LETTERS

Comment on Neuronal networks in epileptic encephalopathies with CSWS

To the Editors:

I read with great interest the work of Japaridze et al[1] in *Epilepsia*.

They wrote: "An activation of spike and wave activity during slow sleep provides a clear argument for involvement of the thalamocortical network. Synchronization of epileptiform spikes and slow oscillation during slow sleep may involve mechanism similar to one described by Steriade and colleagues . . .."

Our question is: What is the nature of the discharges? Are they really "generalized spike-and-wave" or regional discharges?

The first publications about ESES spoke explicitly about generalized spike-and-wave discharges. Not only the electromorphology was considered to be "spike-and-wave" but the recent interpretations about the pathomechanism of the discharges also went back to the classical generalized spike wave pattern, similarly to the present interpretation of Japaridze et al..[2,3] However, focal/regional discharges were frequently reported.[3–6] Beaumanoir[7] already pointed out that "during ESES, the interictal EEG abnormalities during wakefulness are similar to those before ESES, but are usually more marked."

The last overview of the Tassinari group[8] is summarized as follows: "The EEG during wakefulness shows usually focal, or multifocal, slow spikes with frequent associated diffuse slow spikes and waves. In a proportion of cases, the EEG can show features similar to what one observes in "idiopathic" focal ("Rolandic," frontal or, less frequently, parietooccipital) epilepsies or syndromes. Figure 9 of Tassinari et al.[8] shows a clear-cut map of a focal/regional parietotemporal discharge, nothing to do with the classical bilateral spike-wave pattern.

Thus doubts can be raised about the existence of a unitary mechanism of ESES because discharges show heterogenic forms; they are bilateral spike-waves but in the majority of cases are focal/regional discharges like in Rolandic or in other focal idiopathic childhood epilepsies. The literature is astonishingly poor in studies that analyze the potential fields of the ESES discharges. In our study[9] from the 33 (18 lesional and 15 nonlesional) children with ESES, only 3 (<10%) (two nonlesional and one lesional) showed the classical generalized spike and wave field. It was characterized by bilateral more or less symmetric distribution, with a uniform dipole (anterior negative and posterior positive half-fields) without unihemispheral phase reversal. All the other patients regardless of lesional or nonlesional etiology showed unihemispheral phase reversals of their discharges with anterior, medial, and posterior localization along the Sylvian fissure as an axis, almost equally distributed. Thus we can say that in our material showing lesional and nonlesional cases in 54.5:46.5% rate, the overwhelming majority had spike fields similar to what we observe in focal/regional childhood idiopathic hyperexcitability syndromes. This finding enlightens our lack of detailed knowledge about the nature of the discharges, and raises the possibility that the majority of the discharges might reflect a more circumscript regional network and that their electromorphology, spatial distribution, and functional properties are not similar to the classical generalized spike-wave pattern.

DISCLOSURE

I have no conflicts of interest to disclose. I confirm that I have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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In response: Neuronal networks in epileptic encephalopathies with CSWS

To the Editors:

In his commentary of our article,[1] Prof. Péter Halász points out an important issue of the nature of epileptiform discharges during electrical status epilepticus in sleep (ESES) and offers a thorough review of the topic. Furthermore, due to the diversity of the epileptiform discharges, which are mainly focal/regional discharges or bilateral spike-waves,[2] he raises doubt about the existence of unitary mechanism of ESES and suggests that most of the discharges might reflect a more confined regional network.[3]

A better understanding of the morphology and localization of the epileptiform discharges during ESES is an important issue. However, as noted by Dr. Halász, there are only few studies analyzing the potential fields of ESES discharges.[4] We concur with Dr. Halász that heterogeneity of discharges can be responsible for differences in clinical presentations of patients with ESES, and can be used as an argument against the existence of the unitary mechanisms of ESES discharges.

Similar to the observations of previous authors,[2,3,5–7] we observed that most our patients exhibited regional discharges with mainly centrotemporal or parietooccipital predominance. However, we did not focus on detailed and systematic analyses of the morphology and localization of discharges. The aim of our previous study was to investigate the unifying mechanisms that generate background oscillations, as opposed to epileptiform discharges, of patients with ESES. As such, localization of the discharges or differences in seizure forms were not taken into account.

We would argue that the delta frequency oscillations observed during the acute phase of continuous spikes and waves during sleep (CSWS) represent a unified network signal that is significantly associated with the coherent sources we observed.[8] Furthermore, we believe that the complexity of the observed network may explain the diversity of neurophysiologic deficits characteristic of this condition.

The high temporal resolution that electroencephalography (EEG) provides, in conjunction with advancements in source analysis methods, allowed a description of the hierarchical association. This enabled us to identify the thalamus, together with the mesial temporal and parietal regions, as the epicenter of the network. Based on the results obtained from the directionality analyses, we concluded that the posteromedial cortical region is merely a precipitator, which acts on the thalamocortical network and facilitates the development of epileptiform discharges.

We strongly agree that the detailed and systematic analyses of the morphology of spike and wave discharges, in addition to studies focused on networks underlying epileptiform discharges in ESES, are topics of great interest, both of which we hope will be the focus of future research pursuits.

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Disclosure

None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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The new ILAE seizure classification: 63 seizure types?

Dear Editors,

We have read with great interest the ILAE position papers on the new seizure classification.[1,2] The papers nicely describe the reasoning behind the proposed new terminology of seizure types. However, not all names generated by the proposed algorithm are mentioned in the text. A detailed list with the names of all seizure types is necessary for standardization of nomenclature and communication between centers. To prevent the potential confusion generated by translation into other languages, codes attributed to each seizure type would be helpful. This became obvious when we attempted to implement the new ILAE seizure classification into the revised version of SCORE (Standardized Computer-based Organized reporting of EEG [electroencephalography])[3] by a taskforce of the International Federation of Clinical Neurophysiology, comprising 39 experts. Using the reasoning described in the ILAE position papers, we propose such a list, containing 63 seizure types (Table 1).

The other practical question concerns negative myoclonus. This is not mentioned in the new classification. We were wondering what the reason could be: (1) The authors do not consider that there is evidence for such a seizure type, although several studies indicated its existence and that its correct diagnosis can have therapeutic implications[4–8]; (2) it should be described under myoclonic seizure types, adding "negative" in free text, as a descriptor; (3) it should be described as an atonic seizure—of very short duration. In the "Instruction manual,"[2] it is stated that wherever possible, prior accepted definitions from the ILAE Glossary of 2001[9] were maintained, in order to support continuity of usage. Terms no longer recommended

Table 1. List of seizure types according to the new ILAE seizure classification

Three-step classification			Name of seizure type	Code
Focal onset	Aware	Motor onset—not further specified	Focal aware motor-onset seizure	I.A.01
		Myoclonic	Focal aware myoclonic seizure	I.A.02
		Clonic	Focal aware clonic seizure	I.A.03
		Tonic	Focal aware tonic seizure	I.A.04
		Atonic	Focal aware atonic seizure	I.A.05
		Automatisms	Focal aware automatism seizure	I.A.06
		Hyperkinetic	Focal aware hyperkinetic seizure	I.A.07
		Nonmotor onset—not further specified	Focal aware nonmotor onset seizure	I.A.08
		Behavior arrest	Focal aware behavior arrest seizure	I.A.09
		Sensory	Focal aware sensory seizure	I.A.10
		Emotional	Focal aware emotional seizure	I.A.11
		Cognitive	Focal aware cognitive seizure	I.A.12
		Autonomic	Focal aware autonomic seizure	I.A.13
		Onset not further specified	Focal aware seizure	I.A.14
	Impaired awareness	Motor onset—not further specified	Focal impaired awareness motor onset seizure	I.B.01
		Myoclonic	Focal impaired awareness myoclonic seizure	I.B.02
		Clonic	Focal impaired awareness clonic seizure	I.B.03
		Tonic	Focal impaired awareness tonic seizure	I.B.04
		Atonic	Focal impaired awareness atonic seizure	I.B.05
		Automatisms	Focal impaired awareness automatism seizure	I.B.06
		Hyperkinetic	Focal impaired awareness hyperkinetic seizure	I.B.07
		Nonmotor onset—not further specified	Focal impaired awareness nonmotor onset seizure	I.B.08
		Behavior arrest	Focal impaired awareness behavior arrest seizure	I.B.09
		Sensory	Focal impaired awareness sensory seizure	I.B.10
		Emotional	Focal impaired awareness emotional seizure	I.B.11
		Cognitive	Focal impaired awareness cognitive seizure	I.B.12
		Autonomic	Focal impaired awareness autonomic seizure	I.B.13
		Onset not further specified	Focal impaired awareness seizure	I.B.14

Continued

Table 1. Continued.

Three-step classification			Name of seizure type	Code
	Awareness not known or not specified	Motor onset—not further specified	Focal motor seizure	I.C.01
		Myoclonic	Focal myoclonic seizure	I.C.02
		Clonic	Focal clonic seizure	I.C.03
		Epileptic spasms	Focal epileptic spasm	I.C.04
		Tonic	Focal tonic seizure	I.C.05
		Atonic	Focal atonic seizure	I.C.06
		Automatisms	Focal automatisms seizure	I.C.07
		Hyperkinetic	Focal hyperkinetic seizure	I.C.08
		Nonmotor onset—not further specified	Focal nonmotor seizure	I.C.09
		Behavior arrest	Focal behavior arrest seizure	I.C.10
		Sensory	Focal sensory seizure	I.C.11
		Emotional	Focal emotional seizure	I.C.12
		Cognitive	Focal cognitive seizure	I.C.13
		Autonomic	Focal autonomic seizure	I.C.14
		Onset not further specified	Focal seizure	I.C.15
	Focal to bilateral tonic–clonic		Focal to bilateral tonic–clonic seizure	I.D.01
Generalized Onset	Motor	Onset not further specified	Generalized motor seizure	II.A.01
		Myoclonic	Generalized myoclonic seizure	II.A.02
		Myoclonic–atonic	Myoclonic–atonic seizure	II.A.04
		Myoclonic–tonic–clonic	Myoclonic–tonic–clonic seizure	II.A.04
		Clonic	Generalized clonic seizure	II.A.05
		Epileptic spasm	Generalized epileptic spasm	II.A.06
		Tonic	Generalized tonic seizure	II.A.07
		Atonic	Generalized atonic seizure	II.A.08
		Tonic–clonic	Generalized tonic–clonic seizure	II.A.09
	Absence	Typical	Typical absence seizure	II.B.01
		Atypical	Atypical absence seizure	II.B.02
		Myoclonic absence	Myoclonic absence seizure	II.B.03
		Eyelid myoclonia	Eyelid myoclonia with absence / without absence	II.B.04
Unknown onset	Motor	Tonic–clonic	Tonic–clonic seizure of unknown onset	III.A.01
		Epileptic spasm	Epileptic spasm with unknown onset	III.A.02
		Motor—not further specified	Motor seizure with unknown onset	III.A.03
	Nonmotor	Behavior arrest	Behavioral arrest with unknown onset	III.B.01
		Nonmotor—not further specified	Nonmotor seizure with unknown onset	III.B.02
	Unknown		Unclassified seizure	III.C.01

for use are omitted. The 2001 Glossary[9] recognized negative myoclonus as a specific seizure type, distinct from (positive) myoclonus, and this clinical entity is commonly used in clinical practice. Therefore, it would be important to highlight its placement in the seizure classification.

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None of the authors has any conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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Response to the numbering of seizure types

To the Editors:

We thank the authors for their kind attention to the 2017 ILAE seizure type classification. Our target audience comprised general clinicians, patients with epilepsy, and the public (for the basic classification) and neurologists, epileptologists, and researchers (for the expanded classification). To keep the classification usable for this audience, the Classification Task Force chose to abbreviate only the most important seizure types, for example, FAS for focal aware seizure and FIAS for focal impaired awareness seizure. We have no objection to the suggested numbering system for use by specialized groups using the computerized SCORE system.

The question of negative myoclonus was not discussed extensively by our Task Force. The 2017 classification is not comprehensive and it omits mention of a number of seizure types. The distinction of negative myoclonus seizures from focal or generalized atonic seizures can be difficult. Diagnosis is confounded by nonepileptic negative myoclonus in the form of asterixis. Despite these diagnostic issues, it would be acceptable to indicate that myoclonic seizures can have either positive or negative manifestations. Future research about this entity may clarify where negative myoclonus best fits into a classification.

Disclosures of Conflict of Interest

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Novel *SMC1A* variant and epilepsy of infancy with migrating focal seizures: Expansion of the phenotype

To the Editors:

Symonds et al.[1] recently reported 10 females with frameshift or splice-site variants in Structural Maintenance Of Chromosomes 1A (*SMC1A*) with acquired microcephaly, severe developmental delay, cardiac malformations, and drug-resistant epilepsy, with a new association of seizure clustering. Herein, we report two further female infants, with novel de novo pathogenic variants in *SMC1A*, one of whom had epilepsy of infancy with migrating focal seizures (EIMFS), a phenotype not previously described in association with this gene.

Female one was born full term, the second child of nonconsanguineous Irish parents. Antenatal and birth course were uneventful. Early developmental milestones were achieved. She presented at 7 weeks with clusters of focal seizures that responded to phenobarbital and clonazepam. Aged 17 weeks, during a febrile illness, focal seizures with apnea emerged with associated developmental regression. Seizures were refractory to multiple therapies (carbamazepine, valproate, topiramate, pyridoxal-5-phosphate, phenytoin, and ketogenic diet) until she died at age 9 months. At 8 months, she had no head control, visual fixation, or vocalization, and there was acquired microcephaly (occipitofrontal circumference (OFC) 50th percentile to 0.4th percentile over 8 months) and profound axial hypotonia. She was nondysmorphic. Electroencephalography (EEG) was normal at age 7 weeks, and at 5 months showed a slow asymmetric background (left slower than right). At age 8 months, EEG showed features of EIMFS. Multiple focal seizures arose in the left hemisphere with simultaneous and sequential independent seizures arising from the right. Interictal EEG showed multifocal spike and poly-spike bursts and persistent background slowing. Trio whole exome sequencing identified a novel de novo heterozygous c.1114delG resulting in a premature stop codon (pVal372*) in *SMC1A* (GRCh39/hg17, NM_006306.3). The deleted nucleotide is in an acceptor splice site and is predicted to influence non-sense–mediated messenger RNA (mRNA) decay. Further details, including previous neurometabolic and genetic investigation, and postmortem neuropathology findings are previously outlined (patient 12 of McTague et al.).[2]

The second female identified had a de novo splice-site variant in *SMC1A* (g.10734G>A) with a phenotype similar to those reported by Symonds et al.[1] She presented with clusters of focal seizures (7 weeks of age) and later developed clusters of tonic seizures (4 months), infantile spasms (9 months), and rare generalized tonic–clonic seizures (13 months). Treatment with multiples antiepileptic drugs and ketogenic diet had no sustained effect on the frequency of seizure clusters. Other features included antenatal and postnatal microcephaly (OFC 0.4^{th} percentile), dysmorphic features (small hands and feet, incomplete single palmar creases, big hallux bilaterally extended), atrial septal defect, severe developmental delay, and profound hypotonia. She died at age 3 years. Multiple EEG studies demonstrated a slow background with frequent epileptiform discharges, maximally left temporal.

In our cohort of Irish patients with unexplained early onset epileptic encephalopathy (EOEE), loss of function variants in *SMC1A* were identified in two cases accounting, for 2.7% of this population (and 5% of females), indicating that *SMC1A* encephalopathy may be an underrecognized diagnosis in females with EOEE. The identification of a loss-of-function variant in *SMC1A* in EIMFS expands the phenotype, number of genes, and mechanisms contributing to this devastating electroclinical syndrome.

Disclosure

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ANNOUNCEMENTS

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Journeés française de l'Epilepsie (JFE)

9–12 October 2017
Palais du Pharo, Marseille, France
Organized by La Ligue Française contre l'Epilepsie (LFCE)
Website: http://www.jfe-congres.fr/

2017 CLAE Scientific Meeting

13–15 October 2017
Vancouver, BC, Canada
Website: https://canadianleagueagainstepilepsy.wildapricot.org/2017-Meeting

Other Congresses

Advanced International Course: Bridging Basic with Clinical Epileptology – 6

17–28 July 2017
San Servolo (Venice), Italy
Course Directors: Giuliano Avanzini and Marco de Curtis
Information

7th International Summer School for Neuropathology and Epilepsy Surgery (INES 2017)

22–25 July 2017
State University of Campinas – UNICAMP, Brazil
Flyer

11th Baltic Sea Summer School on Epilepsy (BSSSE 11)

6–11 August 2017
Tartu, Estonia
Clinically oriented, and focused on comprehensive aspects of diagnosis and treatment of epilepsy.
Announcement: Program, fees, and more information | Past BSSSE Schools | Website: www.epilepsiestiftung-wolf.de

XIV Workshop on Neurobiology of Epilepsy (WONOEP) 2017

28 August–1 September, 2017
Mon St Benet, Barcelona, Spain
Announcement | WONOEP Report

Eighth Caucasian Regional School of Clinical Epileptology (CRSSCE-VIII)

13–18 September 2017
Dilijan, Armenia

XIII World Congress of Neurology

16–21 September 2017
Kyoto, Japan
Website: www.2017.wcn-neurology.com/

Cleveland Clinic Epilepsy Update & Review Course

23–25 September 2017
InterContinental Hotel & Bank of America Conference Center, Cleveland, Ohio, USA
Program | Website – Register by August 15 and save!

3rd International Epilepsy Symposium: New Insights into Epilepsy

29 – 30 September 2017
Berlin, Germany More information

ISPN 2017, 45th Annual Meeting of the International Society for Pediatric Neurosurgery

8–12 October 2017
Denver, Colorado, U.S.A.
Early Registration Deadline 14 August 2017
ISPNMeeting.org

12–14 October 2017
International Workshop on Onchocerciasis-Associated Epilepsy (OAE)

ANA 2017: American Neurological Association Annual Meeting

15–17 October 2017
San Diego, CA, U.S.A.
Website

7th Eilat International Educational Course: Pharmacological Treatment of Epilepsy

15–20 October 2017
Jerusalem, Israel
Website: www.eilatedu2017.com – Course and bursary information, applications

4th European Congress of NeuroRehabilitation (ECNR)

25–28 October 2017
SwissTech Convention Center, Lausanne, Switzerland
www.ecnr-congress.org

2nd Moroccan Congress of Neurophysiology

26–28 October
The First African and Middle Eastern Seminar of Clinical Neurophysiology and Movement Disorders Conference Center Mohammed VI, Rabat City, Morocco
Website: Speakers, program, registration

2018 Congresses

12th World Congress on Controversies in Neurology (CONy)

22–25 March 2018
Warsaw, Poland
CONy 2018 Website

2nd International Training Course on Neuropsychology in Epilepsy

15–20 April 2018
Domaine de Châteauneuf, Provence, France Information

31st International Congress of Clinical Neurophysiology (ICCN) of the International Federation of Clinical Neurophysiology (IFCN)

1–6 May 2018
Washington, DC, U.S.A.
ICCN 2018 Website: http://iccn2018.acns.org/

4th International Congress on Brain and Mind

3–5 May 2018
Brno, Czech Republic
Read about the previous Brain and Mind congress

12th Asian and Oceanian Epilepsy Congress

21–24 June 2018
Bali, Indonesia
Website: www.epilepsybali2018.org

Regional Congresses

13th European Congress on Epileptology

26–28 August 2018
Vienna, Austria
website: www.epilepsyvienna2018.org

6th Global Symposium on Ketogenic Therapies for Neurological Disorders

5–8 October 2018
Embracing Diversity, Global Implementation and Individualized Care
International Convention Center Jeju, Jeju, Korea
Website: www.ketoconnect.org