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THE EFFECTIVENESS OF TREATMENT ON LENNOX GASTAUT SYNDROME: REVIEW ARTICLE

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Abstract

Background: Lennox-Gastaut Syndrome (LGS) is typically before the age of 8, it can persist into adulthood. The seizures associated with LGS include tonic seizures, atonic seizures (drop attacks), and atypical absence seizures. Intellectual and developmental disabilities are common in individuals with LGS, impacting their overall cognitive functioning. Additionally, behavioral and psychiatric issues may also be present. The exact cause of LGS is often unknown, and treatment options are challenging, typically involving a combination of medications and supportive therapies to manage symptoms. Early diagnosis and a multidisciplinary approach are crucial in addressing the complex needs of individuals with Lennox-Gastaut Syndrome. **Aim:** To overview Lennox Gastaut Syndrome and its pharmacological management. **Methods:** This review included articles obtained by an online search through scientific websites such as PubMed using several keywords. Results: We obtained several articles and included only those focused on the syndrome.

Keywords:
LGS, LGS management, Diagnosis of LGS, Epilepsy, Seizures.

Introduction:

Lennox-Gastaut Syndrome (LGS) presents a challenging landscape in the realm of epilepsy, characterized by its evolution throughout adolescence and adulthood, albeit with rare occurrences of late onset. Its diagnostic hallmark lies in the absence of tonic seizures, juxtaposed with a spectrum of seizure types including atypical absence, atonic, and generalized tonic-clonic seizures. Notably, LGS can manifest either de novo or as a progression from severe infantile seizure disorders such as West syndrome.

Central to the clinical presentation of LGS is the concurrent presence of cognitive decline alongside generalized slow spike-wave discharges, typically measuring less than 3 Hz on electroencephalography (EEG). These features serve as pivotal diagnostic indicators, contributing to the complexity of managing this syndrome.

Regrettably, therapeutic options for LGS are encumbered by limited efficacy, and prognosis tends to be predominantly bleak. In this review, we endeavor to offer a comprehensive understanding of LGS and its management landscape, elucidating the multifaceted challenges entwined with this intricate and often refractory epilepsy syndrome.

Materials and methods:

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Scientific articles that related to the present topic were obtained by Searching through reputable scientific databases like PubMed, ResearchGate, and Google Scholar using specific keywords related to Lennox-Gastaut Syndrome (LGS) is a systematic way to gather relevant literature.
Since we've obtained 15 articles were published between the years 2004-2017 and selected 5 based on relevance and recency, this suggests a focused and refined approach to your literature review. It's crucial to include recent studies to ensure that your information is up-to-date and reflects the latest developments in the field.

Discussion:

LGS defnition, epidemiology, and symptoms:

The defnite defnition of LGS is still elusive, however, there are 2 key criteria to describe prevail, they are the abnormal EEG which consists of an interictal pattern of diffuse and slow spike-wave (SSW) less than 3 Hz, and the occurrence of multiple seizure types [1]. The annual incidence of LGS ranges from 0.2-2.8 per 10000 births in Europe, while the prevalence is higher reaching 5% among all epilepsies and 10% among those of childhood epilepsy. LGS begins between the ages of 2-8 years old with a peak at 3-5 years [2].

All of the new AEDs were found to be appropriate for adjunctive treatment of refractory partial seizures in adults. Gabapentin can be effective for the treatment of mixed seizure disorders, and gabapentin, lamotrigine, oxcarbazepine, and topiramate for the treatment of refractory partial seizures in children [3]. LGS is primarily a syndrome of childhood; although long term prognosis is poor with regard to cognitive outcome, seizures become less troublesome into adulthood [4]. The common adverse events (reported by >or=10% of patients receiving rufnamide) were somnolence (24.3% with rufnamide vs 12.5% with placebo) and vomiting (21.6% vs 6.3%) [5].

An improvement in the management of Lennox-Gastaut syndrome requires a better understanding of the pathophysiology of this disorder and the development of animal models in which to test new compounds [6]. (LGS) is a severe pediatric epilepsy syndrome characterized by mixed seizures, cognitive decline, and generalized slow (<3Hz) spike wave discharges on electroencephalography [7]. Lennox-Gastaut syndrome is one of the most severe epileptic encephalopathies of childhood onset. The cause of this syndrome can be symptomatic (ie, secondary to an underlying brain disorder) or cryptogenic (ie, has no known cause) [8].

A large number of epilepsy-related diseases in childhood, adulthood, and old age are not enumerated here because the seizures are not distinctively different from other seizure types and are not critical for diagnosis [9]. LGS is a devastating rare childhood epilepsy syndrome, the term was first used in 1969 [10]. LGS is de novo in cryptogenic cases which represent 30%, and it can result from injuries of the brain that may result from infections, several malformations (brain tumor, dysplasia), and pre-or peri natal insult [11]. Early diagnosis of KGS is difficult as some symptoms such as cognitive decline don’t appear at the onset of the seizures; however, the syndrome will develop during a few months to years and then symptoms appear [12,13]. Impairment of cognitive function can be seen within 5 years of LGS onset in 20-60% of patients, while 75-95% of patients develop cognitive deterioration [14]. The hallmark of LGS is tonic seizures [15], which occur in 17-92% of patients during slow sleep, the duration lasts for a few seconds to 1 minute. Whereas Vatonic and absence seizures may appear later or become difficult to recognize in younger children [16].

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In the long term, patients with this condition still have intractable seizures, intellectual disability, behavioral problems, and physical comorbidities. The aim of this study was to describe the clinical and EEG characteristics of a group of adults with Lennox-Gastaut syndrome [17]. Atonic seizures are characterized by a loss of tone suddenly that involves the whole body or the head only. Atypical absence seizures duration lasts from 5-30 seconds, and they are associated with a decrease or even loss of consciousness. Other clinical features appear frequently including learning difficulties and comorbid sleep and behavior, whereas partial and myoclonic seizures are less common [18].

Diagnosis:

The diagnosis is usually poor, so an accurate diagnosis is necessary for better counseling regarding both clinical outcome and course [18]. LGS is characterized by 3 electroclinical features including specific EEG patterns, mental slowing or/and regression, and multiple types of seizures [2]. For an accurate diagnosis, several factors should be considered, sleep EEG recording which is mandatory to diagnose LGS.

Tonic seizures occurrence from the presence of paroxysmal fast rhythms and/ or sleep are the diagnostic criteria for LGS [15,18]. The second factor that should be considered is MRI, which is required to investigate the presence of structural abnormalities such as tuberous sclerosis complex, brain tumor, or malformation, these conditions may help in diagnosis and guide in deciding the treatment strategy [2]. The final factor that is important for accurate LGS diagnosis is genetic investigations, Although LGS is highly heterogeneous [19,20], and no single gene is specific for it, genetic testing can help in determining the etiology and consequent recurrence of risks as well as avoiding the unnecessary diagnostic investigations [21]. The genes that may be investigated include GABRB3, DMN1, SCN1A, SLC2A1, and STXBP1 [22].

Treatment:

In LGS children it is challenging to control seizures, although with the advancement in medicine, more than 9% of LGS children have drug-resistant epilepsy [23]. LGS remains an incredible therapeutic challenge for practitioners and poses immense risk and morbidity for afflicted individuals well into adulthood [24]. The medical treatment of LGS involves 6 antiseizure medications that have been held by the FDA and they include lamotrigine, rufinamide, clonazepam, clobazam, topihydramate, and felbamate [25]. Although the combination of some antiseizure medicine shows a synergetic effect, side effects can additively occur and hence make the seizure worse and often cause increased sedation and behavioral problems, so balancing side effects with seizure control using rational polypharmacy is a challenge [26]. Lennox-Gastaut syndrome (LGS) is a severe, chronic, epileptic encephalopathy, primarily with childhood onset, which is charactered 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 [27]. However, standard treatments showed in Epidemiological follow-up data and review of adults with LGS that there is a very low likelihood of remission in the long term, proving the challenge of managing seizures [15,26]. Meta-analysis wasn't possible as the studies differ in designs, criteria considered, and outcomes, however, the conclusion obtained was that there was no drug was highly effective in LGS over the others, and some drugs including lamotrigine (LTG), rufinamide (RUF), felbamate (FLB) and topiramate (TPM) may be useful

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to be used additively and clobazam (CLB) is useful for drop attack [26]. Here we will present different antiepileptic drugs licensed in the USA and Europe.

1-Lamotrigine (LTG):

It was licensed by the USA [28] and Europe [1], for LGS seizures. In phase III placebo-controlled RCT of 169 LGS patients, LGT showed effectiveness and it was tolerated and LGS treatment [29]. LGT was well tolerated and showed a statistically significance reduction in seizure frequency in double-blind compared to placebo-controlled individuals [30]. Sodium Valproate (VPA) which wasn't licensed for use in LGS [22] inhibits LTG metabolism [31], however, the combination of LTG with VPA is recommended for early treatment of LGS, hence it is necessary to decrease the LTG dose, and monitor the dose for adjustment [32].

2- Rufinamide (RUF):

It is another drug that has been approved in Europe and the USA as adjunctive treatment for LGS seizures. The effectiveness of RUF was shown in phase III placebo-controlled RCT which was conducted on 138 LGS patients. Another study [33] was performed on 124 patients with open-label extension long-term use of RUF for a median of 432 days and showed that seizure frequency was reduced, and tolerability was observed in the initial trial and on the long-term follow-up [33]. RUF also showed good tolerability and favorable efficacy when used as adjunctive therapy for adults [34].

In an open-label extension study following 3 months of multicenter placebo-controlled RCT, it was found that there was a change in the frequency of tonic-atonic seizures related to the frequency at the start of the study, and adverse events were either mild or moderate except for transient seizure aggravation in 3 patients, the adverse events that led to cessation of RUF included drug eruption, worsening of underlying autism and decreased appetite [35].3-

3- Topiramate (TPM):

This drug has been licensed as an adjunctive drug for LGS seizures in the USA and Europe [35,36]. Its effectiveness was found in LGS treatment in phase III conducted on 98 LGS patients in placebo controlled RCT [37]. In an open-label extension study, TPM showed that it was well tolerated and patients who retained therapy for ≥3 years were 71%, only 5% of patients showed behavioral problems [38]. TPM may cause behavioral and cognitive adverse events and rarely it may cause Stevens.

4- Clobazam (CLB):

This drug was licensed in the USA as an adjunctive therapy for LGS seizures [39], whereas in Europe it was licensed as an adjunctive treatment for epilepsy. A placebo-controlled phase III RCT study reported the effectiveness of CLB [40]. Open-label extension long-term study was conducted on patients who completed this RCT and the previous phase II study [41] and it was found that over the long term, there was a reduction in seizure frequency and drop attack with a median of -82% and -92% respectively from the baseline after 3 years, whereas after 5 years there was more reduction in seizure frequency -85%, while the drop attack slightly increases -91% [42]. Both behavioral and cognitive adverse events are associated with CLB, also there is a high risk for tolerance, however, it was reported that only one-third of patients showed tolerance [43,44]. The risk of tolerance made CLB recommended to be used on an intermittent basis over 3-5 days. Regular use can be considered when drop attacks are problematic, however it should be used with caution. CLB can be used in the treatment of LGS in case of crisis episodes and difficult phases such as prolonged absences and cluster seizures [22].

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European Medicines Agency (EMA) didn't approve felbamate (FLB) for use and in the USA, FLB carries a black box warning, it is licensed only for LGS patients who suffer severe epilepsy or those who respond inadequately to other treatments [22].

5- Levetiracetam (LEV):

LEV is a pyrrolidone derivative that was developed from piracetam [45], it is an effective drug for generalized onset myoclonic and tonic-clonic seizures as well as focal onset seizures [46]. It is assumed that it performs its effect by acting on presynaptic neurotransmitter release by binding to the glycoprotein synaptic vesicle protein 2A (SV2A), which is a part of the membrane of presynaptic neurotransmitter-containing vesicles in neural dendritic cells and neurons [47]. The mechanism of LEV binding to SV2A is not clear, but it is suggested that this protein is incorporated in the exocytosis of neurotransmitters, which is downregulated by either of reduction of calcium inward currents or other mechanisms [48]. It was postulated that LEV modulates neuronal cell function by several pharmacological mechanisms including u-opioid receptors, serotogenic, and alpha 2 adrenergic signaling [49]. LEV acts as a modulator for intraneural calcium levels by inhibiting the N-type calcium channel [47].

6-Perampanel (PER):

Is it an additive treatment for both focal onset seizures as well as generalized tonic-clonic seizures in patients older than 12 years [50]? PER was approved by the FDA and EMA in the USA and Europe respectively as an adjunctive therapy for partial onset seizures. After that, it was licensed by EMA to be used as an adjunctive treatment for primary generalized tonic-clonic seizures [51]. PER is an oral drug that is administrated once daily, it has a long have life of 15 h. the recommended dose start with 2mg/day, however it can be increase to 12mg/day [52]. Pre-clinical studies in vivo were performed on rat, and they demonstrated that PER reduced severity and duration of motor seizure significantly and showed inhibitory effects in focal secondary generalized seizures [53-55]. Tolerability and efficacy of PER was demonstrated in a multicentre, randomized, double blinded, placebo-controlled study for generalized tonic-clonic seizures [51]. It showed a good tolerability and efficacy in three clinical trials versus placebo [56-59]. A multicentre study from Spain showed that PER was safe and a good efficacy for drug-resistant epilepsy individuals including adolescents and elder individuals, however adverse effects should be monitored for patients [60]. Another study reported that the rate of adverse effects caused the cessation of PER, and it was fairly effective in heterogenous group of adolescent and children with very refractory epilepsy [52]. It reduces the glutamatergic transmission by acting on AMOA receptors as highly selective noncompetitive antagonist. As it is noncompetitive antagonist, high concentrations of synaptic glutamate will not affect its activity. Calcium inward currents are reduced in sub-cortical and cortical brain regions by the action of PER on AMPA receptors. The straightforward posology and favorable pharmacokinetic profile make this drug a logical choice as an add-on AED. With future clinical experience, as more patients are treated, further evidence of efficacy will be reported [61]. These drugs represent a welcome addition to the armamentarium of practitioners, but it remains to be seen how they will affect the landscape of thermoresistant epilepsy [62].

Conclusion:

LGS is a rare syndrome that affects male more than females, it develops de novo or from brain injuries. The pharmacological treatment of LGS showed poor and low efficacy. There are few studies on the

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effect of pharmacological treatment, also there are adverse events resulting from these therapies. Further studies should be performed, and development of new therapies is necessary

Review

Lamotrigine (LTG) IN THE Treatment of Lennox-Gastaut Syndrome (LGS):

1. **Licensing and Approval:**
   - Lamotrigine (LTG) has received approval for the treatment of LGS both in the USA and Europe.
2. **Clinical Trials and Effectiveness:**
   - A phase III placebo- controlled Randomized Control Trial (RCT) involving 169 LGS patients demonstrated the effectiveness of LTG in LGS treatment.
   - The trial indicated that LTG was well-tolerated, and it showed statistically significant reduction in seizure frequency when compared to the placebo group.
3. **Combination Therapy:**
   - Sodium Valproate (VPA), although not licensed for in LGS, inhibits the metabolism of LTG.
   - Despite VPA not being directly approved for LGS, the combination of LTG with VPA is recommended for early LGS treatment.
   - It is crucial to decrease the LTG dose when combining it with VPA and closely monitor the dosage for necessary adjustments.

Rufinamide (RUF) in the Treatment of Lennox-Gastaut Syndrome (LGS):

1. **Approval and Licensing:**
   - Rufinamide (RUF) has received approval as adjunctive treatment for LGS seizures in both the USA and Europe.
2. **Approval and Licensing:**
   - Rufinamide (RUF) has received approval as adjunctive treatment for LGS seizures in both the USA and Europe.
3. **Clinical Trials and Efficacy:**
   - A phase III placebo-controlled Randomized Control Trial (RCT) involving 138 LGS patients demonstrated the ecceftiveness of RUF as an adjunctive treatment.
   - Another study with a long-term open-label extension, conducted on 124 patients with a median of 432 days of RUF use, showed a reduction in seizure frequency and observed tolerability from the initial trial to the long-term follow-up.
4. **Tolerability and Efficacy in Adults:**
   - Rufinamide (RUF) exhibited good tolerability and favorable efficacy when used as adjunctive therapy for adults with LGS.
5. **Open-label Extension Study:**
   - An open-label extension study, following a multicenter placebo-controlled RCT for 3 months, found a change in the frequency of tonic-atonic seizures related to the study's initiation.
   - Adverse events were generally mild or moderate, with transient seizure aggravation reported in 3 patients.
   - Adverse events leading to cessation of RUF included drug eruption, worsening of underlying of underlying autism, and decreased appetite.

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Topiramate (TPM) as Adjunctive Treatment for Lennox-Gastaut Syndrome (LGS):

1. **Licensing and Approval:**
   - Topiramate (TPM) has been licensed as an adjunctive drug for LGS seizures in both the USA and Europe.
2. Clinical Trials and Efficacy:
   - In a phase III placebo-controlled Randomized Control Trial (RCT) involving 98 LGS patients, TPM demonstrated effectiveness in the treatment of LGS.
3. **Long-term Tolerability:**
   - An open-label extension study indicated that TPM was well-tolerated, with a retention rate of 71% in patients who continued therapy for ≥3 years.
   - Only 5% of patients showed behavioral problems during this long-term follow-up.
4. **Adverse Events:**
   - TPM, while effective, may cause behavioral and cognitive adverse events.
   - Rarely, it may lead to serious conditions such as Stevens-Johnson syndrome.

Clobazam (CLB) as Adjunctive Therapy for Lennox-Gastaut Syndrome (LGS):

1. **Licensing:**
   - Clobazam (CLB) has been licensed in the USA as an adjunctive therapy for LGS seizures. In Europe, it is licensed as an adjective treatment for epilepsy in general.
2. **Clinical Trials and Efficacy:**
   - A placebo-controlled phase III Randomized Control Trial (RCT) study reported the effectiveness of CLB
3. **Long-term Study and Reduction in Seizure Frequency:**
   - An open-label extension long-term study was conducted on patients who completed the RCT and a previous phase II study.
   - Over the long term, CLB demonstrated a reduction in seizure frequency and drop attacks, with median reductions of -82% and -92% respectively from the baseline after 3 years.
   - After 5 years, there was further reduction in seizure frequency (-85%), while the drop attack slightly increased (-91%)
4. **Adverse Events and Tolerance:**
   - Both behavioral and cognitive adverse events are associated with CLB.
   - There is a high risk for tolerance, but it was reported that only one-third of patients showed tolerance
5. **Usage Recommendations:**
   - Due to the risk of tolerance, CLB is recommended to be used on an intermittent basis over 3-5 days.
   - Regular use can be considered when drop attacks are problematic but should be used with caution.
   - CLB can be utilized in the treatment of LGS during crisis episodes and difficult phases such as prolonged absences and cluster seizures.

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Felbamate (FLB) and Regulatory Status:

- The European Medicines Agency (EMA) did not approve felbamate (FLB) for use.
- In the USA, felbamate carries a black box warning and is licensed only for LGS patients who suffer severe epilepsy or those who respond inadequately to other treatments.

Levetiracetam (LEV) in the Treatment of Seizures:

1. **Chemical Derivation:**
   - Levetiracetam (LEV) is a pyrrolidone derivative that was developed from piracetam.
2. **Effectiveness and Indications:**
   - LEV is known to be effective for generalized onset myoclonic and tonic-clonic seizures, as well as focal onset seizures.
3. **Mechanism of Action – SV2 Binding:**
   - It is assumed that LEV exerts its effects by acting on presynaptic neurotransmitter release through binding to glycoprotein synaptic vesicle protein 2A (SV2A).
   - SV2A is a component of the membrane of presynaptic neurotransmitter-containing vesicles in neural dendritic cells and neurons.
4. **Mechanism of Binding to SV2A:**
   - The exact mechanism of LEV binding to SV2A is not clear, but it is suggested that SV2A is involved in the exocytosis of neurotransmitters.
   - LEV is thought to downregulate this process, potentially by reducing calcium inward currents or other mechanisms.
5. **Modulation of Neuronal Cell Function:**
   - LEV has been postulated to modulate neuronal cell function through various pharmacological mechanisms, including u-opioid receptors, serotonergic, and alpha-2 adrenergic signaling.
6. **Inhibition of N-type Calcium Channel:**
   - LEV acts as a modulator for intraneural calcium levels by inhibiting the N-type calcium channel.

Perampanel (PER) as an Adjunctive Treatment for Seizures:

1. **Approval and Indications:**
   - Perampanel (PER) has been approved by the FDA and EMA in the USA and Europe, respectively, as an adjunctive therapy for partial onset seizures. Later, it was licensed by the EMA as an adjunctive treatment for primary generalized tonic-clonic seizures.
2. **Administration and Recommended Dose:**
   - PER is an oral drug administered once daily with a long half-life of 15 hours.
   - The recommended starting dose is 2mg/day, with the possibility of increasing it to 12mg/day.
3. **Pre-clinical Studies:**
   - Pre- clinical studies in vivo on rats demonstrated that PER significantly reduced the severity and duration of motor seizures and exhibited inhibitory effects in focal secondary generalized seizures.
4. **Tolerability and Efficacy in Clinical Trials:**
   - Tolerability and efficacy of PER were demonstrated in a multicentre, randomized, double-blinded, placebo-controlled study specifically for generalized tonic-clonic seizures.

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- Three clinical trials versus placebo also showed good tolerability and efficacy.
- A multicentre study from Spain indicated that PER was safe and effective for drug-resistant epilepsy individuals, including adolescents and older individuals. However, careful monitoring of adverse effects is recommended.

5. **Adverse Effects and Discontinuation:**
   - A study reported that adverse effects led to the cessation of PER, although it was found to be fairly effective in a heterogeneous group of adolescents and children with very refractory epilepsy.
6. **Mechanism of Action – Glutamatergic Transmission:**
   - PER reduces glutamatergic transmission by acting on AMPA receptors as a highly selective noncompetitive antagonist.
   - Being a noncompetitive antagonist means that high concentrations of synaptic glutamate will not affect its activity.
   - PER also reduces calcium inward currents in sub-cortical and cortical brain regions through its action on AMPA receptors.

TITLE	AUTHOR	PUBLISHER	YEAR	DOI	LINK	SUMMARY
Following catastrophic epilepsy patients from childhood to adulthood	Tracy A Glauser	PUBMED	2004	10.1111/j.0013-9580.2004.05005.x.	Following catastrophic epilepsy patients from childhood to adulthood - PubMed (nih.gov)	As individuals with severe epilepsies progress from childhood to adulthood, it becomes necessary to adapt and explore new therapeutic approaches. Nevertheless, the objective of ensuring the highest possible quality of life while minimizing both seizures and adverse effects remains constant. By

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						staying informed about the evolving needs of patients, clinicians can devise suitable care plans. The clinical manifestations of catastrophic epilepsies may evolve over time, but by comprehending the patient's condition's natural progression, clinicians can facilitate a smoother transition from childhood to adulthood.
The synaptic vesicle protein SV2A is the binding site for the antiepileptic drug levetiracetam	Berkley A Lynch	PUBMED	2004	10.1073/pnas.0308208101.	The synaptic vesicle protein SV2A is the binding site for the antiepileptic drug levetiracetam - PubMed (nih.gov)	In this study, we present evidence that the synaptic vesicle protein SV2A serves as the specific binding site for levetiracetam (LEV), a novel antiepileptic drug that exhibits a distinct activity profile

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						in animal models of seizure and epilepsy. Our findings demonstrate that the LEV-binding site is predominantly found in synaptic vesicles, and further analysis using photoaffinity labeling of purified synaptic vesicles reveals that it possesses an apparent molecular mass of approximately 90 kDa. Importantly, our experiments with brain membranes and purified synaptic vesicles from mice lacking SV2A clearly indicate that SV2A is essential for LEV binding, as they do not

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						exhibit any binding of a tritiated LEV derivative.
Epileptic Encephalopathies in Childhood: The Role of Genetic Testing	Johannes R Lemke	PUBMED	2015	doi: 10.1055/s-0035-1552623.	Epileptic Encephalopathies in Childhood: The Role of Genetic Testing - PubMed (nih.gov)	The epileptic encephalopathies encompass a diverse range of neurodevelopmental disorders distinguished by significant epileptic activity linked to developmental regression. Confirming the genetic makeup and categorizing a clinical diagnosis in an individual can offer assurance in treatment choices, prognosis, and assessment of seizure recurrence risks. Additionally, it can help avoid unnecessary diagnostic investigations.
Treatment of	Rob	PUBME	2016	doi:	Treatment of	Thirty-one

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Adults with Lennox-Gastaut Syndrome: Further Analysis of Efficacy and Safety/Tolerability of Rufinamide	McMurray	D		10.1007/s40120-016-0041-9.	Adults with Lennox-Gastaut Syndrome: Further Analysis of Efficacy and Safety/Tolerability of Rufinamide - PubMed (nih.gov)	adults between the ages of 18 and 37 diagnosed with LGS were treated with either rufinamide (n = 21) or placebo (n = 10). In the rufinamide group, three patients did not complete the trial. The median reduction in seizure frequency from baseline was -31.5% for rufinamide compared to +22.1% for placebo (P = 0.008) for all seizures, and -54.9% versus +21.7% (P = 0.002) for drop attacks. Response rates were 33.3% for rufinamide versus 0% for placebo (P = 0.066) for all seizures, and 57.1% versus 10.0% (P =

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						0.020) for drop attacks.
Clobazam in the treatment of Lennox-Gastaut syndrome	Joan A Conry	PUBMED	2009	doi: 10.1111/j.1528-1167.2008.01935.x.	Clobazam in the treatment of Lennox-Gastaut syndrome - PubMed (nih.gov)	In both the high-dose and low-dose groups, the weekly drop seizure rates showed a significant decrease compared to the baseline. However, the reduction was notably higher in the high-dose group. A significantly larger number of patients in the high-dose group experienced reductions in drop seizures of 25% or more, 50% or more, and 75% or more, in comparison to the low-dose group. Additionally, more patients in the high-dose group achieved a complete elimination of drop seizures,

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						although this difference was not statistically significant.

Additional Information

Disclosures

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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