touchEXPERT BRIEFING

Improving disease screening in Lennox-Gastaut syndrome

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Online Activity Details

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https://www.touchneurologytmc.com/epilepsy/learning-zone/improving-disease-screening-in-lennox-gastaut-syndrome

This content is for healthcare professionals in the US only.

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Learning Objectives

After watching the touchEXPERT BRIEFING activity, you should be able to:

- ✓ Describe the importance of avoiding delays and ensuring an accurate diagnosis for all patients with LGS, in addition to current screening and diagnostic challenges
- ✓ Outline the key features of the REST-LGS tool, and how it was developed and validated
- ✓ Discuss the diagnostic and management implications of the REST-LGS tool to help ensure a timely and accurate LGS diagnosis for patients of all ages

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Disclosures

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Dr Piña-Garza has served as advisor and has been part of the speaker bureau for Aquestive therapeutics, Eisai, Greenwich Biosciences, Jazz Pharmaceuticals, Marinus, Neurelis, SK life science, Sunovion, Supernus and UCB pharma. He also receives royalties from Elsevier for his published book.

Patricia McGoldrick, NP, MPA, MSN

Patricia McGoldrick has received honoraria from Greenwich Biosciences, Eisai, Jazz Pharmaceuticals, LivaNova, Sunovion, Neurelis, Marinus and UCB, and has participated as an investigator in clinical trials for Eisai, Greenwich Biosciences, NeuroPace, Neurelis, UCB and Zogenix.

Dr Steven Wolf, MD

Dr Wolf has received advisory board, speaker bureau and research support from Aquestive/Cataylist, Biomarin, Eisai Pharma, Jazz Pharmaceuticals, LivaNova, Longboard Pharma, Neurelis, Neuropace, SK Life Science, Sunovion, Takeda Pharma and UCB/Zogenix.

Dr Kathryn Davis, MD

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LGS: the importance of avoiding diagnostic delays and ensuring accurate diagnosis

Burden of LGS

LGS exerts a significant burden on patients, families and healthcare systems

- Increased risk of mortality[1,2] (14x higher in children with vs without LGS[2])
- Frequent hospitalizations due to complications[2,5]
- Multiple seizures per day of variable types[3,4]
- Adverse effect on caregiver emotional wellbeing, physical health, social activities and work productivity[6]
- Frequent intellectual impairment and cognitive delay[4]
- Commonly necessitates frequent HCRU and high costs[2,5]

1. Strzelczyk A, et al. *Epilepsy Behav*. 2021;115:107647; 2. Autry AR, et al. *J Child Neurol.* 2010;25(4):441-7;
3. Auvin S, et al. *Epilepsy Behav*. 2021;123:108239; 4. Camfield PR. *Epilepsia*. 2011;52(s5):3–9; 5. Reaven NL, et al. *Epilepsy Behav*. 2018;88:66–73;
6. Gallop K, et al. *Epilepsy Behav*. 2021;124:108324
HCRU, healthcare resource utilization LGS, Lennox-Gastaut syndrome

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Importance of an accurate diagnosis

LGS is likely under-detected, resulting in under-treatment[1]

Delayed diagnosis

- Seizures decrease brain function[2]
- Continued mortality risk[3]
- Recurrent falls, injuries and hospitalizations[4,5]

Accurate diagnosis

- Avoids suboptimal treatment selection, which can worsen seizures and cause AEs[5-7]
- Allows for correct treatment selection[5]
  - Improved seizure control and reduced cognitive worsening[5]

1. Wolf SM, et al. REST-LGS tool: Real-world use to screen for LGS and improve access to care. Presented at the American Epilepsy Society Annual Meeting in Nashville, TN USA; Dec 5, 2022; 2. Archer JS, et al. *Front Neurol.* 2014;5:25; 3. Strzelczyk A, et al. *Epilepsy Behav.* 2021;115:107647; 4. Reaven NL, et al. *Epilepsy Behav*. 2018;88:66–73; 5. Arzimanoglou A, et al. *Lancet Neurol* 2009;8:82–93; 6. Perucca E, et al. *Epilepsia* 1998;39:5–17; 7. Glauser TA. *Epilepsy Behav* 2004;5:25–32.
AE, adverse event; LGS, Lennox-Gastaut syndrome

Current screening and diagnostic challenges in LGS

LGS screening and diagnosis

Screening

Assessment in adults is uncommon as LGS onset usually occurs at <8 years of age and screening is typically performed by pediatric neurologists.[1,2]

Childhood: characteristic presentation[1,3]

Multiple seizure types

Most commonly tonic seizures, atypical absences and atonic types

Developmental delay

Increases over time with a loss of skills

Abnormal EEG

2–2.5 Hz in the interictal EEG and GPFA during sleep

1. Arzimanoglou A, et al. *Lancet Neurol* 2009;8:82–93; 2. Piña-Garza JE, et al. *Epilepsy Behav*. 2019;90:148-153; 3. Specchio N, et al. *Epilepsia*. 2022;63(6):1398-1442.

EEG, electroencephalogram; GPFA, generalized paroxysmal fast activity; LGS, Lennox-Gastaut syndrome

Current challenges in LGS screening and diagnosis

Individual symptoms may change with age[1,2]

Seizure types

May evolve over time (commonly fewer atonic and persistent nocturnal tonic seizures)

Developmental delay

Progression to cognitive impairment and behavioral disorders

Abnormal EEG

Majority of patients no longer show SSW in adulthood

Incomplete patient records

Particularly EEG results, previous medications and age of seizure onset[1,3]

Caregivers

Patients are frequently living in residential care, supported by individuals unaware of their medical history[2]

LGS is particularly difficult to identify in adults

1. Piña-Garza JE, et al. *Behav Case Rep*. 2016;5:38-43; 2. Ferlazzo E, et al. *Epilepsy Res*. 2010;89(2-3):271-7; 3. Wolf SM, et al. REST-LGS tool: Real-world use to screen for LGS and improve access to care. Presented at the American Epilepsy Society Annual Meeting in Nashville, TN USA; Dec 5, 2022.

EEG, electroencephalogram; LGS, Lennox-Gastaut syndrome; SSW, slow spike and wave

The Refractory Epilepsy Screening Tool for LGS (REST-LGS): key features and development

Key features of the REST-LGS tool

Goal of the REST-LGS: increase the detection of LGS[1]

Major criteria

- ≥2 seizure types?
- Seizure onset <12 years of age?
- Cognitive impairment since childhood?[a]
- History of EEG with generalized SSW discharges (<2.5Hz)?

If yes, 3 point per item

Minor criteria

- Persistent seizures despite trial of ≥2 anti-seizure medications?
- Evidence of seizure-related helmet use, or head or face injuries?
- History of VNS, ketogenic diet or epilepsy surgery?
- ≥1 EEG abnormality?[b]

If yes, 1 point per item

Score: >11 (Likely LGS), 8–11 (possible LGS), <8 (unlikely LGS)[2]

[a]May include past or current learning difficulties, history of special education, autism, intellectual disabilities or developmental delays; [b]multifocal spikes, symptomatic generalized discharges, generalized polyspikes, generalized periods of attenuation of background/electrodecrement, or paroxysmal fast activity.

1. Piña-Garza JE, et al. *Epilepsy Behav.* 2019;90:148-53; 2. Wolf SM, et al. REST-LGS tool: Real-world use to screen for LGS and improve access to care. Presented at the American Epilepsy Society Annual Meeting in Nashville, TN USA, December 5, 2022.

EEG, electroencephalogram; LGS, Lennox-Gastaut syndrome; REST-LGS, Refractory Epilepsy Screening Tool for LGS; SSW, slow spike-and-wave; VNS, vagal nerve surgery

Development of the REST-LGS tool

Conceptualized and designed using the Modified Delphi Consensus process[1]

Reliability and validity assessed by blinded screening of patients with LGS or DRE by expert and non-experts at 2 large epilepsy centers (100 patients per center)[1]

- Moderate to very good agreement in the majority of REST-LGS criteria between experts and non-experts
- Most patients with LGS met 3 major and 2–3 minor criteria, while most patients with DRE met 1 major and 1–2 minor criteria

Blinded retrospective real-world chart review of 100 adults with DRE and intellectual and developmental disabilities in residential care by 2 primary care providers[2]

- After unblinding, of the 74 patients without a previous LGS diagnosis, 57% (n=42) were rated as likely or possible LGS cases
- Of the 26 patients with a previous diagnosis of LGS, 12 had extensive missing data, highlighting the challenge of diagnosing adults

1. Piña-Garza JE, et al. *Epilepsy Behav*. 2019;90:148-53l 2. Wolf SM, et al. REST-LGS tool: Real-world use to screen for LGS and improve access to care. Presented at the American Epilepsy Society Annual Meeting in Nashville, TN USA; Dec 5, 2022.
DRE, drug-resistant epilepsy; LGS, Lennox-Gastaut syndrome; REST-LGS, Refractory Epilepsy Screening Tool for LGS

The REST-LGS tool: implications for a timely and accurate LGS diagnosis

Contexts where the REST-LGS can be used

Non-specialist physicians
In the office of HCPs without extensive knowledge of LGS or neurology, particularly those managing adult patients

Residential care facilities
Caregivers supporting patients in residential care homes

Family
Families of potential patients and other people who interact with them

HCP, healthcare practitioners; REST-LGS, Refractory Epilepsy Screening Tool for LGS

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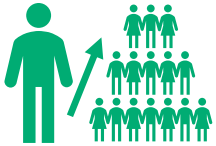
Implications of the REST-LGS tool

Increased recognition of LGS
As LGS accounts for up to 10% of childhood epilepsies,[1] the REST-LGS tool may increase LGS detection even among neurologists



Screening ease
Simple administration of the REST-LEG facilitates the screening of a larger number of potential patients

Early diagnosis and access to specialized care/treatment
Identifying a patient as potentially having LGS allows the possibility of diagnostic evaluation and if the LGS diagnosis is confirmed, specialized care and treatment

1. Camfield PR. *Epilepsia*. 2011;52(s5):3–9;.
LGS, Lennox-Gastaut syndrome; REST-LGS, Refractory Epilepsy Screening Tool for LGS

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Summary

Summary

1. LGS exerts a large burden on patients, caregivers and healthcare systems; timely and accurate diagnosis, which is particularly challenging in adults can reduce disease burden
2. The REST-LGS, which includes 8 questions, is simple to administer and is able screen for the likelihood of potential LGS in undiagnosed patients, including adults in the real-world
3. The REST-LGS can be used by non-specialist physicians to improve LGS screening and diagnosis, facilitating access to specialized care

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