SPECIAL ARTICLE

Practice guideline summary: Sudden unexpected death in epilepsy incidence rates and risk factors

Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the American Epilepsy Society

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ABSTRACT

Objective: To determine the incidence rates of sudden unexpected death in epilepsy (SUDEP) in different epilepsy populations and address the question of whether risk factors for SUDEP have been identified.

Methods: Systematic review of evidence; modified Grading Recommendations Assessment, Development, and Evaluation process for developing conclusions; recommendations developed by consensus.

Results: Findings for incidence rates based on 12 Class I studies include the following: SUDEP risk in children with epilepsy (aged 0–17 years) is 0.22/1,000 patient-years (95% confidence interval [CI] 0.16–0.31) (moderate confidence in evidence). SUDEP risk increases in adults to 1.2/1,000 patient-years (95% CI 0.64–2.32) (low confidence in evidence). The major risk factor for SUDEP is the occurrence of generalized tonic-clonic seizures (GTCS); the SUDEP risk increases in association with increasing frequency of GTCS occurrence (high confidence in evidence).

Recommendations: Level B: Clinicians caring for young children with epilepsy should inform parents/guardians that in 1 year, SUDEP typically affects 1 in 4,500 children; therefore, 4,499 of 4,500 children will not be affected. Clinicians should inform adult patients with epilepsy that SUDEP typically affects 1 in 1,000 adults with epilepsy per year; therefore, annually 999 of 1,000 adults will not be affected. For persons with epilepsy who continue to experience GTCS, clinicians should continue to actively manage epilepsy therapies to reduce seizures and SUDEP risk while incorporating patient preferences and weighing the risks and benefits of any new approach. Clinicians should inform persons with epilepsy that seizure freedom, particularly freedom from GTCS, is strongly associated with decreased SUDEP risk. ***Neurology*® 2017;88:1674–1680**

GLOSSARY

AAN = American Academy of Neurology; **AED** = antiepileptic drug; **CI** = confidence interval; **GTCS** = generalized tonic-clonic seizures; **SUDEP** = sudden unexpected death in epilepsy.

Editorial, page 1598

Supplemental data at Neurology.org

This document summarizes information provided in the complete guideline, available at Neurology.org. Appendix e-6, cited in the full guideline (data supplement), is available at Neurology.org.

Sudden unexpected death in epilepsy (SUDEP) is a poorly understood and catastrophic risk of epilepsy. The sensitive nature of discussions of this infrequent but important risk with patients and families has prompted the need for evidence-based information about SUDEP. The goal of this practice guideline is to examine evidence for the SUDEP incidence rate in epilepsy populations and for prognostic factors

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Approved by the Guideline Development, Dissemination, and Implementation Subcommittee on November 7, 2015; by the AAN Practice Committee on January 17, 2016; by the AES Guidelines Committee on November 11, 2016; by the AES Council on Clinical Activities on November 11, 2016; by the AES Executive Committee on November 14, 2016; by the AES Board of Directors on November 30, 2016; and by the AAN Institute Board of Directors on January 11, 2017. This practice guideline was endorsed by the International Child Neurology Association on August 27, 2016.

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for SUDEP occurrence. This in turn will inform an honest and balanced discussion when clinicians counsel people about SUDEP, and provide insight into areas where more clinical research is needed.

Two questions were asked:

1. What is the incidence rate of SUDEP in different epilepsy populations?
2. Are there specific risk factors for SUDEP?

DESCRIPTION OF THE ANALYTIC PROCESS This practice guideline broadly follows the process delineated in the 2004 American Academy of Neurology (AAN) guideline development process manual,[1] with the exception of the processes for formulating conclusions and recommendations, which follow the processes explained in the 2011 AAN guideline development process manual.[2]

In 2010, the AAN Guideline Development, Dissemination, and Implementation Subcommittee and the Guidelines Committee of the American Epilepsy Society convened a panel of experts to develop this practice guideline. The guideline panel engaged an independent medical librarian to search the MEDLINE and Embase databases from earliest available article to November 2010. The panel then performed an identical search in April 2015 to include articles published since November 2010. The keywords for both searches were SUDEP or (sudden and [unexplained or unexpected] and death) combined with the traditional medical subheadings (MeSH) for epilepsy (epilepsy/abnormalities or epilepsy/classification or epilepsy/complications or epilepsy/drug effects or epilepsy/drug therapy or epilepsy/epidemiology or epilepsy/ethnology or epilepsy/etiology or epilepsy/genetics or epilepsy/mortality or epilepsy/physiopathology or epilepsy/prevention and control or epilepsy/therapy) with limits of humans, plus all child: 0–18 years or all adult: 19+ years. Literature types were limited to clinical trial; randomized controlled trial; comparative study; controlled clinical trial; evaluation studies; journal article; multicenter study; research support; NIH, extramural, research support; NIH, intramural, research support; non–US gov't, research support; US gov't, non PHS, research support; or US gov't, PHS, validation studies. Finally, the guideline panel specifically searched causes implicated in SUDEP (i.e., cardiac arrhythmias and preictal autonomic dysfunction), where the hypotheses were tested.

This search yielded 1,068 abstracts, all of which were reviewed for relevance by at least 2 panel members working independently of each other; 744 abstracts were not relevant to provide answers to the questions. Of the remaining 324 abstracts, 2 panel members then obtained the full articles and reviewed them independently for inclusion. Reviewed articles were entered into a database application through an online questionnaire. Seventy articles had data for inclusion, and 254 were excluded because they failed to address the questions, employ an adequate SUDEP definition, or use an appropriate epilepsy comparison group in the prognostic studies. The available literature consisted of multiple Class I articles for incidence, and therefore articles rated Class II or lower were excluded because the Class II publications did not address populations not otherwise encompassed by the Class I articles. Several Class I and multiple Class II articles were available for prognostic questions.

Included articles were required to state that the SUDEP definition provided by Nashef,[3] Annegers,[4] and Leestma et al.[5] was used or to describe criteria in accordance with these definitions. These definitions share the following criteria, and the guideline panel included any article that incorporated these criteria in its SUDEP definition: (1) the patient had epilepsy by reasonable criteria without reference to the criteria used for epilepsy; (2) deaths by drowning, trauma, or status epilepticus were excluded; (3) death could have occurred after a witnessed seizure; (4) other competing causes of death were excluded.

The guideline panel used 2 of the AAN's evidence-based schemes to rate articles: the screening criteria for the incidence question and the prognostic criteria for the risk factor question.

Question 1: What is the incidence of SUDEP in different epilepsy populations? Twelve Class I studies provided incidence rate data.[6–17] Imprecision in study findings resulted in moderate confidence in the evidence for SUDEP rates in childhood and low confidence in the evidence for SUDEP rates in adulthood and overall (table 1). Because of imprecision in the incidence study results with a lack of overlap of 95% confidence interval (CIs) between several comparable study populations, the guideline panel performed a random-effects meta-analysis to provide summary measures of the absolute or relative risk of SUDEP. In addition, to explore reasons for heterogeneity in the absolute risk of SUDEP reported, the panel conducted a meta-analysis of subgroups of studies

Table 1 Conclusions for sudden unexpected death in epilepsy (SUDEP) incidence

Population	SUDEP/1,000 patient-years (confidence interval)	Confidence
Overall	0.58 (0.31–1.08)	Low
Childhood	0.22 (0.16–0.31)	Moderate
Adulthood	1.2 (0.64–2.32)	Low

including different groups of patients with epilepsy (e.g., children vs adults). These meta-analyses have significant unexplained heterogeneity, which may suggest the presence of other unknown or unexplored risk factors.

Rationale for recommendations 1 and 2. Our systematic review found that the SUDEP risk in children with epilepsy is 0.22/1,000 patient-years (95% CI 0.16–0.31). The SUDEP risk increases in adults to 1.2/1,000 patient-years (95% CI 0.64–2.32). There is considerable uncertainty regarding the estimates of the adult risk.

People with epilepsy and their families prefer to be informed of the individual's risk for a catastrophic event such as SUDEP, even when the probability of the event is low.[18] This preference is subject to cultural influences. After being informed of an adverse event, people commonly overestimate the risk of that adverse event happening to them.[19] Such overestimation unduly increases anxiety related to an adverse event. Overestimation can be lessened by presenting the risk as the probability of both having and not having the event,[20] and by using numbers in addition to words[19] and frequencies rather than percentages to convey the risk.[21]

Incidence recommendation 1: SUDEP incidence in children. Clinicians caring for children with epilepsy should inform the children's parents or guardians that (Level B for the following):

1. There is a rare risk of SUDEP.
2. In 1 year, SUDEP typically affects 1 in 4,500 children with epilepsy; in other words, annually, 4,499 of 4,500 children will not be affected by SUDEP.

Incidence recommendation 2: SUDEP incidence in adults. Clinicians should inform adult persons with epilepsy that (Level B for the following):

1. There is a small risk of SUDEP.
2. In 1 year, SUDEP typically affects 1 in 1,000 adults with epilepsy; in other words, annually, 999 of 1,000 adults will not be affected by SUDEP.

Question 2: Are there any risk factors for SUDEP? Six Class I[14,22–26] and 16 Class II articles[6,7,17,23,27–38] provided evidence for this question. Table 2 summarizes the results.

Rationale for recommendation 3. Our systematic review found that a major risk factor for SUDEP is the presence and frequency of generalized tonic-clonic seizures (GTCS). For example, people with 3 or more GTCS per year have a 15-fold increased risk of SUDEP. This relative risk increase translates to an absolute risk of up to 18 deaths per 1,000 patient-years for people with frequent GTCS.[29]

The large SUDEP risk increase from GTCS, coupled with epilepsy monitoring unit evidence[39] demonstrating that a GTCS was always the precipitating event of SUDEP, strongly suggests that GTCS are not just associated with SUDEP but, rather, are in the causal path to SUDEP. From this, it seems reasonable to infer that improved control of an individual's GTCS will result in a reduced risk of SUDEP. Thus, a reduction in SUDEP risk is an additional benefit to the many benefits resulting from improved seizure control.

As with all benefits associated with improved seizure control, the potential benefit of SUDEP risk reduction needs to be balanced with the risks and burdens associated with antiseizure therapies.

Recommendation 3. For persons with epilepsy who continue to experience GTCS, clinicians should continue to actively manage epilepsy therapies to reduce seizure occurrences and the risk of SUDEP while incorporating patient preferences and weighing the risks and benefits of any new approach (Level B).

Rationale for recommendation 4. GTCS are clear risk factors for SUDEP, and nocturnal seizures may also increase risk. These findings, in conjunction with the observation that postictal respiratory depression is a major mechanism in SUDEP,[39] suggest that unwitnessed nocturnal seizures and postictal respiratory depression can cause SUDEP.

Moreover, the presence in the bedroom of another individual at least 10 years of age and of normal intelligence is associated with a decreased SUDEP risk. These results imply that a bedroom observer could detect seizures, check on the patient, and provide sufficient stimulation to prevent respiratory arrest. This association does not indicate that these interventions directly mitigate the mechanism that causes SUDEP.

If it were in accordance with patient and family circumstances and values, nocturnal supervision

Table 2 Conclusions for sudden unexpected death in epilepsy (SUDEP) risk factors

Factor	OR (CI)	Confidence level
Presence of GTCS vs lack of GTCS	10 (17–14)	Moderate
Frequency of GTCS	OR 5.07 (2.94–8.76) for 1–2 GTCS per year and OR 15.46 (9.92–24.10) for >3 GTCS per year	High
Not being seizure-free for 1–5 y	4.7 (1.4–16)	Moderate
Not adding an AED when patients are medically refractory	6 (2–20)	Moderate
Nocturnal supervision (risk reduction)	0.4 (0.2–0.8)	Moderate
Use of nocturnal listening device (risk reduction)	0.1 (0–0.3)	Moderate

Abbreviations: AED = antiepileptic drug; CI = confidence interval; GTCS = generalized tonic-clonic seizure; OR = odds ratio.

could reduce SUDEP risk; however, providing nighttime observation might be overly burdensome and intrusive.

Recommendation 4. For persons with frequent GTCS and nocturnal seizures, clinicians may advise selected patients and families, if permitted by their individualized epilepsy and psychosocial circumstances, to use nocturnal supervision or other nocturnal precautions, such as the use of a remote listening device, to reduce SUDEP risk (Level C).

Rationale for recommendation 5. One of the most consistent findings of this review is that many factors that are indicators of uncontrolled epilepsy, including having GTCS, having frequent GTCS, and the absence of seizure freedom, are strongly associated with SUDEP.

Usually, people with epilepsy and their families prefer to be informed of factors that are associated with an increased risk of a catastrophic event such as SUDEP. Patients are especially interested in factors that might reduce their risk even when a causal link between the factor and a reduction in risk has not been established. Knowledge of these risk factors might suggest behaviors that could modify the risk factors (e.g., improved therapy adherence[40]), increase the person's sense of control, and reduce the anxiety that comes from awareness of the risk. Less severe seizure types, such as focal seizures or myoclonic seizures, are not proven to be associated with increased SUDEP risk, but individuals who have them often remain at risk for GTCS in the setting of therapy nonadherence. Therefore, therapy adherence to maintain freedom from GTCS is important even when an individual is not experiencing this severe seizure type.

Recommendation 5. Clinicians should inform patients with epilepsy that seizure freedom, particularly freedom from GTCS (which is more likely to occur with medication adherence), is strongly associated with a decreased risk of SUDEP (Level B).

Additional conclusions (no recommendations made). The evidence is low that the following factors are associated with altering SUDEP risk:

1. Nocturnal seizures (associated with increased risk)
2. Any specific antiepileptic drug (AED) (none associated specifically with increased risk)
3. Lamotrigine use in women (associated with increased risk)
4. Never having been treated with an AED (associated with increased risk)
5. Number of AEDs used overall (associated with increased risk)
6. Heart rate variability (not associated with increased risk)
7. Extratemporal epilepsy (associated with increased risk)
8. Intellectual disability (associated with increased risk)
9. Male sex (associated with increased risk)
10. Anxiolytic drug use (associated with increased risk)

The evidence is very low or conflicting that the following factors are associated with altering SUDEP risk:

1. Overall seizure frequency when evaluated by using all seizure types
2. Medically refractory epilepsy vs not having well-controlled seizures defined as no seizures in the last year
3. Monotherapy vs polytherapy
4. Carbamazepine, phenytoin, or sodium valproate levels that are above, below, or within the reference range
5. Psychotropic drug use
6. Mental health disorders, lung disorders, or alcohol use
7. Lamotrigine use in people with highly refractory epilepsy
8. Frequent changes in AEDs
9. Therapeutic drug monitoring
10. Undergoing a resective epilepsy surgical procedure (although current research does not rule out the possibility of a beneficial effect or, further, the potential effect of epilepsy surgery on reducing GTCS frequency and epilepsy severity on reducing SUDEP risk)
11. Engel outcome of epilepsy surgery (although current research does not rule out the possibility of a beneficial effect and, further, the potential effect of epilepsy surgery on reducing GTCS frequency and epilepsy severity on reducing SUDEP risk)
12. Vagus nerve stimulator use for more than 2 years (however, current research does not rule out the possibility of a beneficial effect and, further, the potential effect of epilepsy surgery on reducing GTCS frequency and epilepsy severity on reducing the risk of SUDEP)
13. Epilepsy etiology, whether idiopathic or localization-related
14. Structural lesion on MRI
15. Duration of epilepsy
16. Age at epilepsy onset
17. Postictal EEG suppression

SUGGESTIONS FOR FUTURE RESEARCH

1. Systematic methods should be developed to identify and report the incidence of SUDEP in

different epilepsy populations in order to obtain a better understanding of the incidence and causes of this devastating condition.
2. Educational efforts are needed to improve the forensic knowledge of SUDEP among professionals such as medical examiners, coroners, and pathologists in order to help determine, and document on death certificates, the etiology in individuals, and in order to improve overall knowledge of this condition.
3. Research to identify preventable risk factors should be supported and encouraged so that future clinical trials will be conducted to reduce SUDEP occurrence. Of particular importance is to better understand (1) the relationship between the nature, severity, and duration of epilepsy and the occurrence of SUDEP and (2) whether current treatments affect the risk of developing SUDEP.
4. Because of (1) risks identified with frequent GTCS, (2) the fact that one study shows more SUDEP events occur in people in placebo arms of trials, and (3) increased SUDEP risk, serious consideration should be given to avoid assigning people with frequent GTCS to placebo for long periods.

CONFLICT OF INTEREST The American Academy of Neurology and the American Epilepsy Society are committed to producing independent, critical, and truthful practice guidelines. Significant efforts are made to minimize the potential for conflicts of interest to influence the recommendations of this practice guideline. To the extent possible, the AAN and the AES keep separate those who have a financial stake in the success or failure of the products appraised in the practice guidelines and the developers of the practice guidelines. Conflict of interest forms were obtained from all authors and reviewed by an oversight committee prior to project initiation. AAN and AES limit the participation of authors with substantial conflicts of interest. The AAN and the AES forbid commercial participation in, or funding of, practice guidelines projects. Drafts of the practice guidelines have been reviewed by at least 3 AAN committees, at least 1 AES committee, a network of neurologists, *Neurology*® peer reviewers, and representatives from related fields. The AAN Guideline Author Conflict of Interest Policy can be viewed at aan.com. For complete information on this process, access the 2004 AAN process manual.[1]

AUTHOR CONTRIBUTIONS

Dr. Harden: study concept and design, acquisition of data, analysis or interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content, study supervision. Dr. Tomson: study concept and design, acquisition of data, analysis or interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content. Dr. Gloss: study concept and design, acquisition of data, analysis or interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content. Dr. Buchhalter: study concept and design, acquisition of data, analysis or interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content. Dr. Cross: study concept and design, acquisition of data, analysis or interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content. Dr. Donner: study concept and design, acquisition of data, analysis or interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content. Dr. French: analysis or interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content. Dr. Gil-Nagel: study concept and design, acquisition of data, analysis or interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content. Dr. Hesdorffer: study concept and design, acquisition of data, analysis or interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content. Dr. Smithson: study concept and design, acquisition of data, analysis or interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content. Dr. Spitz: study concept and design, acquisition of data, analysis or interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content. Dr. Walczak: analysis or interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content. Dr. Sander: analysis or interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content. Dr. Ryvlin: analysis or interpretation of data, drafting/revising the manuscript, critical revision of the manuscript for important intellectual content.

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DISCLOSURE

C. Harden has received royalties from Wiley and UpToDate and has served as a contributing editor for *Epilepsy Currents*. T. Tomson has served as the associate editor of *Epilepsia*; is a member of the editorial boards of *Epilepsy Research*, *Epileptic Disorders*, and the *European Journal of Clinical Pharmacology*; has received honoraria from Sun Pharmaceuticals, UCB, Eisai, and Bial; has served as a member of an expert panel for sudden unexpected death in epilepsy (SUDEP) adjudication in clinical trials of lamotrigine sponsored by GlaxoSmithKline; and has received research support from UCB, GlaxoSmithKline, Bial, Eisai, Novartis, Stockholm County Council, and Citizens United in Research for Epilepsy (CURE). D. Gloss serves as an evidence-based medicine consultant for the American Academy of Neurology (AAN) and has served as an associate editor (risk of bias classification) for *Neurology*®. J. Buchhalter has received funding for travel from the AAN; serves on an editorial advisory board for *Pediatric Neurology* and *Epilepsy Currents*; has served as a consultant to UCB, Upsher-Smith Laboratories, and Eisai; and has performed clinical procedures/imaging studies related to the content of this practice guideline, including EEG and video EEG (25%) and epilepsy surgery evaluation. J. Cross has served as a member of the editorial boards of *Developmental Medicine*, *Child Neurology,* and the *European Journal of Child Neurology*; has a patent for C10 in the treatment of epilepsy; has received royalties for a chapter on childhood epilepsy in *Brain Diseases of the Nervous System* and as editor of *Paediatric Epilepsy*; has received research support from the UK National Institute for Health and Research (NIHR), the European Framework FP7, the Charles Wolfson Foundation, Action Medical Research, and Sparks; and has sat on advisory boards for Vitaflo, Sanofi, Eisai, Viropharma, and Zogenix, for which remuneration is paid to her department. E. Donner has received research support from the Canadian Institutes of Health Research, Dravet Canada, and SUDEP Aware. J. French has served as a consultant for Acorda, Biotie, Eisai Medical Research, GlaxoSmithKline, Impax, Johnson & Johnson, Lewis County General Hospital, Marinus, Novartis, Pfizer, Sunovion, SK Life Science, Supernus Pharmaceuticals, UCB, Upsher-Smith, and Vertex; has received grants from Eisai Medical Research, the US Epilepsy Research Foundation, the Epilepsy Study Consortium, the Epilepsy Therapy Project of the Epilepsy Foundation, Lundbeck, Pfizer, and UCB; and is president of the Epilepsy Study Consortium. All consulting is done on behalf of the Consortium, and fees are paid to the Consortium. New York University receives salary support from the Consortium. A. Gil-Nagel has received personal compensation from Bial, Eisai, GSD Pharma Consulting, UCB Pharma, and Pfizer; has received funding for travel from Bial, Eisai, and GlaxoSmithKline; has served as an editor for *Seizure, Neurologia,* and *Revista de Neurologia*; has served on speakers bureaus for Bial, Eisai, GlaxoSmithKline, and UCB Pharma; and asserts that the information he provides his patients in his epilepsy clinic may be influenced by the results of this practice guideline. D. Hesdorffer is a member of the SUDEP Institute and of the Executive Committee of the North American SUDEP Registry; has served on scientific advisory boards for Upsher-Smith and Acorda; has served as a consultant for Cyberonics; has received funding for travel from the International League Against Epilepsy; has served as an associate editor of *Epilepsia*; has served on the editorial board for *Epilepsy and Behavior*; has served as a contributing editor for *Epilepsy Currents*; and has received funding from the NIH, the Centers for Disease Control and Prevention, the Epilepsy Consortium, the Patient Centered Outcome Research Institute, Finding a Cure for Epilepsy, The Epilepsy Study Consortium, and the Icahn School of Medicine at Mount Sinai (for consulting work on an injury prevention grant). W. Smithson has served on a scientific advisory board for the Sanofi UK consensus guidelines on women with epilepsy, has received travel funding for the Partners Against Mortality in Epilepsy conference on SUDEP (Washington 2016), has received publishing royalties from Blackwell Publishing for the *ABC of Epilepsy*, has received financial support in the form of funding for a general practice research infrastructure from the NIHR (UK), and has given expert witness testimony for the Fatal Accident Inquiry Dundee 2012 (2 cases of SUDEP). M. Spitz has received personal compensation and honoraria for serving on an advisory board for UCB, has received travel funding from Cyberonics (to see the site/factory), has received financial support for a US Department of Defense Study on closed head injury, and has given expert testimony, prepared an affidavit for, and acted as a witness or consultant regarding a legal proceeding. T. Walczak serves on a scientific advisory panel tracking incidence of SUDEP in follow-up of patients treated with the NeuroPace RNS System. Compensation goes directly to his academic department and does not increase his salary. J. Sander is based at University College London/University College London Hospitals, which receives funding from the UK Department of Health's NIHR Biomedical Research Centres; has served on advisory boards for UCB and Eisai; has received speaker honoraria from GlaxoSmithKline, Eisai, UCB, Lundbeck, and Teva; serves on the editorial board of the *Lancet Neurology*; and receives research support from the Dr. Marvin Weil Epilepsy Research Fund, the Epilepsy Society (UK), the Netherlands Epilepsy Fund, Eisai, GlaxoSmithKline, WHO, and EU FP7. His current position is endowed by the Epilepsy Society (UK). P. Ryvlin has served as a chair of the Scientific Advisory Committee for the annual meeting of the French League Against Epilepsy; has received travel funding and honoraria from GlaxoSmithKline, Eisai, Janssen Cilag Pty. Ltd., Cyberonics, Medtronic, and UCB Pharma (in order to participate on industry-funded advisory boards or symposia); has served as a journal editor for *Epilepsia, Epilepsy Research, Epileptic Disorders,* and *Epilepsy Research and Treatment*; has served on speakers bureaus for Eisai, GlaxoSmithKline, and UCB Pharma for a symposium at the European and International Epilepsy Congress (in order to participate on advisory boards or symposia); and has received financial support in the form of a European FP7 grant (EURIPIDES) and grant/research program funding from national (French) entities, including 2 PHRC (Programme Hospitalier de Recherche Clinique), 1 INSERM-DHOS (Institut National de la Santé et de la Recherche Médicale-Direction de l'Hospitalisation et de l'Organisation des Soins) Translationnelle, and 1 Contrat d'Interface INSERM. Go to Neurology.org for full disclosures.

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