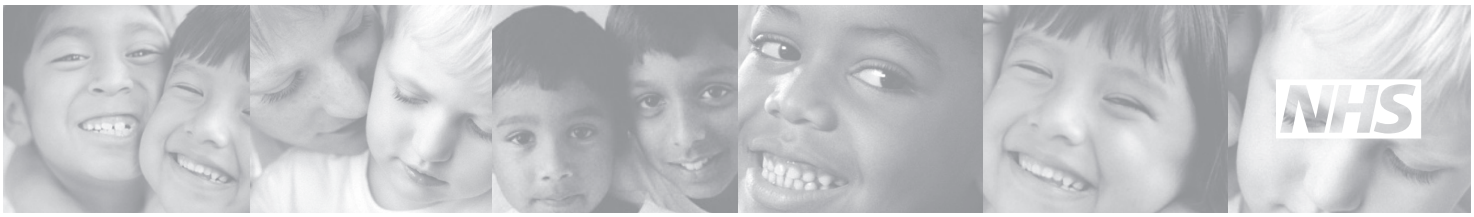
In general terms, about half the children make a reasonable recovery, a quarter have a partial recovery and the remaining quarter have very significant persisting difficulties with language, behaviour or general learning ability.

Children with a good outcome regain ability in spoken language and tend to score within the average range for their age group on formal assessments. However, they often experience subtle difficulties, such as trouble with short-term memory and problems listening when there is background noise. Those with a moderate outcome have some degree of language difficulty but spoken language will be their main means of communication. Even children with a poor language outcome, who never recover spoken language, may become very proficient at British Sign Language, and go on to lead a full and independent adult life, often within the hearing-impaired community.

In general, the longer the active period, the worse the outcome. Children who develop LKS at an older age and when their language is more mature, tend to do better, as do those who respond promptly to medication. Where children lose skills in addition to language, it is often the problems with social communication that pose the greatest barriers to recovery.

Adjustment and support

LKS can be both bewildering and distressing for the child and their family. Some children are aware of their lost abilities and can become frightened and/or frustrated. They are vulnerable to poor self-esteem and low mood. It is important to support the child as much as possible, providing opportunities for them to spend time with their existing friends, but also creating chances for them to find new friends who might experience similar difficulties, perhaps drawn from other children with language or learning difficulties or even from the deaf community.



For parents, there is the very painful experience of watching their child lose skills. In addition to the anxiety and distress caused by visible seizures and the need for medication or other treatments, parents must find ways to support their child who suddenly cannot understand the world as they did before, who may be distressed and frightened, and who may show behaviour that is extremely difficult to manage and an apparent 'personality change'. Many parents report that the behavioural changes in their child, particularly aggression and sleep disturbance, are the hardest parts to manage.

Having a child with LKS inevitably affects the whole family. As well as the demands of caring for their child with LKS, there are also the needs of other siblings to consider, who may be confused and resentful of the attention paid to their brother or sister. Brothers and sisters may need information about LKS and guidance on their role, particularly if their sibling's behaviour or personality has changed.

As stated earlier, LKS is very fluctuant and so is difficult to predict, which can be particularly discouraging. It is a rare diagnosis and there is often little knowledge amongst local professionals about the syndrome. This means that parents may have to invest a significant amount of time speaking to local education and health services about their child's needs. These needs can vary over time and it is important that support can be accessed when windows of opportunity arise.

Parents may face a large number of differing views and approaches by professionals, which can be daunting, confusing and exhausting. It is common for parents to feel completely overwhelmed at times. This is made more difficult by the lack of an identifiable 'event' such as a head injury or infection, with which to explain such a dramatic effect on their child. It is important for parents to identify local sources of support and to focus on practical issues such as their child's educational and emotional needs, rather than try to be overwhelmed by the search for a cause. Details of some helpful organisations follow in the next section.

Improving clinical care and research

We have a number of initiatives to advance knowledge and clinical management of LKS, including a registered database of clinical information and various research projects such as a genetics project. If you are invited to take part in a research project, you will be given full written information about the study. There is no obligation to participate and your decision will not affect your child's treatment in any way, now or in the future. You can also withdraw from the project at any time without explanation.

Further information and support

Within GOSH, the **Developmental Epilepsy Clinic** in the Wolfson Neurodisability Service can offer support and advice. Call them on 020 7405 9200 ext. 1144 or visit their website at www.gosh.nhs.uk/gosh/clinicalservices/Neurodisability.

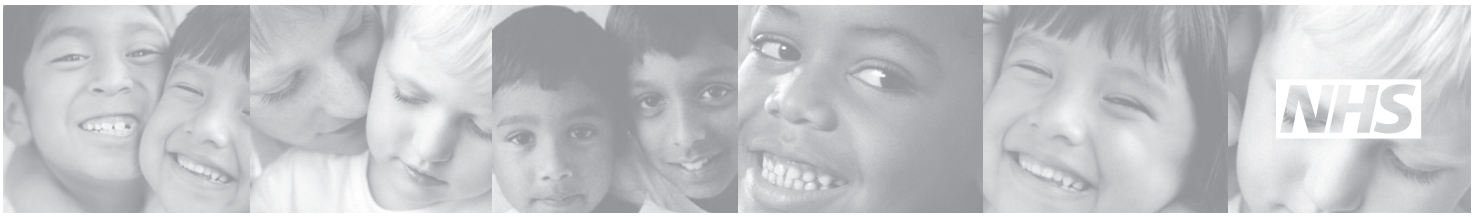
There is currently no active support group within the UK dedicated to Landau Kleffner syndrome, although Friends of LKS (FOLKS) hopes to become active again. The umbrella organisation **Contact a Family** may be able to put you in touch with another family affected. Call their helpline on 0808 808 3555 or visit their website at www.cafamily.org.uk

Useful contacts

AFASIC is an organisation offering support and advice to anyone affected by speech and language difficulties. Call their helpline on 0845 355 5577 or visit their website at www.afasic.org.uk

The **National Deaf Children's Society (NDCS)** support families of children with LKS. Call their helpline on 0808 800 8880 or visit their website at www.ndcs.org.uk.

The **Hyperactive Children's Support Group** can offer support and advice to parents of hyperactive children. Call them on 01243 539



966 or visit their website at www.hacsg.org.uk

The **National Attention Deficit Disorder Information and Support Service** provide information and resources about Attention Deficit Hyperactivity Disorder. Visit their website at www.addiss.co.uk.

I CAN offers support and advice to anyone affected by communication difficulties. Call their helpline on 0845 225 4073 or visit their website at www.ican.org.uk In addition, they also run two speciality speech and language schools, one in Surrey and one in Nottinghamshire.

Independent Parental Special Education Advice (IPSEA) advises families about special educational needs of all kinds. Call their helpline on 0800 0184 016 or visit their website at www.ipsea.org.uk

Makaton® is a type of sign language used by many children and young people. Visit their website at www.makaton.org for further information.

Your school SENDCo, GP or paediatrician will refer your child to community speech and language therapy (SLT) services. For further information relating to SLT you can contact the Royal College of Speech and Language Therapists on 020 7378 3012 or visit their website at www.rcslt.org

Definitions and explanations

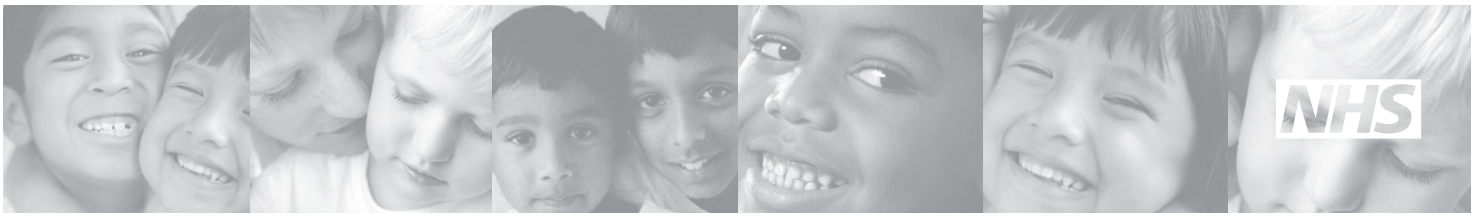
We try to avoid medical terminology as much as possible when we are communicating with you, but inevitably some jargon creeps in to our discussions. The following pages contain definitions and explanations to help you understand some commonly used terms.

- **Child development**
  This is the process by which children change and increase in their abilities in all areas, such as movement, language and social skills, over time. It is viewed as a continuous process that depends on the maturation of the child's brain. The brain is not fully developed at birth. It grows and makes important connections or 'wiring' throughout the early years of life. Generally, children follow a predictable sequence, for example sitting before walking, although at different speeds. For the younger child, development is often assessed by considering skills in different areas, such as gross motor (sitting and walking for instance), fine motor (including hand usage), vision, language, cognitive ability (such as puzzles or problem solving) and personal-social skills. For older and more able children, it is common to concentrate on language and cognitive (non-verbal intelligence) skills.

- **Developmental delay**
  This means that a child's development is not as advanced as would be expected for their age, so it is often reported as 'age equivalent'. This normally occurs when the child's rate of development is slower than usual.

- **Catch up**
  Parents often think that a child can be stimulated to 'catch up' and then perform at the same level as children of a similar age. This does not generally happen, as it requires development at a faster rate than normal. Most delayed children make steady progress at a slower rate than other children of the same age and make predictable gains in learning, but never 'catching up'.

  The case for children with LKS is different. These children generally had normal early development and were increasing their skills at the normal rate. During the active phase of LKS, they then lose language skills (regression) and if treatment for LKS is successful, they will show progress in their language skills and may well appear to 'catch up' and learn at an increased rate, often in response to steroid medication. What is actually happening, however, is recovery of their previous developmental path and retrieval of skills that were inaccessible to them in the acute (active) phase due to the effect of LKS on their brain. Unfortunately this is not always the case in LKS and some children do not



recover their lost skills at this time.

At the end of the active phase of LKS, children or adolescents are often left with residual impairments. They then tend to make steady developmental progress. For some, this progress is at an increased rate and their language skills improve and may approach their peers. Others may show new learning, but at a slower rate and continue to have significant difficulty with language. For some young people who have recovered from LKS, there is evidence of continuing progress after the age of 20 which is unusual. In this case they would benefit from continuing in education and should be encouraged and supported to do this.

- **Regression**
  This is the loss of previously acquired skills, so that the child appears to have returned to an earlier stage in their development. Loss of skills can sometimes affect one particular skill and not another so the child has an uneven profile. For example a child may still be able to read words, but no longer understand the words they read. This may leave the child with isolated retained skills from their previous abilities, which can mask their lost skills.
- **Seizures**
  These happen when part of the brain develops uncontrolled electrical activity, which stops the normal function of that part of the brain and produces the features that occur in the clinical seizure. EEG recordings will pick up electrical changes (discharges) over the area of brain affected or even over the entire brain if the seizure activity involves the whole brain (generalised seizure).

  In clinical seizures, there is an obvious change that occurs for the person during the seizure. This change depends on the part of the brain having the seizure and a person may twitch and jerk, go blank for a few seconds or even experience a strange taste or smell.

  In subclinical seizure activity, there is no obvious change such as jerking, even though an EEG records electrical seizures. These subclinical electrical seizures affect acquired skills such as language, social communication or abstract thought. In LKS, the main seizures are subclinical and occur during sleep.
- **Convulsive status epilepticus**
  This is where a seizure that causes convulsions (where the muscles move out of control), lasts for a long time, usually more than 30 minutes. It can also occur if one seizure follows another without the person regaining consciousness in between. It is dangerous and needs urgent treatment.
- **Non-convulsive status**
  This also occurs when seizures are very prolonged or follow one after another without a break. However, in this case, the seizures do not cause convulsions but typically cause fluctuations in awareness and jerkiness.
- **Electrical Status Epilepticus during Sleep (ESES)**
  This is a specific type of non-convulsive status in which continuous discharges of electrical activity occupy most of sleep. It is particularly associated with the active phase of LKS and linked to intellectual deterioration and loss of language. It may also be referred to as Continuous Spike and Wave in Sleep (CSWS). This electrical activity can persist for months or even years.

Compiled by staff from the Developmental Epilepsy Clinic
in collaboration with the Child and Family Information Group
Great Ormond Street Hospital for Children NHS Foundation Trust, Great Ormond Street, London WC1N 3JH
www.gosh.nhs.uk

 Ref: 2016F0942