COMMENTARY

Commentary on the 1st International Summer School for Neuropathology and Epilepsy Surgery (INES 2013) held in Erlangen, Germany, September 16–20, 2013

Epilepsy surgery is increasingly available as a successful treatment option in patients with drug-resistant focal epilepsies when associated with distinct brain lesions. Reliable neuropathologic work-up of epilepsy-associated brain lesions represents, therefore, an important diagnostic tool in clinical epileptology, and the International League Against Epilepsys international classification of epilepsies recognizes a large spectrum of neuropathologic substrates as potential predictors of each patients disease progression and treatment response. However, histopathologic standards are not yet available for all different lesions encountered in patients with epilepsy, nor are they very well accepted or disseminated among the diagnostic pathology community. In addition, the microscopic diagnosis of epilepsy-related surgical brain specimens remains challenging due to the broad spectrum of disease variants. The European Commission of the International League Against Epilepsy (ILAE-CEA) launched a first neuropathology teaching course aimed at colleagues who are engaged in the diagnostic evaluation of patients with drug-resistant focal epilepsy. Thirty-seven colleagues from 25 nations participated at this first INES summer school in Erlangen, Germany (Fig. 1A). Most participants had a medical training record in pathology or neuropathology, although some had their background also in neurology, neurosurgery, neuroradiology, neuropsychology, or neurosciences. This multidisciplinary group composition fostered fruitful discussions during the week that were considered most helpful to appreciate the value but also limitations of histopathology diagnosis in epilepsy surgery.

The group was trained during 5 days by six distinguished tutors (Dr. Eleonora Aronica, Amsterdam; Dr. Albert Becker, Bonn; Dr. Ingmar Blumcke, Erlangen; Dr. Hajime Miyata, Akita; Dr. Harvey Sarnat, Calgary; and Dr. Maria Thom, London). Each tutor mentored his/her own group of six to seven students, helping them to microscopically review and discuss a series of 112 glass slides obtained from 31 surgical specimens selected to cover the large spectrum of epilepsy-related brain lesions and their variants, that is, the new ILAE classification of hippocampal sclerosis (first day), epileptic encephalitis and vascular disorders (second day), long-term epilepsy–associated brain tumors (third day), and the ILAE classification of focal cortical dysplasia as well as other malformations of cortical development (fourth and fifth days). This valuable series of histopathologic glass slides was prepared by the course organizers in Erlangen to offer each student free access to microscopic review and to familiarize with helpful and recommended special stainings, including a large panel of immunohistochemistry. All information was made available also by a special course booklet summarizing case presentation, protocols for neuropathologic workup in epilepsy surgery, as well as several histopathologic review articles introducing all major entities of epileptogenic brain lesions. We also invited distinguished speakers experienced in the field of clinical epileptology (Dr. Eugen Trinka, Salzburg; Dr. Christian Bien, Bielefeld; Dr. Karl Rössler, Erlangen; Dr. Hans Holthausen, Vogtareuth; and Dr. Fernando Cendes, Campinas), who always started the days teaching program with a topic-related plenary lecture introducing the principles of adult or childhood epileptology, modern imaging techniques, or neurosurgical procedures.

In addition to these practical teaching sessions, the interdisciplinary discussion and training environment in the microscope lecture room offered an encouraging spirit to foster clinical and scientific interest in the field of surgical neuropathology. The students evaluation achieved exceptional rating scales, which support the courses structure with enough room and space for face-to-face teaching, as well as group discussions during case presentation and plenary lectures. Not to forget, our social events were very well anticipated and regarded helpful for building professional networks.

Scholarships were made available from the International Society of Neuropathology (ISN, Fig. 1C) and International Brain Research Organization (IBRO, Fig. 1B), which allowed also participants from low-income countries to attend this course.

CEA-ILEA support will be available also for next years second INES in Erlangen. The dates will be announced on the course website at www.epilepsie-register.de or available at personal request from the course director (bluemcke@uk-erlangen.de).

Both faculty and participants were confident that this course was most helpful to train in this rapidly emerging discipline with its new diagnostic classification schemes and many still ill-defined disease categories, covering a

Figure 1.
(**A**) INES group from bottom row left to right: *Jinmei Lie*, Chengdu, China; *Se Hoon Kim*, Seoul, South Korea; *Eva Lobner*, Copenhagen, Denmark; *Francesco Deleo*, Milano, Italy; *Beatrice Paradiso*, Ferrara, Italy; *Laura Zaldumbe*, Santander, Spain; *Raffaele Nunziata*, Milano, Italy; *Laura Flores-Sarnat*, Calgary, AB, Canada; *Juana Villeda Hernandez*, Mexico City, Mexico; second row left to right: *Vega Karlowee*; Semarang, Indonesia; *Sandra Orozco Suarez*; Mexico City, Mexico; *Ludmilla Shishkina*, Moscow, Russia; *Facundo Las Heras*, Santiago, Chile; *Ovidiu Tica*, Oradea, Rumania; *Harvey Sarnat* (tutor), Calgary, AB, Canada; *Hajime Miyata* (tutor), Akita, Japan; third row left to right: *Sophie Hamelin*, Grenoble, France; *Monica Mezmezian*, Buenos Aires, Argentina; *Lily Pal*, Lucknow, India; fourth row left to right: *Savo Raicevic*, Belgrade, Serbia; *Anne Sieben*, Gent, Belgium; *Elane Magno*, Sao Paulo, Brazil; *Theo Kraus*, Munich, Germany; *Roberto Spreafico* (lecturer), Milano, Italy; *Karl Rössler* (lecturer), Erlangen, Germany; *Francine Oliveira*, Porto Alegre, Brazil; *Ingmar Blumcke* (course director and tutor), Erlangen, Germany; fifth row left to right: *Gianluca Marucci*, Bologna, Italy; *Tuomas Rauramaa*, Kuopio, Finland; *Clinton Paul Turner*, Auckland, New Zealand; *Paul Gallagher*, Glasgow, Scotland; *Maria Thom* (tutor), London, United Kingdom; *Ricardo Taipa*, Porto, Portugal; last row on top from left to right: *Muchou Joe Ma*, Orlando, FL, U.S.A.; *Eleonora Aronica* (tutor), Amsterdam, The Netherlands; *Alexey Kislyakov*, Moscow, Russia; *Roland Coras* (course director), Erlangen, Germany; *Harald Stefanits*; Vienna, Austria; *Marc Polivka*, Paris, France; *Antonia Jakovcevic*, Zagreb, Croatia; *Jan Bauer* (lecturer), Vienna, Austria; *Andrew Gifford*, Randwick, NSW, Australia; *Albert Becker* (tutor), Bonn, Germany; *Fabio Rogerio*, Campinas, Brazil. (**B**) IBRO scholarships received (from left to right) *Antonia Jakovcevic* (Zagreb, Croatia), *Savo Raicevic* (Belgrade, Serbia), *Ricardo Taipa* (Porto, Portugal), *Fabio Rogerio* (Campinas, Brazil) and *Ovidiu Tica* (Oradea, Romania). (**C**) Tutors, lecturers, and ISN scholars from left to right: *Hajime Miyata* (tutor from Akita, Japan); *Ingmar Blumcke* (course director and tutor from Erlangen, Germany), *Fernando Cendes* (lecturer from Campinas, Brazil), *Lei Liu*, Beijing, China; *Facundo Las Heras*, Santiago, Chile; *Roberto Spreafico* (Lecturer from Milano, Italy); *Vega Karlowee*, Semarang, Indonesia; *Monica Mezmezian*, Buenos Aires, Argentina; *Francine Oliviera*, Porto Alegre, Brazil.

huge spectrum of brain malformations, inflammatory disease, degeneration, and tumors.

Looking forward to meeting you next year in Erlangen!

Disclosure

None of the authors have any conflicts to declare. INES 2013 was financially supported by ILAE-CEA (Commission on European Affairs of the Intl League against Epilepsy), IBRO (International Brain Research Organization), ISN (International Society of Neuropathology) and Roche Diagnostics Deutschland GmbH (Mannheim, Germany). I confirm that I have read the Journals position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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A meta-analysis of complications of subdural electrode placement

To the Editors:

We recently read with great interest an article by Arya et al.[1] In this study, the authors conducted a PubMed search to identify studies that reported adverse events related to subdural electrode (SDE) implantation and invasive electroencephalography (EEG) monitoring. A total of 21 studies with 2,542 patients met the authors search criteria and were included in the systematic review and meta-analysis. Of note, in the methods section of the study, the authors stated that studies that included patients who were undergoing invasive monitoring with depth electrodes had been excluded.

We noted that in one of the studies included in their review,[2] the rates of infectious and hemorrhagic complications (1.8% and 0.8%. respectively) were surprisingly low. Upon reading this report by Tarnriverdi et al., it is clear that electrode placement for intracranial monitoring was performed using depth electrodes only and not with subdural grids. In fact, this study includes 491 patients who underwent stereo-electroencephalography (SEEG), and is the largest such report of intracranial monitoring using depth electrodes from North America. Unfortunately, this is the largest series included in the meta-analysis by Arya et al.

In addition, another report by Wellmer et al.,[3] which comprises the second largest cohort used in the meta-analysis, reports adverse effects of invasive evaluations using a mix of various types of intracranial monitoring techniques, with at least 127 (49%) of 260 patients undergoing placement of depth or strip electrodes only, without a craniotomy. It is well known that complications from SEEG differ from those associated with SDE placement[3–6] and as such, the meta-analysis may not reflect an accurate rate of adverse events associated with SDE placement. Given that at least 618 patients from these two series (fully 24.3% of the patients) that are included in this meta-analysis, underwent a procedure with a markedly distinct adverse event profile, it calls into serious question the validity of the meta-analysis. Pooling two distinct classes of patients does not comply with several of the tenets of the QUOROM or PRISMA statements regarding meta-analysis.[7,8] We encourage the authors to make amendments to their report to precisely report the incidence of adverse events after the placement of SDEs.

Disclosure

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

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In response to comments on Adverse events related to extraoperative invasive EEG monitoring with subdural grid electrodes: A systematic review and meta-analysis

To The Editor-in-Chief

We are thankful to Drs. Tandon and Esquenazi for interest in our work. As mentioned in our Methods section, only those studies were excluded which reported patients with only depth electrodes.[1] We included the studies that provided data about both subdural and depth electrodes. The study by Tanriverdi et al.[2] reports data from a total of 6,415 electrodes including 2,943 depth electrodes (45.9%) and 2,490 cortical electrodes (38.8%). The rest were reference and ground electrodes (also subdural). This study also reports data about surgical morbidity of various epilepsy surgery procedures. While calculating pooled prevalence estimates for our study, we used a value for our denomina-

tor that was imputed from the ratio of depth and other electrodes. However, we had no choice but to extrapolate their raw percentages as being applicable to both depth and cortical electrodes. For regression analysis, we evaluated different adjusted models, but we presented only the best models based on commonly used criteria, as detailed in our paper. We have already mentioned this limitation in our study and cautioned the reader that the estimates are biased and most likely represent conservative figures. Similar argument holds true for the study by Wellmer et al.[3] We agree with Drs. Tandon and Esquenazi that this is an imperfect data synthesis. However, as we have repeatedly pointed out in our paper: there is extensive variability in reporting surgical morbidity associated with invasive epilepsy evaluation and the estimates that we have generated, although biased and likely conservative, represent the currently available data and draw attention to the heterogeneity in practice and data reporting.

Disclosures

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

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Parietal seizures mimicking psychogenic nonepileptic seizures

To the Editors:

We would like to comment on the excellent article Minimum requirements for the diagnosis of psychogenic nonepileptic seizures: A staged approach by LaFrance et al.[1] In terms of the difficulty of differential diagnosis between psychogenic nonepileptic seizures (PNES) and epileptic seizures, we note that frontal seizures, especially the so-called hypermotor seizures, have been highlighted several times in this article. However, from our experience working within a tertiary epilepsy center in Marseille, the diagnostic difficulties we have more frequently encountered in recent years tend to arise in differentiating parietal lobe seizures from PNES.

In the past 8 years we have seen five patients considered by us after initial assessment to have a fairly high likelihood of PNES, whose events were subsequently shown to be epileptic seizures of parietal origin. The initial impression of probable PNES was reinforced in two patients by short-term video–electroencephalography (EEG) recording of their habitual events, albeit a mild, mainly sensory version of these, with seemingly atypical clinical features, apparently produced or reinforced by suggestion[2] with no surface EEG change.

However, with subsequent long-term video-EEG monitoring, all five patients proved to have parietal epilepsies with epileptic seizures that involved somatosensory illusions, which were painful or certainly unpleasant, usually involving but not limited to the contralateral hemibody. Vertiginous symptoms or altered body perception could also occur. Motor signs were generally scarce in the early phase of the seizure but subtle dystonic posturing, tremor, or dyspraxic-type movements could be observed in the contralateral upper limb, often in the later part of the seizure. There was also frequently an ictal emotional component of fear or anxiety (with associated distressed behavior) and rather subtle alteration of consciousness. One patient had dysarthria. The early, mainly sensory phase of the seizures seemed to wax and wane (during which period the EEG was noncontributory) with a gradual build-up to more obvious motor signs (at which point the EEG showed changes). This waxing and waning pattern could be particularly observed during the EEG hyperventilation test. In two patients the seizure developed over many minutes before terminating in quite sudden secondary generalization (tonic–clonic seizure). All five patients had interictal anxio-depressive symptoms and a tendency for their seizures to be triggered by emotional events. Three patients had parietal lobe dysplasia that was not visible on initial magnetic resonance imaging (MRI) scans but that became evident with repeated, more detailed imaging, one had cryptogenic epilepsy and one had developed epilepsy following meningitis (MRI normal). Three of the five patients have since undergone presurgical evaluation with stereoelectroencephalography (SEEG), of which two have undergone subsequent parietal cortical resection surgery with good outcome.

The diversity of parietal lobe semiology, including polysensory auras and heterogeneous motor manifestations such as dystonia and hyperkinetic behavior, has been previously highlighted.[3–5] An interesting observation in our own and others cases, which could contribute to giving an initial impression of PNES is the rather frequent occurrence of affective ictal and interictal symptoms.[3,5] Although surface EEG is often nonlocalizing in parietal

seizures,[3] SEEG recordings have allowed description of subgroups of parietal seizure organization.[5]

Over the same time period in our center we have not observed similar diagnostic difficulties in differentiating PNES from frontal seizures. Patients with certain forms of parietal seizures represent an interesting group for further study in the context of differential diagnosis from PNES.

Disclosure

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

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In response to comments on Parietal seizures mimicking psychogenic nonepileptic seizures

To the Editors:

We thank Drs. McGonigal and Bartolomei for their remarks on the ILAE nonepileptic seizures (NES) Task Force (TF) Diagnosis paper.[1] We agree with their comments, and we acknowledge that frontal lobe epilepsy (FLE) seizures have been well described in the literature and are in many ways different enough from psychogenic NES (PNES) (with FLEs predominantly nocturnal occurrence, short duration, stereotyped semiology) that diagnostic mistakes involving FLE are becoming less of an issue.[2,3]

Our charge in the TF was to provide a logical and practicable framework for diagnosing PNES and differentiating them from epileptic seizures, one that could be used by a wide range of clinicians, rather than categorizing all potential diagnostic scenarios. We are aware that there are a number of problematic situations in which neurologic and cardiovascular phenomena, such as epileptic seizures and syncope, may appear to have the characteristics of PNES, or may trigger PNES.[4] The letter of Drs. McGonigal and Bartolomei illustrates two important points related to the differential diagnosis for PNES. First, as noted in the epilepsy literature,[5] parietal lobe epileptic seizures can be mistaken for PNES, especially when presenting with some atypical features. Second, a scalp-negative ictal EEG is only one element in establishing the PNES diagnosis, of the three necessary diagnostic components (history, semiology, EEG) in our criteria (Table 2). As noted in the ILAE NES TF paper,[1] The event described should be clinically incompatible with simple partial seizures (whether small motor seizures, or experiential seizures) or hypermotor frontal lobe seizures in which ictal EEG changes may be lacking.

The clinical observations in Drs. McGonigal and Bartolomeis cases are welcome. As many in the field know, no matter how experienced and careful you are, there will sometimes be cases in which your first impression is subsequently proven wrong. The more we know about brain-behavior disorders and the neuropsychiatry of seizures, the better it is for patients and clinicians.

Disclosure

The authors have no conflicts of interest. We confirm that we have read the Journals position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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ANNOUNCEMENTS

2014 Congresses

4th Course on Epilepsy Surgery (EPODES)

13–17 January, 2014 Brno, Czech Republic. Registration deadline 1 November, 2013. http://www.ta-service.cz/epodes2014/.

5th SEEG Course on Seizures of the Motor System

4–8 February, 2014; Venice, Italy. More information from seeg@ant-congres.com or +33 (0) 4 67 10 92 23.

30th International Congress of Clinical Neurophysiology (ICCN) and 58th Annual Meeting of the German Society for Clinical Neurophysiology and Functional Imaging (DGKN) 2014

19–23 March, 2014 at Estrel Hotel and Convention Center Berlin, Germany. www.iccn2014.de.

3rd International Congress on Epilepsy, Brain and Mind

3–5 April, 2014 Brno, Czech Republic.
Congress website: www.epilepsy-brain-mind2014.eu.

The 8th World Congress on Controversies in Neurology (CONy)

8–11 May, 2014 in Berlin, Germany. http://www.comtecmed.com/CongressPreView.aspx?cid=129.

2nd African Epilepsy Congress

22–24 May, 2014; Capetown, South Africa. www.epilepsycapetown2014.org.

4th NARCCE (North American Regional Caribbean Conference on Epilepsy)

22–24 May, 2014 Bay Gardens Resorts, St. Lucia.
Congress Website**:** www.epilepsycaribbean.org/narcce-2014.html.

11th European Congress on Epileptology

29 June–3 July, 2014 in Stockholm, Sweden. http://www.epilepsystockholm2014.org/.

Dianalund Summer School on EEG and Epilepsy (DSSEE), 2nd edition

3–19 July, 2014, Dianalund, Denmark.
Advanced course on EEG and its application in the field of epilepsy.
Announcement: http://www.ilae.org/Visitors/Congress/congressinfo/DSSEE2-2014-Announcment.pdf.

2014 World Tuberous Sclerosis Complex (TSC) Conference

July 3–6, 2014 in Washington, D.C. http://www.tsalliance.org/worldTSCconference.

2014 San Servolo epilepsy summer course: Bridging Basic with Clinical Epileptology

20 July–1 August 2014, San Servolo (Venice), Italy.
Announcement: http://www.ilae.org/Visitors/Congress/congressinfo/SanServolo-announcement-2014.pdf.
Email: epilepsysummercourse@univiu.org.

8th Baltic Sea Summer School on Epilepsy (BSSSE 8)

3–8 August, 2014, Trakai, Lithuania.
Application deadline April 15, 2014
Information: http://www.ilae.org/Visitors/Congress/congressinfo/BSSSE8_2014.pdf.
Contact: petra.novotny@wolfstiftung.org.

10th Asian and Oceanian Epilepsy Congress

7–10 August; Singapore. http://www.epilepsysingapore2014.org/.

EPNS Research Meeting 2014

12–13 September, 2014, Bucharest, Romania.
Forum for researchers in the area of Pediatric Neurology,
Announcement: http://www.ilae.org/Visitors/Congress/congressinfo/EPNS-2014-Announcement.pdf.

8th Latin American Congress on Epilepsy (8th LACE)

17–20 September, 2014, Buenos Aires, Argentina.
Website: http://www.epilepsycongress.org/8o-congreso-latinoamericano-de-epilepsia-8th-latin-american-epilepsy-congress/.

Canadian League Against Epilepsy (CLAE) Biennial Meeting

17–19 October, 2014 in London, Ontario, Canada.
More information available soon.

2015 Congresses

31st International Epilepsy Congress

6–10 September, 2015; Istanbul.

NORTHWESTERN FEINBERG SCHOOL OF MEDICINE
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The Davee Department of Neurology, seeks an **EPILEPTOLOGIST** with fellowship training to join the Comprehensive Epilepsy Center, Department of Neurology at Northwestern University, Chicago with appointment as a non-tenure eligible full-time **ASSISTANT/ASSOCIATE PROFESSOR**. Must be BE/BC in Neurology and Neurophysiology. Primary responsibilities include routine, ambulatory and continuous video-EEG interpretation, participation in epilepsy surgery evaluations, evaluation and management of epilepsy patients, intraoperative monitoring and teaching of students, residents and fellows. The individual will join a group of four epileptologists. The program includes an Epilepsy Monitoring Unit for noninvasive and invasive surgical and diagnostic evaluations, an active ICU continuous EEG service, daily intraoperative monitoring cases, and a dedicated Women's Neurology program. Opportunities are available to join or develop clinical and basic research related to epilepsy and to participate in administrative or educational leadership and in program development. Northwestern University Feinberg School of Medicine and Northwestern Memorial Hospital are located directly in downtown Chicago along Lake Michigan and offer a unique lifestyle in one of the most exciting cities in the country

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Stephen Schuele, MD, MPH
Northwestern University,
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