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WORLD NEUROLOGY

THE OFFICIAL NEWSLETTER OF THE WORLD FEDERATION OF NEUROLOGY

Nodding Syndrome Baffles Researchers

BY JENNIE SMITH
Elsevier Global Medical News

The cause of nodding syndrome, a progressive seizure and developmental disorder of unknown cause affecting children and teenagers, has remained elusive since the condition was first described in a remote mountain region of Tanzania in the early 1960s, then decades later in northern Uganda and what is now South Sudan, but recent efforts have begun to narrow down the possibilities.

Mental retardation and generalized or complex partial seizures are among the most frequent abnormalities reported along with involuntary head nodding, which starts in children aged 5-15 years. Few children are known to have recovered from nodding syndrome, although antiepileptic medications have been shown to help reduce seizures in some cases.

In 2005, a multinational team working in Tanzania documented impaired consciousness and other supportive signs of epileptic seizures and EEG-confirmed epileptic activity with head nodding (*Epilepsia* 2008;49:2008-15). And in 2010, the US-based Centers for Disease Control and Prevention (CDC) documented that head nodding in northern Uganda was a manifestation of seizures that cause brief lapses in muscle tone due to alterations in brain function.

COURTESY DR. SUDHIR BUNGA/CDC

Dr. Carlos Navarro-Colorado (left) from the US Centers for Disease Control and Prevention consults with South Sudanese families whose children are affected by the devastating disease known as nodding syndrome. Reports suggest a rise in the number of cases.

In a Jan. 27 report on a 2011 case-control study from two communities in South Sudan, CDC investigators found, based on physical and neurological examinations; clinical, family, and epidemiologic histories; and laboratory investigations, that the syndrome there is, in fact, the same as that observed

See **Nodding Syndrome** • *page 12*

INSIDE

WFN Looks at e-Learning, Telemedicine Options

BY MORRIS FREEDMAN, MD,
RIADH GOUIDER, MD,
TIM PATTERSON, BA
eLearning Task Force, WFN

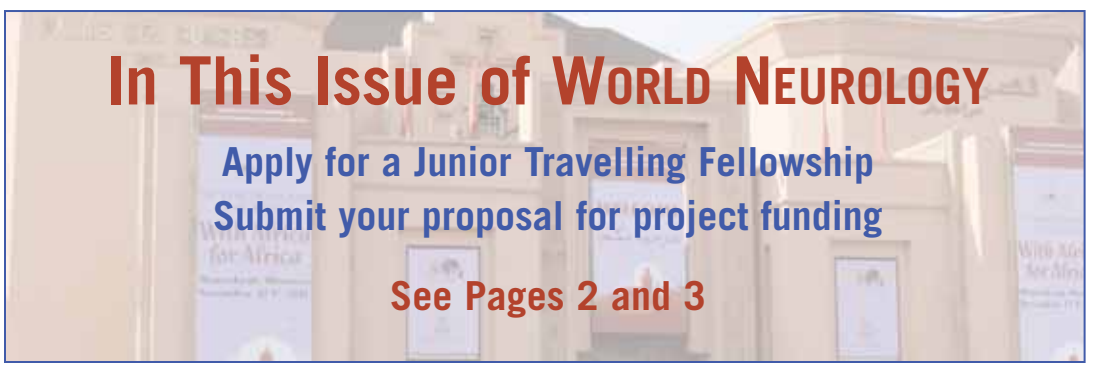
A survey by the World Federation of Neurology (WFN) to assess e-learning needs and capabilities for distance learning using electronic technologies found that there is significant support for online learning (e-learning) and telemedicine among member societies. However, although there is good access to online distance learning technology, cost and time constraints might be a hindrance to some societies going online.

The survey was organized by the eLearning Task Force of the WFN Education Committee. The task force is cochaired by Dr. Morris Freedman and Dr. Riadh Gouider, WFN delegates from Canada and Tunisia. Tim Patterson (Canada) serves as a consultant to the task force.

Fifty-four of the WFN's 113 member societies responded (response rate, 47.8%. The distribution of society responses by geographical region was: Asia, 18 societies; South America, 6; Europe, 18; North America, 4; and Africa, 8.

The response rates for developing countries was almost double that of developed countries at 56.5% and 29.5%, respectively. This observation requires further study, but it raises the possibility that representatives from developing countries responded at a higher rate because they perceive a greater need than those from developed countries for increased CME using distance learning technologies. In addition, WFN member societies support e-learning and telemedicine, with the survey showing that 62% of member societies strongly encourage online distance learning. Twenty-eight percent somewhat encouraged this. Other key findings are discussed on page 8.

See **e-Learning** • *page 8*



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EDITOR IN CHIEF'S COLUMN

MARK HALLETT, MD

Web Access Trumps Physical Barriers

My farewell editorial in 2007 as Editor-in-Chief of the *Journal of Clinical Neurophysiology* was titled, "Editing the journal in a time of revolution." In it, I described the transition, common around that time, from a paper-based manuscript submission process to an online submission system. Although that was not too long ago, it is almost difficult to remember working with those paper manuscripts. The revolution continues in many ways. People communicate by Facebook and Twitter as well as e-mail. Landline telephones are becoming unnecessary, replaced by cell phones. And the cell phone itself is gradually morphing into the "smart phone." Faxing is on the decline and will likely disappear. Soon, everyone will have their medical histories and whole genome recorded in a small chip embedded in their forearms. And so on.

The current issue of World Neurology has two reports dealing with continuing progress in the electronic revolution (pages 1 and 8). The e-Learning Task Force of the World Federation of Neurology's Education Committee has evaluated the desirability and capability of e-learning. There is considerable interest in this, especially from neurologists in developing countries. The advantages of e-learning programs are considerable. Materials can be developed and used repeatedly at times that are convenient to each person. Electronic resources are not yet universal, but their accessibility is certainly increasing rapidly, including in developing countries. Cost continues to be a barrier in some locations, but in the long run, online learning will likely be a more efficient, less costly form of education.

Neurologists in Canada and Tunisia have organized joint behavioral neurology rounds through teleconferencing. This is an excellent use for the methodology as well as telemedicine, allowing for patient cases to be presented remotely from selected centers and for participating neurologists to assess and discuss the cases and recommend medical care. There appear to be no barriers to neurologists interacting no matter where they are. This is a great area for the WFN to take the lead and to promote high-quality education and patient care worldwide. ■

It's WFN Dues Time

The World Federation of Neurology 2012 annual fees for your member society are now due. The subscription is unchanged at £3.00 per individual neurologist.

It is very important the WFN maintains an up-to-date list of all of our members. If there are any changes to your officers or members and/or their contact details, please advise us as soon as possible.

If you did not send a complete list of all of your members last year, please do so now. The list should include the following:

- Names,
- E-mail addresses, and
- Full mailing addresses.

The information is for the sole use of the WFN, such as mailing World Neurology, and will not be made available to any third party.

For further information, contact Keith Newton or Laura Druce at info@wfneurology.org. ■

2012 Junior Travelling Fellowships

This year, the World Federation of Neurology is again able to offer Junior Travelling Fellowships for young neurologists from low- or lower middle-income countries to attend approved international meetings.

Thirty fellowships will be awarded. Applicants should hold a post not above that of associate professor and be no older than 42 years of age.

Those interested in applying for a fellowship should send us:

- The name and dates of the meeting they wish to register for,
- A CV and bibliography,
- A letter of recommendation from the head of their department, and
- An estimate of expenses, to a maximum of £1,000.

If the applicant plans to present a paper or poster at the meeting, then an abstract should be included in the application materials.

Applications should be sent to:

- The World Federation of Neurology, Hill House, Heron Square, Richmond, Surrey, TW9 1EP United Kingdom; or
- Faxed to +44 208 439 9499; or
- E-mailed to info@wfneurology.

Applications must be received at the WFN office no later than **Friday, March 23, 2012**. The awards will be announced as soon as possible thereafter.

In past years, World Neurology has invited travelling fellows to write brief reports on their experiences and lessons learned at the meetings they attended. Among the highlights for most fellows have been the opportunities to attend presentations by renowned experts, to learn about current therapies and advances in neurology, and to meet neurologists from other countries. On page 6 of this issue, B.K. Bajaj of India reports on going to the Asia Pacific Stroke Conference. ■

World Neurology

World Neurology, an official publication of the World Federation of Neurology, provides reports from the leadership of the WFN, its member societies, neurologists around the globe, and news from the cutting edge of clinical neurology. Content for **World Neurology** is provided by the World Federation of Neurology and IMNG Medical Newswire.

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PRESIDENT'S COLUMN

A Call for 2012 Projects Proposals

VLADIMIR HACHINSKI, MD

Last year, for the first time in its 55-year history, the World Federation of Neurology invited proposals from its membership for educational or applied research projects in neurology and the applied neurosciences, as part of its activities as a registered charitable organization and its mission to "foster quality neurology and brain health worldwide."

I chaired the grants committee that reviewed the proposals, together with Charles Warlow (UK), Emre Murat (Turkey), and Jun Kimura (USA, Japan). We awarded funds for 10 projects (see box) based on the following criteria:

▶ **Relevance.** How does the project address the mission of the WFN?

▶ **Value.** What is the return for invested effort, funds, or time? Priority is given to low-cost, high-impact projects.

▶ **Viability.** Is this a limited-time project with a measurable outcome, or an initiative that will grow and become institutionalized? If the latter, who will assume responsibility after the WFN's initial involvement?

▶ **Synergy.** Is there synergy within the WFN; among committees, initiatives, and task forces; and with other organizations, outside partners, and governmental and nongovernmental organizations, funding agencies, and the like? Does the project have potential for publicity and fundraising?

▶ **Evaluation.** How will the outcome be measured?

I am pleased now to announce the 2012 competition. This year, the committee will be made up of leaders from the major brain organizations. They will serve as individuals, but we hope they will identify projects of mutual interest that they can recommend to their respective organizations for joint funding. Through this arrangement, we hope that we become familiar with what others are doing; that one or more organizations may choose to cofund a project; and, by having a greater number of potential sources of funding, it may be possible to carry out more substantial projects.

The 2012 committee members are: Peter Black (USA), World Federation of Neurosurgical Societies; Hugh Chugani (USA), International Child Neurology Association; William Carroll (Australia), Multiple Sclerosis Research Australia; Richard Hughes (UK), European Federation of Neurological Societies; Pierre Magistretti (Switzerland), International Brain Research Organization; Solomon Moshe (USA), International League Against Epilepsy; Bo Norrving (Sweden), World Stroke Organization, Bruce Sigsbee (USA), American Academy of Neurology; and Günther Dueschl (Germany), The Movement Disorder Society.

Where the Money Went in 2011

Project	Year 1	Year 2
Bringing EMG/NCV* to Zambia	$16,290	
Cognitive clinics worldwide	35,213	
Revision of ICD-10	50,000	$50,000
Stroke survey**	19,758	10,445
Pediatric neurology elect training	9,000	
Neurology training for non-neurologists	3,000	
Education grant for Asian neurology	12,755	12,755
Neurology training in Afghanistan	9,800	
Children with epilepsy	20,000	
Training and retraining child neurologists	15,000	15,000

*EMG = electromyography (equipment), NCV = nerve conduction velocity (testing equipment); **Jointly funded by the WFN, World Stroke Organization
Note: Dollar amounts are US dollars.

To apply for funding, submit a letter of intent and a brief CV to Rebecca Clarke (Rebecca.clarke@lhsc.on.ca) by March 1, 2012.

The letter should be organized under the heading, "Letter of Intent Application Form," with the subheadings: Title of project; Name of sponsoring group, names of project leader(s), and their affiliations; Description of project, including aims, methodology, timelines, and outcomes (1,000-word limit); and Budget.

The application timeline will be:

▶ **March 15,** letter of intent due,

▶ **March 31,** applicants notified of results,

▶ **May 15,** applications due,

▶ **June 15,** applicants learn final results,

▶ **July 1,** funding begins.

The growing burden of brain disorders and the global shrinking of resources pose new challenges that call for novel solutions. By broadening our approach and focusing our activities, we can have an impact greater than the sum of our individual efforts. Together we can do more. ■

WFN Updates and Enhances Its Web Site

The World Federation of Neurology launched its revised web site, www.wfneurology.org, during the World Neurology Congress in November 2011. The new look is clean and user friendly, with rotating photographs from past congresses, and an announcement for the next WCN, in Vienna in 2013.

The new-look homepage has two features: WFN News, for Federation-related matters, and Neurology News, which carries international news that is relevant to neurology. The content for these features will change regularly to keep the homepage current and interesting. Members of the Web Site Committee hope that this will encourage neurologists to visit the site frequently for routine updates on issues that interest them. (My web committee colleagues are Chiu K. Man, webmaster; Donna Bergen, global networks; Wolfgang Grisold and Steven Sergay, education; Walter Struhal, social networks and news; Keith Newton and Laura Druce, executive office.)

The primary purpose of the web site is to inform neurologists of the ongoing work of the WFN, to offer educational programs, and to provide an interactive space, both open and password-protected as appropriate, for officers, committee members, and member societies to carry out WFN activities. The main sections are: About Us, Education, Global Networks, Publications, Member Societies, and Meetings and Congresses. We have also added social networking capabilities in recognition of the importance of attracting young neurologists to WFN. The content of each of section is as follows:

▶ **About Us.** This section provides demographic information about the WFN, lists the Federation's officers, committees, and describes ongoing projects such as the African, Asian, and Latin American Initiatives.

▶ **Education.** The Education Committee's activities and structures are highlighted in this section, which features information for practicing neurologists, neurologists in training, medical students, and nonneurologists who provide neurological care. The section includes or will include downloadable WFN education programs; CME accreditation and meeting endorsement; WFN quality standards; and information about opportunities for neurologists, including the WFN Junior Travelling Fellowships and education grants.

▶ **Global Networks.** Members of the WFN's World Brain Alliance – the European Brain Council, International Brain Research Organization, International Child Neurology Association, International League Against Epilepsy, World Federation of NeuroRehabilitation, World Federation of Neurosurgical Societies, World Psychiatric Association, and the World Stroke Organization – all have links to the new web site. Through the World Health Organization link (found under the tab, Other Neuroscience Organisations and Agencies), users will have access to the WHO's online publications in neurology and other areas of medicine and public health. Links to international neurology subspecialty organizations are found under the Global Neurology Subspecialty Liaisons tab. Their meetings and educational conferences will be featured on the WFN's webpages. Each of the WFN's Applied Research Groups has a webpage for posting its membership, activities, and plans, and to use for easy communication within each group.

JEROME ENGEL. JR., MD, PHD

Dr. Engel is the Editor-in-Chief of the WFN web site. He is director of the UCLA Seizure Disorder Center, David Geffen School of Medicine, Los Angeles, Calif., USA.

▶ **Publications.** These pages include full content of past and current issues of WORLD NEUROLOGY, a link to *Journal of the Neurological Sciences* web site, and full content of *Seminars in Clinical Neurology*. The *Seminars* texts, which can be downloaded free of charge, are for neurologists who are practicing in countries with limited resources, tropical conditions, and/or sociopolitical concerns that are not generally addressed in standard textbooks.

▶ **Member Societies.** This section presents the contact information for all of the WFN member societies and links to their web sites. Member societies that do not have web sites can create a site in this space.

▶ **Meetings and Congresses.** These pages will provide information and links for future meetings and congresses to be held by WFN and its member societies. They will also carry content from previous World Congresses, and a calendar of other events of interest to neurologists.

Social Networks

As a novel initiative, the WFN will regularly broadcast news online on Twitter (twitter.com/wfneurology) and Facebook (www.facebook.com/wfneurology). The target group for these services are mainly Generation Y neurologists, the "digital natives." These channels will provide information on all news items published in the news section of the WFN web site and will remind young neurologists about WFN initiatives such as the Junior Travelling Fellowships and education grants. In addition, the WFN aims to use the unique interactive features of these services though its presence on the social networks.

Comments regarding the web site can be sent to the Web Site Committee at info@wfneurology.org. ■

NEUROLOGICAL HISTORY

Piecing Together Electricity's Role in Nerve Function

As far back as the second century AD, the Alexandrian physician Galen suggested that animal spirits drove nerve function, and that view – that the animal spirits were a volatile substance that flowed through hollow nerves and caused muscles to move – prevailed until the late 18th century. At that time, Benjamin Franklin's discoveries and theories about electricity became known and scientists began to explore whether electricity might be the key to explaining nerve function.

BY PETER J. KOEHLER, MD, PHD

Dr. Koehler is a neurologist in the department of neurology at the Atrium Medical Centre, Heerlen, the Netherlands. Visit his web site at www.neurohistory.nl.

It had been known for a long time that several kinds of fish, such as catfish and rays, could cause numbness. In 1714, the influential French scientist René-Antoine Ferchault de Réaumur explained the numbness as the "effects of a very lively percussion, operated by a curious apparatus of muscles placed under the back of the animal." There was one fish, found in creeks of Dutch colonies in the north of South America, Surinam, and surroundings that had a very strong numbing effect. Colonists who had experienced the effect of the Leyden jar, (an early capacitor discovered by Pieter van Musschenbroek in 1745) realized that the shocking, numbing effect of the "tremble eel" felt similar that of the jar and that the numbness from the eel might have been caused by electricity.

The Leyden professor of natural history Jan Nicolas Sébastien Allamand (1713-87; of Swiss origin) published his correspondence with the colonists in Essequibo, a Dutch colony in what is now Guyana, in the *Proceedings of the Dutch Society of Sciences* (of Haarlem) in 1756:

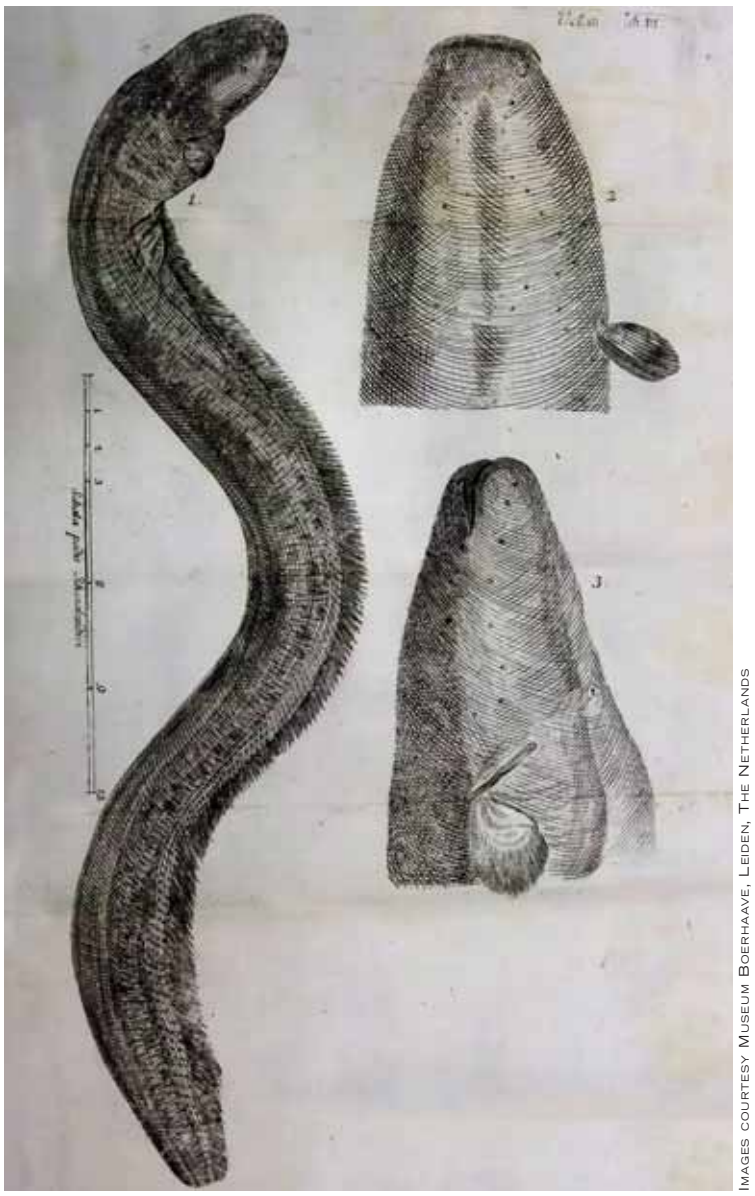
Almost two years have past since I received a fish from Mr. [van] 's Gravesande, general director of the Volksplanting of Issequebo; a fish that the inhabitants of the place consider a kind a eel; although basically it is a fish, called Gymnoti.

Allamand's correspondent, Laurens Storm van 's Gravesande (1704-1775) was administrator and secretary of the Dutch West-Indies Company and informed Allamand about his observations:

The experiment was done with an eel called a tremble fish, and what I had written to you about it in my previous letter is true. It produces the same effect as the electricity that I felt with you, while holding [my] hand in a bottle [Leyden jar] that was connected to an electrified tube by an iron wire.

The effect of the fish is much stronger than that of rays: If one touches the fish, it does not give off fire or sparks, similar to the apparatus for electricity. But for everything else it is the same; yes, even much stronger, because if the fish is big and lively, the shock produced by the animal will throw anyone who touches it to the ground, without exception, and one feels it throughout the whole body.

At the time, electricity was gradually introduced for treatment of various afflictions, as Allamand had reported in the *Proceedings* several years previously. For example, Abbé Nollet in cooperation with Sauveur F. Morand and Joseph Marie F. de la Sône at the Charité Hôpital in Paris tried to get body parts that had been affected by paralysis to move on application of an electric pulse from the Leyden jar, but were not successful (1746). A year later, the Swiss professor of experimental philosophy and mathematics, Jean Jallabert, was able to produce contractions in the arm of person with right hemiplegia and shortly thereafter of his own, healthy, arm muscles.



IMAGES COURTESY MUSEUM BOERHAAVE, LEIDEN, THE NETHERLANDS

The tremble eel that Linnaeus (1766) named *Gymnotus electricus* is known today as *Electrophorus electricus*.

The Leyden jar, discovered in1745, was of fundamental importance in the medical application of electricity.

Allamand wrote that clinical trials with electricity usually did not produce great medical benefits. Nevertheless, he found an exception with a young girl suffering from affectum paralytico-spasmodicum, who, after an intense terror, displayed hemiparesis, fits, and aphasia. Following electrical treatments, her speech improved, but she was not as fluent as she had been before her illness. She showed more recovery of her other impaired functions (*Verhandelingen Hollandsche Maatschappye der Weetenschappen Haarlem* 1754;1:485-497).

COLONISTS REALIZED THE EFFECTS OF THE TREMBLE EEL WERE SIMILAR TO THOSE OF THE LEYDEN JAR AND MIGHT BE CAUSED BY ELECTRICITY.

In another letter by a certain Van der Lott (1762) we read the following passage:

[A 9-year-old boy] suffered from obstruction of the nerves in such a way that his arms and legs were crooked. Each day, this gentleman threw the boy in a tub of water with a large Conger-eel of the black variety, which shocked the boy so powerfully that he crept out on all fours.

It was not easy to transport a live eel to Europe, although several dead eels had been taken to European cities, including Amsterdam, where specimens were collected and drawn for books. In the 1770s at the Royal Society in London, scientists proved that the eels did indeed discharge an electrical current after they drew a spark at the time of a living eel's discharge, a fundamental criterion at the time. The finding endorsed the Italian scientist Luigi Galvani's concept of animal electricity based on his findings that the legs of dead frogs would move when touched by a spark of electricity. However, due to the opposition of Allesandro Volta, an Italian physicist who was also studying electricity, and the lack of refined measuring methods, it was several decades before the nerve action potential was measured by the German physiologist Emil du Bois-Reymond in 1843.

It is apparent that during the century that elapsed between colonists' first realization that the eel produced electricity, a great number of scientists from various countries made scientific contributions that finally led to the observation of a nerve action potential.

Further reading

Koehler PJ, Finger S, Piccolino M. The eels of South America: Mid-eighteenth century Dutch contributions to the theory of animal electricity. *Journal of the History of Biology* 2009;42:235-251. ■

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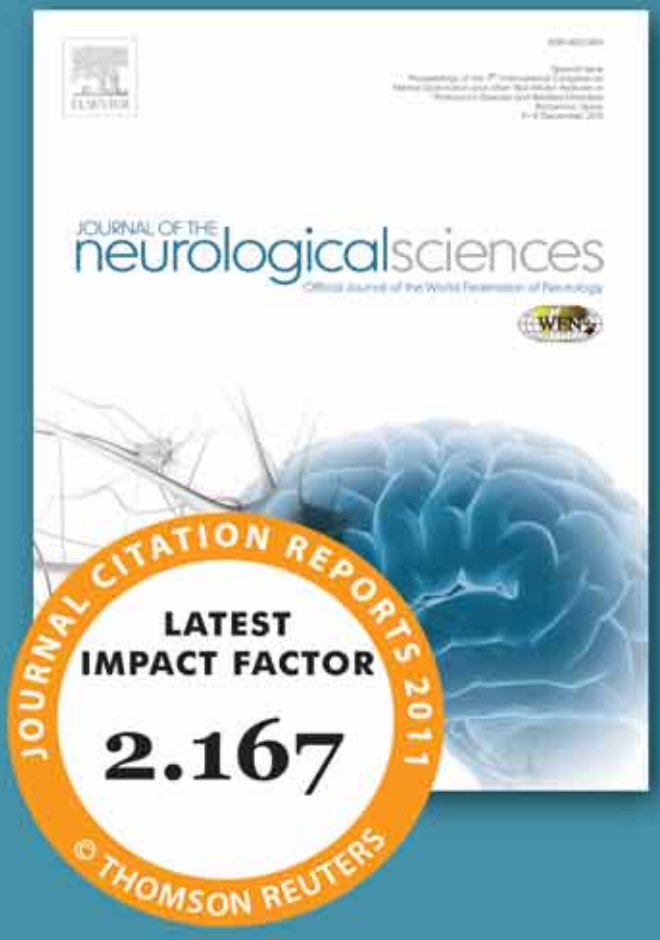

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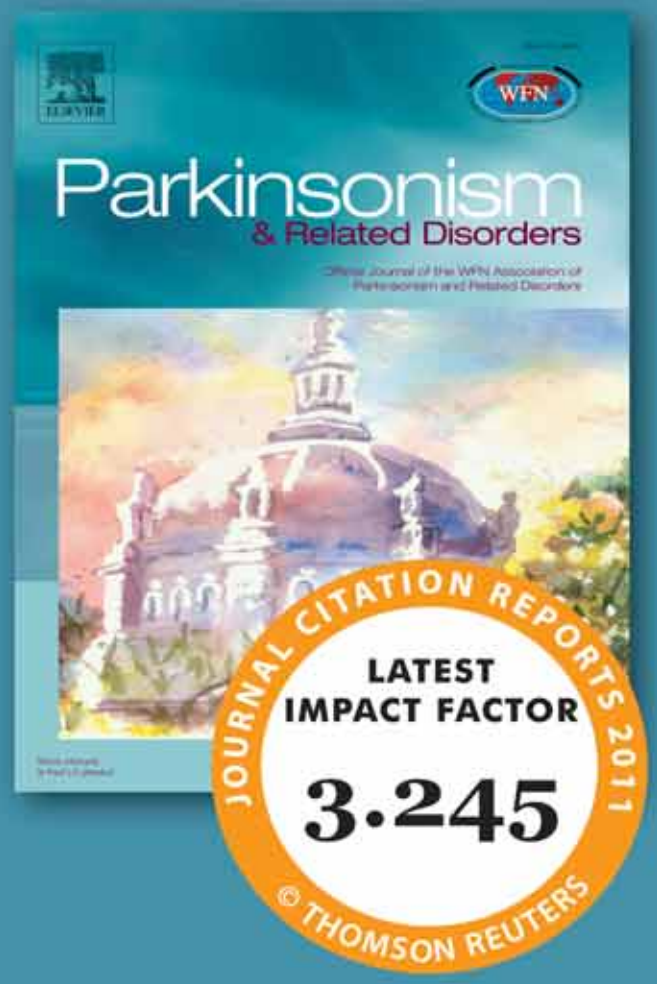

ELSEVIER

WFN JUNIOR TRAVELLING FELLOW

New Experiences, Diverse Perspectives at Stroke Conference

BY B.K. BAJAJ, MBBS, MD, DM

Dr. Bajaj is associate professor of neurology in the Postgraduate Institute of Medical Education & Research at the Dr. Ram Manohar Lohia Hospital, New Delhi, India.

Conferences and workshops are a means of updating one's knowledge, learning new skills, and connecting with other clinicians, scholars, and researchers. My visit to Colombo, Sri Lanka, in November 2011 to attend the Asia Pacific Stroke Conference as a World Federation of Neurology (WFN) Junior Travelling Fellow was an academically enriching experience that exposed me to the diverse perspectives of my fellow neurologists from different parts of the world.

I attended a preconference workshop on transcranial Doppler ultrasound. It was truly a hands-on experience for the participants. We discussed the basic techniques of the test and the methods for obtaining an accurate, functional image of the intracranial arteries. The speakers and instructors were all experts in their fields and superb teachers. The enthusiasm of Dr. Vijay Sharma from National University Hospital, Singapore, was particularly impressive.

There were multiple sessions on the management of acute stroke as well as the rehabilitation of stroke patients. There is little opportunity for exchange of information between physicians from developed and developing countries, but at this conference, we were exposed to the different viewpoints of international experts for the management of stroke. In certain areas, the outlook and the practices of experts from the Eastern and Southeast Asian countries seemed notably different from their colleagues from more developed and technologically advanced countries. A speaker from Japan highlighted the low dose of r-tPA at 0.6 mg/kg body weight as effective and safe in Japanese patients with acute stroke, compared with the recommended 0.9 mg/kg body weight cited in the NINDS-NIH protocol. The attendees vigorously deliberated the study findings, since the drug was given only to those patients in whom there were no early CT signs of ischemia. There was also heated discussion after a presentation by Peter Sandercock and Alan Barber about the use of ABCD scoring in patients with transient ischemic attack. On a personal note, I found Dr. N.V. Ramani's analysis of the evidence-based management of malignant middle cerebral artery infarct highly informative.

The concept of separate stroke units is not new to places such as the United States and most European countries. In contrast, many developing Asian countries such as India do not have the most basic neurology facilities and struggle to provide neurological care. The noncommunicable disease burden in such countries is significant, and financing to provide the basic infrastructures for managing conditions such as stroke should be considered at the global level. Many of the tertiary-care teaching hospitals in developing countries are not equipped to handle stroke patients. The obstacles to delivering the best possible stroke treatment in many Asian countries are formidable.

In addition, there are few rehabilitation experts in developing countries. This absence of appropriate rehabilitative measures leaves many patients with a suboptimal level of functional ability, which adversely affects the quality of life of many stroke patients.

But there are ways in which developing countries can meet the challenges of being underresourced. Dr. Tissa Wijeratne from Australia suggested that a hospital could start a special stroke care facility by designating a few beds for stroke patients only and by drawing on the expertise of different medics and paramedics without having the sophisticated infrastructure and paraphernalia in place first. However, some attendees disagreed with his suggestion. They questioned the feasibility of such an arrangement and whether it would ever be able to replicate the results seen in better equipped stroke units.

It was clear that we need to look into new ways and means of delivering advanced neurological services to underdeveloped countries. This can happen only through cooperation and exchange between neurologists from developed and developing countries, and the WFN is doing much to foster this exchange in its bid to improve neurological care and ensure expertise in neurology in the less developed regions of the world. I am thankful to the WFN for awarding me a travel grant to attend APSC 2011 and in helping me see things from a different perspective. ■

Neurosciences Training at Sudan Meeting

BY OSHEIK ABU'ASHA SEIDI, MD

The Sudanese Society for Neurosciences will hold a 2-day training course in the clinical neurosciences during Feb. 22-23, in Khartoum, Sudan, ahead of its 4th International SSNS Conference from Feb. 25-26.

The purpose of the Fourth Clinical Neurosciences Course will be to address the clinical and practical challenges in delivering neurological care in Sudan and to update participants on therapies and the diagnosis and management of neurological diseases. It will be held at the Education, Examinations and Training Centre at Soba University Hospital, the teaching hospital for the University of Khartoum's faculty of medicine.

Among the topics covered during the sessions are neuro-anatomy, history taking, the neurological exam, neuroradiology, neurophysiology, neurology in women, neuro-rehabilitation, pediatric neurology, and neurological investigations. There will also be sessions on stroke, epilepsy, peripheral neuropathies, movement disorders, CNS infections, dementia, neuron disorders, headache, and neurosurgery.

At the end of the second day, there will be a clinical stations session. Experienced neurologists will be present at 18 stations to present cases and field participants' questions. The 10-minute demonstrations will include three stations each on pediatric neurology and clinical neurophysiology, as well as a "challenging case" competition and a range of other clinical cases, from hemiplegia, to movement disorders and ataxia, and others.

The course was planned by the local organizing committee, Osheik A. Seidi, Mohamed Nagib, Eetidal Abu Albashr, Sarah Misbah El Sadig, Isam Izzeldin, Husam Abu Obeida, Muaz Abdelatif, Mohamed Khalafalla Saeed; and its supporting team, Mutakil Imam, Assim Mamoun, and Shad Hamid.

The international faculty is Hadi Manji, Mathew Pitt (London, UK), Victor Patterson (Belfast, UK), Ashraf Ghobashy (Cairo, Egypt), Abdelaziz Mirghani (Jeddah, Saudi Arabia), John Nixon (Preston, UK), and Khalid Awad (Kuwait).

For more information, e-mail: info@medicaluofk.net. To reserve a space in the course, e-mail Muna El Bahi at munaelbahi4@yahoo.co.uk, or phone +249-915-566-1412. Placement in the course is done on a first come, first serve basis up to 100 participants. ■

Dr. Seidi *is registrar and clinical lecturer in the department of neurology, Sunderland Royal Hospital, UK, and consultant to the faculty of medicine and Soba University Hospital, University of Khartoum, Sudan.*

Calendar of International Events

2012

XIII Pan American Congress of Neurology
March 4-8
La Paz, Bolivia
www2.kenes.com/PCN2012

64th Annual Meeting of the American Academy of Neurology
Apr. 21-28
New Orleans, USA
www.aan.com

7th World Congress for NeuroRehabilitation
May 16-19
Melbourne, Australia
www.dcconferences.com.au/wcnr2012/Home

13th Asian Oceanian Congress of Neurology
June 4-8
Melbourne, Australia
www.aocn2012.com

22nd Meeting of the European Neurological Society
June 9-12
Prague, Czech Republic
www.congrex.ch/ens2012

16th Congress of the European Federation of Neurological Societies
Sep. 8-11
Stockholm, Sweden
www.efns.org/efns2012

10th European Congress on Epileptology
Sep. 30-Oct. 4
London, UK
www.epilepsylondon2012.org

8th World Stroke Congress
Oct. 10-13
Brasilia, Brazil
www2.kenes.com/stroke/Pages/Home.aspx

2013

XXI World Congress of Neurology
Sep. 21-26
Vienna, Austria
www2.kenes.com/wcn/Pages/Home.aspx

WORLD SLEEP DAY, MARCH 16, 2012

Annual Event Highlights Ventilatory Disturbances

This year's World Sleep Day (WSD) will take place on Friday, March 16 under the slogan, "Breathe easily, sleep well," highlighting the focus on sleep-related ventilatory disturbances that are so common in our modern society.

WSD is an annual event, intended to be a celebration of sleep and a call to action on important issues related to sleep. It is organized by the World Sleep Day Committee of the World Association of Sleep Medicine (WASM) and aims to reduce the burden of sleep problems on society through better prevention and management of sleep disorders.

BY ANTONIO CULEBRAS, MD

Dr. Culebras is professor of neurology at State University of New York, Upstate Medical University, New York, USA.

The event is cochaired by Liborio Parrino, MD, assistant professor of neurology at Parma University, Italy, and me, with support from WASM's executive director, Allan O'Bryan.

A Platform for Societies

WSD events take place primarily online at www.worldsleepday.org, featuring educational videos, historical videos, education materials, and public service announcements.

World Sleep Day offers a platform for sleep societies, enterprises, and interested practitioners to raise awareness about sleep, its disturbances, and the effects of those disturbances at the local level. Professionals in more than 70 countries have taken advantage of this opportunity on an annual basis.

The first WSD was held in March 2008, under the slogan, "Sleep well, live fully awake." Each successive year since then has operated under a slogan that indicates the focus for that year: 2009, "Drive alert, arrive safe;" 2010, "Sleep well, stay healthy;" and 2011, "Sleep well, grow healthy" with emphasis in children's sleep.

With the focus this year on sleep-related ventilatory disturbances, WSD has adopted the following Declaration of Principles:

- Whereas, sleepiness and sleeplessness constitute a global epidemic that threatens health and quality of life,
- Whereas, much can be done to prevent and treat sleepiness and sleeplessness,
- Whereas, professional and public awareness are the first steps to action,
- We hereby declare that the disorders of sleep are preventable and treatable medical conditions in every country of the world.

A Basic Need

Sleep is a basic human need – it is a crucial component of survival, much like breathing, eating a healthy diet, or getting enough exercise. World Sleep Day has been designed to raise awareness of sleep as a human privilege that is often compromised by the habits of modern life.

Sleep alterations constitute a global epidemic affecting up to 45% of the world's population. Insomnia, obstructive sleep apnea, restless legs syndrome, and sleep deprivation significantly impact physical, mental and emotional health, in addition to affecting work performance and personal relationships. In adults, lack of quality sleep as a result of sleep apnea and other sleep disturbances can lead to health problems including systemic hypertension while increasing the risk of diabetes, heart disease, and stroke. Failure to obtain quality sleep may lead to poor alertness, lack of attention, reduced concentration, decreased workplace and academic productivity, and an increase the risk of motor vehicle accidents.

The first step toward restoring good quality sleep is to maintain adequate sleep hygiene. Violation of the 10 Commandments of Sleep Hygiene (see box) causes poor quality of nocturnal sleep, short duration of sleep, fragmentation of sleep, and serious sleep deprivation. Obstructive sleep apnea (OSA) affects about 4% of adult men and 2% of women. If sleep apnea is not properly managed, it can have a significant impact on a person's health and well-being.

Sleep disturbances are not limited to adults. Poor sleep affects about 25% of the world's children. Lack of quality sleep in children can lead to:

- Obesity,
- Accidental injury,
- Moodiness and emotional problems,
- Aggressiveness and impulsivity,
- Irritability and frustration,
- A change in activity levels (appearing "hyper" or "low energy"), and
- Decreased memory, attention, learning and reasoning, which can impact school function.

To help improve children's sleep hygiene and overall wellness, the WASM has created the 10 Commandments of Healthy Sleep for Children (see box).

Working to Raise Awareness

Participants in WSD include sleep organizations, enterprises, and interested professionals. All of these groups can help raise awareness of sleep disorders by carrying out appropriate activities during WSD that enhance public education on sleep disorders and its treatments.

A number of possibilities may be considered, based on local capabilities and available resources. These include:

- Organization of a public event to create excitement and generate interest in WSD. It may require a significant investment in terms of time and budget, but creates an impact and signifies the importance of public awareness of sleep disorders. Journalists may be invited to the event to obtain immediate access to case studies and take-home messages.

MOST SLEEP PROBLEMS CAN BE MANAGED BY CHANGING BEHAVIORS AROUND SLEEP, WITH MEDICAL OR COGNITIVE BEHAVIORAL THERAPY.

- The event should be primarily themed around the impact of the current year's slogan, "Breathe easily, sleep well." However, you can draw on previous years' slogans. Several examples of public events have been posted on the web site www.worldsleepday.org.
- Distributing patient literature such as booklets, leaflets, and newsletters. Patient information and useful links are also on the web site.
- Set up a driving simulator in a well-populated area such as near a shopping centre to raise awareness of the perils of driving under the influence of sleepiness.

It is often effective to invite a well-known local celebrity to draw attention to the event and provide the media with photo opportunities of the celebrity trying out the driving simulator. Allow the public to participate in activities as well and prepare leaflets or simple sleep questionnaires that highlight WSD and the dangers of falling asleep behind the wheel.

Research, Diagnosis, and Treatment

In summary, more research is needed before we can fully understand sleep and the causes of sleep disorders; and greater emphasis should be placed on the diagnosis and treatment of sleep disorders.

Moreover, most sleep problems can be managed by changing behaviors around sleep, with appropriate medical therapy or cognitive behavioral therapy. Patients suffering from sleep complaints, or who suffer from excessive daytime sleepiness should consult with their physician. ■

The 10 Commandments of Sleep Hygiene ...

1. Fix a time for going to sleep and waking up.
2. If you are in the habit of taking naps, do not exceed 45 minutes of daytime sleep.
3. Avoid excessive alcohol ingestion 2-4 hours before bedtime and do not smoke.
4. Avoid caffeine 6-8 hours before bedtime. This includes coffee, tea, and many sodas, as well as chocolate.
5. Avoid heavy, spicy, or sugary foods 4 hours before bedtime. A light snack before bed is acceptable.
6. Exercise regularly, but not immediately before bed.
7. Use comfortable bedding.
8. Find a comfortable temperature setting for sleeping and keep the room well ventilated.
9. Block out all distracting noise and eliminate as much light as possible.
10. Reserve the bed for sleep and sex. Don't use the bed as an office, workroom, or recreation room.

Visit www.worldsleepday.org, for translations in different languages.

... and Healthy Sleep for Children

1. Make sure your child gets enough sleep by setting an age-appropriate bedtime and wake time.
2. Set consistent bedtime and wake-up times on both weekdays and weekends.
3. Establish a consistent bedtime routine that includes "quiet time."
4. Encourage your child to fall asleep independently.
5. Avoid bright light at bedtime and during the night (including light from television or computer screens) and increase light exposure in the morning.
6. Keep all electronics, including televisions, computers, and cell phones, out of the bedroom and limit use of electronics before bedtime.
7. Maintain a regular daily schedule, including consistent mealtimes.
8. Have an age-appropriate nap schedule.
9. Ensure plenty of exercise and time spent outside during the day.
10. Eliminate foods and beverages containing caffeine.

Visit www.worldsleepday.org, for translations in different languages.

Good Access, but Costs a Barrier

e-Learning • *from page 1*

Internet access. Most WFN member societies have Internet access (79.6%), a web site (60%), online resources (62%), telemedicine capabilities (55.1%), and people familiar with information technology (82%), but only (18%) have a portal. Fifty-four percent of societies have journals, but only 63% of those journals are online.

About 50% of societies with telemedicine capability have Internet Protocol (IP) connectivity, and 50% have access to Integrated Services Digital Network (ISDN). IP connectivity involves a monthly fee and is cheaper than ISDN connectivity. Although we do not have data on earlier connectivity, it is likely that IP connectivity is increasing.

Cost was reported as a barrier to accessing online distance learning by 44.9% of respondents. Time constraints were considered a barrier by 40.8%. These constraints could stall access to online distance learning technology, even though it is readily available.

Teaching programs. A minority of WFN countries (28.6%) have an e-learning teaching program, but 63.3% of respondents use some form of e-learning in postgraduate and continuing medical education (CME) courses. In addition, 53.1% of respondents have participated in a telemedicine event.

These data suggest there are fewer e-learning teaching programs than expected, based on potential to access this resource. This may reflect a need for leaders who can initiate e-learning and telemedicine programs and for experts who can create content for the programs.

MORRIS FREEDMAN, MD

RIADH GOUIDER, MD

TIM PATTERSON, BA

Need for growth. Most respondents (79.6%) find e-learning useful for acquiring clinical skills. This ranked about the same as textbooks (77.68%) and was higher than hospital rotations (63.3%). About half of the respondents (55.1%) strongly agreed that distance learning is useful, and 32.7% somewhat agreed with that, suggesting a need for growth in development of e-learning and telemedicine.

Prioritizing content areas. The respondents indicated that the following fields were most in need of online distance learning courses: movement disorders (79.6%), epilepsy (75.5%), and stroke and vascular neurology (73.5%). This suggests that the initial foci on WFN e-learning and telemedicine programs should include these areas. However, it will be important to include other fields even if the demand is smaller.

CME responsibility. Forty-nine percent of respondents reported that CME was compulsory for maintaining licensure or for other reasons, and most of those respondents (63.3%) said they can obtain CME credits through e-learning. About a third (30.6%) stated that government (national, state, or provincial) was responsible for overseeing CME. From that group, 89.7% stated that responsibility was with the national government. Just over a quarter of respondents (26.5%) said that national neurological societies were responsible for overseeing CME.

For overseeing education in general, 47.9% stated that responsibility was with the government; for 85% of cases, it was at the national government level.

CME is clearly important for WFN society members, and working with national governments and neurological societies, will be a key factor in developing e-learning and telemedicine programs.

Conclusions and Recommendations

- ▶ Countries across the world are very interested in CME using electronic distance learning technologies.
- ▶ Interest for increasing CME opportunities using e-learning and telemedicine may be higher in developing countries than in developed countries.
- ▶ The infrastructure for developing e-learning and telemedicine programs exists in many countries, but cost and time constraints are potential barriers. The WFN could serve as a resource for enabling countries to develop and enhance e-learning and telemedicine capabilities.
- ▶ There may be a need for leaders who can initiate e-learning and telemedicine programs and experts who can create program content. The WFN could provide mentoring in this regard.
- ▶ Areas of focus for e-learning and telemedicine should include movement disorders, epilepsy, and stroke. It is recommended that the WFN collaborate with professional groups that are already active in these areas to further develop distance learning programs to meet the needs of neurologists worldwide.
- ▶ National governments are actively involved in overseeing CME and education in general in a sizeable number of countries surveyed. It will be important for the WFN to work with national governments and neurological societies in developing international e-learning and telemedicine programs. ■

Dr. Freedman *is in the department of medicine, division of neurology, Baycrest, Mt. Sinai Hospital, and University of Toronto; and at the Rotman Research Institute, Baycrest, Toronto, Canada.* Dr. Goudier *is in the department of neurology, Razi Hospital, Tunis, Tunisia.* Mr. Patterson *is in the department of telehealth, Baycrest; vice-chair of Canada International Scientific Exchange Program; adjunct professor at Al Quds University, Abu Deis, West Bank, and York University, Toronto; and telehealth consultant to Jordan University of Science and Technology, Irbid.*

Canada, Tunisia Link Up for Long Distance Education

BY TIM PATTERSON, BA, RIADH GOUIDER, MD, MORRIS FREEDMAN, MD

The first telecast of the Canada-Tunisia Telehealth program was held in late May 2011 – 2 weeks into the Arab Spring Uprising – as part of the weekly City-Wide Behavioural Neurology Rounds, sponsored by University of Toronto's division of neurology, and cochaired by Dr. Morris Freedman and Dr. Sandra Black.

The program was initiated by the e-Learning Task Force of the World Federation of Neurology's (WFN's) Education Committee. It is cochaired by WFN delegates Dr. Riadh Gouider (Tunisia) and Dr. Morris Freedman (Canada), and I am their e-health and production consultant.

Two presenting sites, Razi Hospital in La Manouba, Tunisia, and Baycrest, a Toronto, Canada-based institute that specializes in age-related care and research, were featured in the telecast, which was titled Tunisia-Canada Frontotemporal Dementia Case Conference. After each presentation, Dr. Tiffany Chow, Dr. Nasri Amira, Dr. Mouna Ben Djebara, Dr. Gargouri Amina, Dr. Hizem Yosr, Dr. Gouider, Dr. Black, and Dr. Freedman were discussants for the case. Later, the discussions opened to participants from 14 other Canadian sites.

This successful experience, based on the positive feedback from the participants, encouraged us to schedule other rounds.

Courtesy Benny Kierdal

Canadian participants gather to view case presentations during the first City-Wide Behavioural Neurology Rounds.

From a programming point of view, the Tunisian round was based on two international neurology series initiated in 2005 and 2009. Each series involves a program scripting process, production techniques, and a minimum of two videoconferencing bridges to accomplish the telecast. Each site has a videoconferencing codec with connectivity either in the form of IP or ISDN that connects to the bridges, allowing for synchronous dialogue among sites.

The first international behavioral neurology round was hosted at Baycrest in 2005 under the auspices of the Peter A. Silverman Global eHealth Program and the Canada International Scientific Exchange Program (CISEPO), with sponsorship from the division of neurology, University of Toronto. The rounds have recently also been placed under the auspices of the Canadian Neurological Sciences Federation. American, Argentinian, Brazilian, Canadian, Chilean, Cuban, Israeli, Jordanian, Palestinian, Russian, South African, Spanish, and Swiss (WHO) hospitals have participated.

The audiences and presentations are multidisciplinary and include neurologists, psychiatrists, geriatricians, family physicians, nurses, social workers, occupational therapists, and psychologists, as well trainees in various health care disciplines.

Each international round lasts 75 minutes. Content, usually in the form of case presentations, originates from any of the participating sites. Past topics have included "Corticobasal Degeneration: Beyond the Alien Limb" (led by Dr. Alexander Pantelyat and Dr. Murray Grossman of the University of Pennsylvania, Philadelphia) and "Black and White Spots and Blotches: What Do They Mean on Brain MRI in Aging and Dementia" (Dr. Black).

The participants evaluate the telecasts, which are accredited under the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada.

Neurology residents are the target audience for the second series, which was started in 2009, also under the auspices of the Peter A. Silverman Global eHealth Program and CISEPO. The Neurology International Residents Videoconferencing Exchange is hosted by St. Michael's Hospital in Toronto. The presenting sites rotate among Brazil, Canada, Jordan, and Russia, where neurology residents present their cases and their fellow residents discuss them. Topics have included "Cerebral Arterial Dissection" (presented by Dr. Anna Smirnova, St. Petersburg State Pavlov Medical University, Russia) and "Juvenile Myasthenia Gravis" (Dr. Camila Exposto, Fundacão do ABC, São Paulo, Brazil).

A rewarding outcome of the telecasts is that participating countries come together using health care as a common language and exchange knowledge in a way that is beneficial to their respective societies. ■

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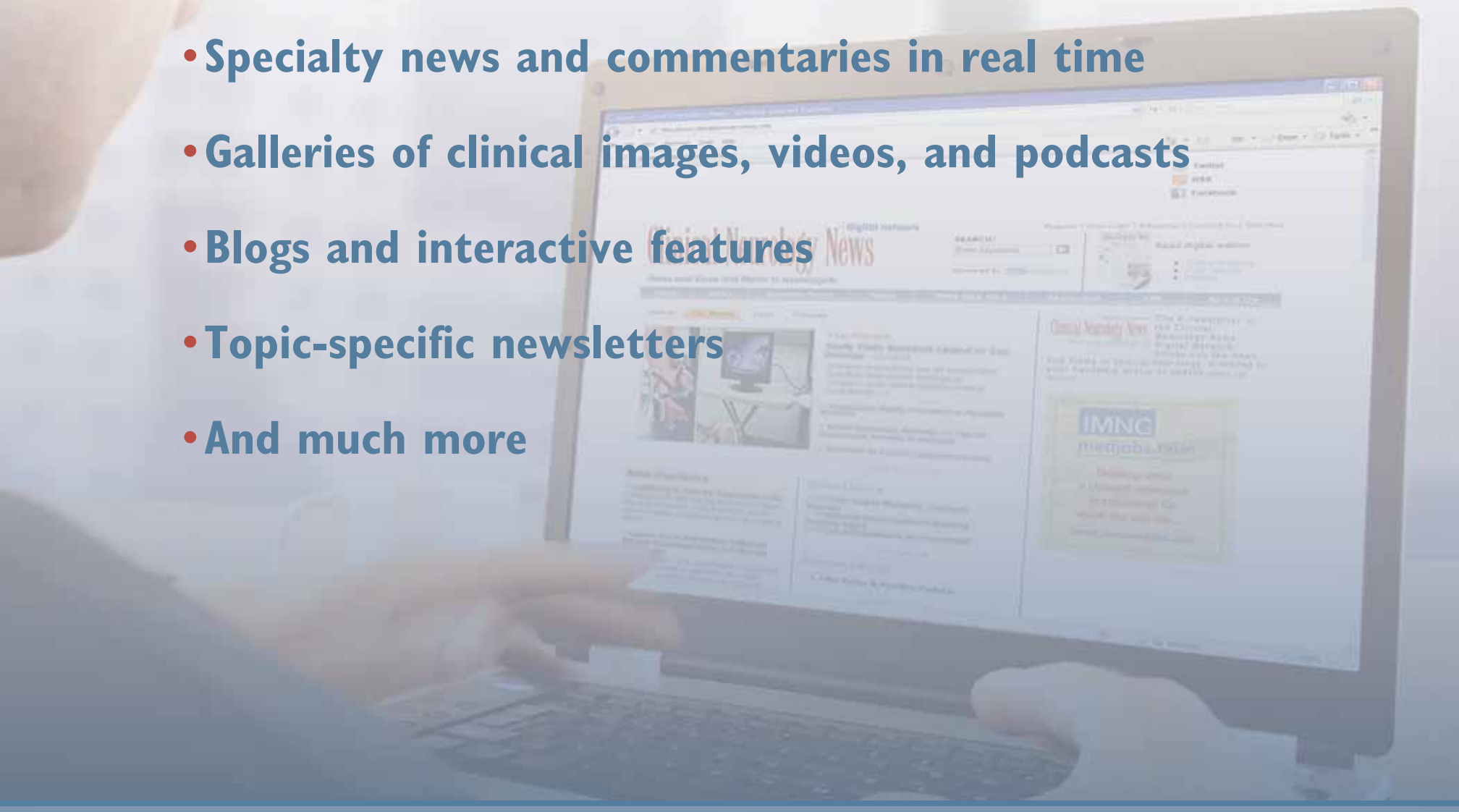

www.clinicalneurologynews.com

New Guideline for Comorbid Epilepsy, HIV Care

BY GRETCHEN L. BIRBECK, MD, MPH, DTMH.

An evidence-based guideline that addresses the potential risk of drug interactions for people with comorbid HIV and epilepsy was released in early January.[1,2] The guideline was developed by a joint committee of the American Academy of Neurology and the World Health Organization through the International League Against Epilepsy and was endorsed by the American Epilepsy Society. It promises to highlight a problem that can likely be ameliorated in developing regions through better communications between specialist physicians and increased patient awareness.

Seizures requiring treatment occur in about 11% of people with HIV; other conditions that may warrant treatment with an antiepileptic drug (AED), such as peripheral neuropathies, are also very common. But the potential pharmacokinetic interactions between AEDs and antiretroviral agents (ARVs) are complex and varied.

Enzyme-inducing AEDs (EI-AEDs; phenobarbital, carbamazepine, and phenytoin) are especially problematic because they may cause more rapid metabolism of protease inhibitors and/or nonnucleotide reverse transcriptase inhibitors resulting in ARV failure, progression to AIDS, and the development of ARV-resistant strains of HIV. AED-ARV combinations can also result in subtherapeutic AED levels. Interactions may also increase the toxicity of either or both AEDs and ARVs. For example, the combination of AZT and zidovudine (AZT) can result in fatal anemia presumably from toxic levels of AZT.

Based on available data, no clear recommendations are made regarding which AED-ARV combinations are optimal, though there are some data for combinations that have not been shown to interact pharmacologically. Unfortunately, there were no published reports on the use of levetiracetam or gabapentin with ARVs, which, given their relative lack of interactions with other medications, are possibly the best options.

The recommendations for the treatment of comorbid HIV and epilepsy are:

- Patients receiving phenytoin may require a lopinavir/ritonavir dosage increase of about 50% to maintain unchanged serum concentrations,
- Patients receiving valproic acid may require a zidovudine dosage reduction to maintain unchanged serum zidovudine concentrations,
- Coadministration of valproic acid and efavirenz may not require efavirenz dosage adjustment,
- Patients receiving ritonavir/atazanavir may require a lamotrigine dosage increase of about 50% to maintain unchanged lamotrigine serum concentrations,
- Coadministration of raltegravir or atazanavir and lamotrigine may not require lamotrigine dosage adjustment,
- Coadministration of raltegravir and midazolam may not require midazolam dosage adjustment,
- Patients may be counseled that it is unclear whether dosage adjustment is necessary when other AEDs and ARVs are combined, and
- It may be important to avoid EI-AEDs in people on ARV regimens that include PIs or NNRTIs, as pharmacokinetic interactions may result in virologic failure, which has clinical implications for disease progression and development of ARV resistance. If such regimens are required for seizure control, patients may be monitored through pharmacokinetic assessments to ensure efficacy of the ARV regimen.

PHOTOS COURTESY DR. GRETCHEN L. BIRBECK

The Salvation Army's Chikankata Mission has well-run, busy antiretroviral and epilepsy clinics, making it the sort of location where the AED-ARV drug interaction concerns are most acute. The mission in Chikankata is 125 km from Lusaka, the capital city of Zambia.

The guideline addresses the risks of drug interactions for people with comorbid HIV and epilepsy, says Dr. Gretchen L. Birbeck, one of the guideline authors.

What does this mean for most patients suffering from both HIV and epilepsy? Although ARV treatment options are expanding in low-income countries, AED availability remains limited in general and in the public sector includes primarily enzyme-inducing AEDs. Furthermore, such regions generally have no capacity for monitoring AED levels or ARV levels.

Perhaps a particular African proverb accurately describes the scenario: "When two elephants fight, the one that suffers most is the grass." In other words, unless or until the donor community, ministries of health, and nongovernmental organizations come together over the issue of epilepsy care in HIV endemic regions, the two elephants of AEDs and ARVs will likely continue to "fight," and people with epilepsy and HIV will continue to be the primary victims of suboptimal AED-ARV regimens. But the potential public health consequences of ignoring this problem should also be of great concern. ■

References

1. Birbeck GL, French JA, Perucca E, et al. Evidence-based guideline: Antiepileptic drug selection for people with HIV/AIDS: Report of the Quality Standards Subcommittee of the American Academy of Neurology and the Ad Hoc Task Force of the Commission on Therapeutic Strategies of the International League Against Epilepsy. *Neurology* 2012;78:139-45.
2. Birbeck GL, French JA, Perucca E, et al. Antiepileptic drug selection for people with HIV/AIDS: Evidence-based guidelines from the ILAE and AAN. *Epilepsia* 2012;53:207-14.

DR. BIRBECK *is the director of the Epilepsy Care Team, Chikankata Hospital, Mazabuka, Zambia, and professor and director of the International Neurologic and Psychiatric Epidemiology Program, Michigan State University, East Lansing, USA.*

Comorbid ADHD Affects Cognition in Epileptic Children

BY HEIDI SPLETE
Elsevier Global Medical News

BALTIMORE – Comorbid attention-deficit/hyperactivity disorder persistently affected the cognitive development of children with epilepsy up to 5 or 6 years after the onset of seizures in a prospective case-control study.

Connie Sung, a doctoral student at the University of Wisconsin, Madison, USA, and colleagues conducted cognitive assessments of 75 children with epilepsy and 62 of their healthy first-degree cousins as controls. They gave the children a comprehensive battery of neurological tests at baseline and at 2 and 5-6 years' follow-up. Average age at last follow-up was 13 years.

At baseline, ADHD and academic performance were significantly associated with neuropsychological impairment across all cognitive domains, but children with epilepsy and no ADHD or academic performance problems had "entirely normal" cognition, compared with controls, Ms. Sung said in a poster at the American Epilepsy Society annual meeting.

The trends persisted after 2 and 5-6 years. Full-scale raw IQ scores after 2 years were about 88 for controls and children with epilepsy without comorbidities, compared with 76 in those with epilepsy and academic performance problems and 68 in those with epilepsy and comorbid ADHD.

The researchers said they had no relevant financial disclosures. ■

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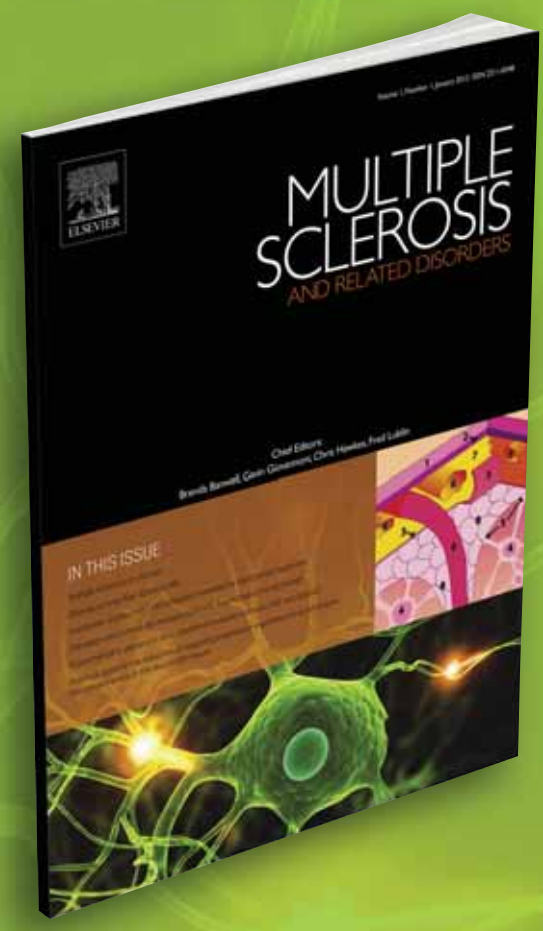

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New Clues to Cause of REM Behavior Disorder in Parkinson's

BY DIANA MAHONEY
Elsevier Global Medical News

REM sleep behavior disorder proved to be significantly associated with cholinergic system degeneration in a cross-sectional, PET imaging study of patients with Parkinson's disease.

Parkinson's disease patients with a history of REM sleep behavior disorder (RBD) demonstrated decreased neocortical, limbic cortical, and thalamic cholinergic innervation relative to those without the parasomnia. The results provide more evidence to suggest that these cholinergic systems are important in the pathophysiology of RBD in Parkinson's disease, according to Dr. Vikas Kotagal of the University of Michigan, Ann Arbor, and his colleagues (Ann. Neurol. 2011 Dec. 9 [doi:10.1002/ana.22691]).

Previous studies have identified RBD and cholinergic system degeneration as independent risk factors for cognitive impairment in Parkinson's disease, but the current findings raise the possibility that the presence of basal forebrain cholinergic dysfunction "may represent a pathological mechanism contributing to the development of dementia in patients who suffer from idiopathic RBD."

The researchers found that the degree of neocortical cholinergic denervation in patients with RBD was "approximately intermediate" between levels seen in Parkinson's patients with and without dementia. A decreased performance in patients with RBD on the verbal-learning test was the only significant difference in cognitive test performance between the groups, which is consistent with previous findings that showed an association between hyposmia in Parkinson's disease, poor performance on verbal-learning testing, and neocortical and limbic cortical cholinergic denervation (Brain 2010;133:1747-54).

VITALS

Major Finding: Patients with RBD had significantly decreased rates of acetylcholinesterase hydrolysis in neocortical, thalamic, and limbic regions on PET imaging.

Data Source: A cross-sectional study of 80 patients with Parkinson's disease without dementia.

Disclosures: The study was funded by grants from the Michael J. Fox Foundation, the Department of Veterans Affairs, and the National Institutes of Health. The authors disclosed potential conflicts of interest with multiple companies, including Pavad Medical, Arena Pharmaceuticals, Guidepoint Global, OrbiMed Advisors, Philips Respironics, Fisher Paykel, K.A.F., Avid Radiopharmaceuticals, MIMvista, and General Electric.

The investigators performed MRI and PET imaging with radiopharmaceuticals for measuring nigrostriatal dopamine, serotonin, and acetylcholine nerve terminals in 80 patients (27 with RBD symptoms, 53 without; mean age, 65 years). They did not have dementia, based on Montreal Cognitive Assessment (MoCA) scores of at least 20.

Patients with RBD had significantly decreased rates of acetylcholinesterase hydrolysis in neocortical, thalamic, and limbic regions. This was unaffected by the activity of dopamine at nigrostriatal nerve terminals. Other covariates such as age, duration of motor disease, or MoCA or Unified Parkinson's Disease Rating Scale scores were not associated with the presence or absence of RBD.

The patients' reports of the severity of symptoms of restless legs syndrome or periodic limb movement disorder, which could be perceived as an RBD mimic by sleep partners, were not associated with the degree of cholinergic activity in a post hoc analysis.

The researchers said their study supports the concept that degeneration or dysfunction in the brain regions that regulate suppression of skeletal muscle during REM sleep – including the cholinergic pedunculopontine nucleus and the lateral dorsal tegmental nucleus, the serotonergic raphe nucleus, and glutamatergic and monoaminergic projections from the parabrachial-precoeruleus regions and the locus coeruleus – causes RBD.

The findings are limited by the reliance on the Mayo Sleep Questionnaire to diagnose RBD vs. polysomnography, as well as the interpretation of decreased [^{11}C]PMP retention as evidence of cholinergic terminal degeneration, the authors noted. "The relationship between cholinergic denervation and RBD symptoms in the study represents a strong correlation, although it does not represent proof of causation," they wrote. "For example, subjects with RBD symptoms in our cohort may have underlying brain changes consistent with a predementia state, which conceivably could confer a stronger association with symptoms of RBD than does the cholinergic deficit that is associated with such a predementia state."

Despite the limitations, the data suggest that "changes in the cholinergic nervous systems within the brainstem and basal forebrain may play a vital role in the pathophysiology of RBD and hence have the potential to offer insight into the underlying heterogeneity of a number of neurodegenerative diseases. Longitudinal observational studies are necessary to further investigate the cause of RBD in [neurodegenerative diseases]," they wrote. ■

Teams Working to Find Origins

Nodding Syndrome • *from page 1*

in northern Uganda (*MMWR* 2012;61:52-4). There is still insufficient evidence to establish whether the Tanzanian cases, which are clinically very similar to those in Uganda and South Sudan, represent the same syndrome.

Nodding syndrome "is devastating for both the children and the caregivers," said Dr. James Sejvar, a CDC neuroepidemiologist who led the field investigations in Uganda and South Sudan, in an interview. "We want to do everything we can to try to determine what's causing it and how best to manage it."

Isolating causes and identifying treatments are especially urgent concerns as cases are reportedly increasing in Uganda and South Sudan, with an estimated 3,000 in Uganda, according to recent media reports there, and 8,000 in South Sudan, according to Dr. Abdinasir Abubakar, a communicable diseases specialist with the World Health Organization in Juba, South Sudan, who is working closely with the CDC investigators. Cases are not reported to be increasing in Tanzania.

Dr. Abubakar said in an interview that although the syndrome is known to have existed for some time in South Sudan, the recent spike in reported cases could only partially be explained by wider awareness and better surveillance. "It's not only local authorities but local NGOs who are saying that more children have been affected," he said. Particularly striking, he said, is that in South Sudan "there are a number of displaced people from another location who did not have nodding. But after the displacement, when they moved to affected areas, after 2 years the children started developing the syndrome."

In Tanzania, Dr. Andrea Winkler, a neurologist at the Technical University of Munich, and investigators from Tanzania, Austria, and Canada have been working with children in an isolated mountain population where nodding syndrome has long been documented, along with a high background incidence of epileptic disorders in general. "I don't know whether we are dealing with the same disease," Dr. Winkler said in an interview, although her team remains "in very close contact" with the CDC team conducting research in South Sudan and Uganda.

South Sudan, Uganda, and Tanzania have contiguous political boundaries, but the communities where nodding syndrome now occurs are isolated from one another. What they are known to have in common is severe poverty and a high rate of infections with *Onchocerca volvulus*, the nematode parasite causing river blindness.

The CDC investigators noted in their new report higher rates of infection with *O. volvulus* in the 38 South Sudan cases (76.3%) than in 38 healthy controls (47.4%). However, *O. volvulus* infection is endemic in many unaffected communities as well.

In their study from Tanzania published in 2008, Dr. Winkler and colleagues saw that more than 80% of children with head nodding had evidence of infection by *O. volvulus*. But they could not find *O. volvulus* antibodies in the children's cerebrospinal fluid, indicating that the infections did not reach the brain. Dr. Winkler said although *O. volvulus* was ruled out for now as a direct cause of nodding, "we cannot exclude the possibility of an autoimmune process [triggered by *O. volvulus*] – for example, a cross reaction of antibodies – though this is highly speculative."

Other potential causes being considered are gene-environment interactions, including a rare genetic disease called pyridoxine-responsive epilepsy, which causes infants to have seizures and that can be corrected by supplementing with vitamin B_6. The CDC, whose field team for nodding disease includes nutrition specialists along with neurologists and infectious disease experts, is still awaiting results of laboratory testing for vitamins A, B_6, and B_{12}; heavy metals; and genetic markers from its South Sudan field study. The CDC plans to conduct additional investigations there in February or March.

IN TANZANIA, AS EARLY AS THE 1960S, PEOPLE KNEW THAT CHILDREN WHO HAD HEAD NODDING WOULD SOONER OR LATER HAVE EPILEPSY.

That genetic factors might be at play would be no surprise to Dr. Louise Jilek-Aall, founder of the Mahenge epilepsy clinic in rural Tanzania and the researcher who originally described head nodding syndrome in 1965. Dr. Jilek-Aall published extensively on epileptic syndromes in rural Tanzania through 2009. Her work helped demonstrate an unusually high background rate of epilepsy in the Mahenge region, along with evidence of familial clustering among nodding cases, and provided the basis for Dr. Winkler and colleagues' continuing investigations.

Dr. Jilek-Aall said in an interview that she was first made aware of head nodding in the beginning of 1960 by the mothers of children with the disorder. "The mothers came with small children of about 4 or 5 [years] and said, 'please can you tell me what to do because this child will get epilepsy.' The children did not show any symptoms of having epilepsy, but the mothers would say the child had been 'nodding the head.' The people knew then that the children who had head nodding would sooner or later have epilepsy, or 'kifafa.' After a few years indeed some of them would begin to get grand mal seizures," she said.

Dr. Jilek-Aall retired to Canada after 5 decades in Tanzania, but her epilepsy clinic, still thriving today, is where Dr. Winkler and colleagues in 2005 recruited their original cohort of 62 patients with head nodding, of whom 53 are still known to be alive. Most of the surviving patients are on antiepileptic medications that the clinic steadily supplies. Because of the clinic, Dr. Winkler said, "I think the situation [in Tanzania] is quite exceptional – you can't compare it with what is going on in Uganda or Sudan at the moment." ■

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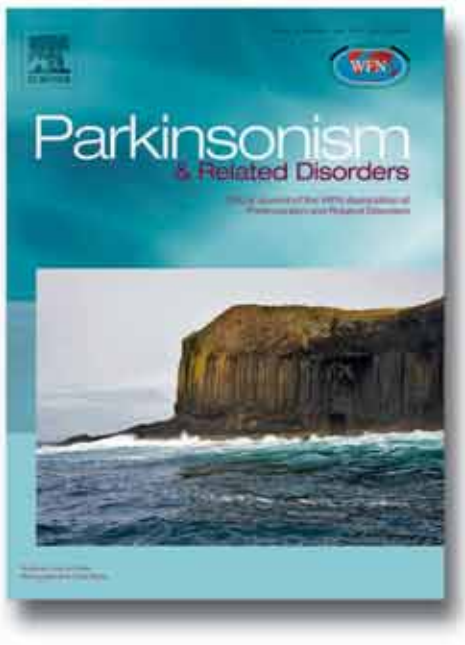

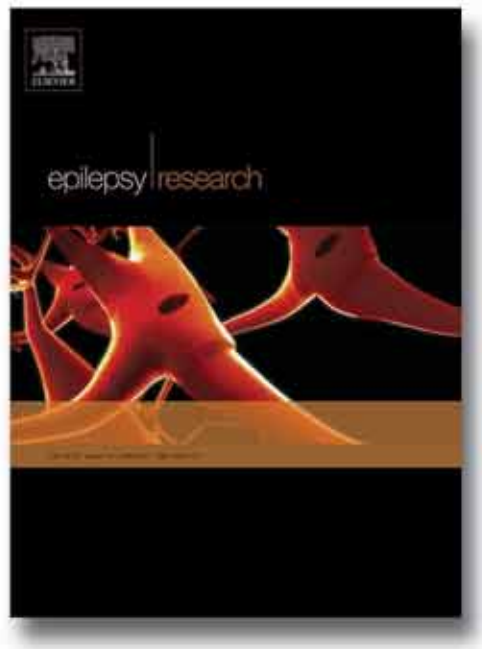

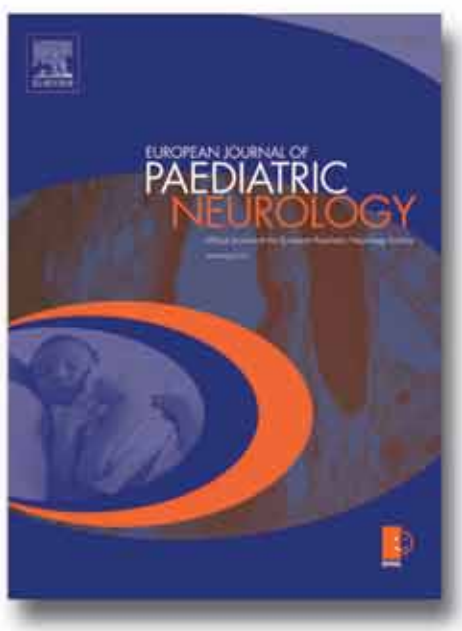

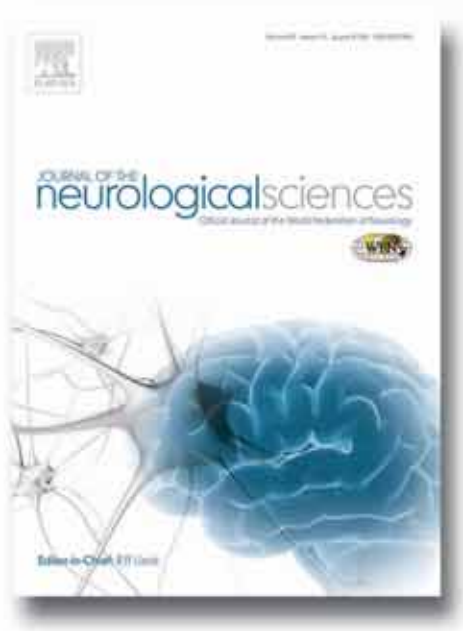

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NEUROLOGY

Movement Disorder Seen in Children With New Narcolepsy With Cataplexy

Authors hope narcolepsy with cataplexy will be added to the differential diagnosis of movement phenomena.

BY DENISE NAPOLI
Elsevier Global Medical News

Childhood narcolepsy with cataplexy frequently presents with a movement disorder that comprises both "active" and "negative" motor disturbances, including tongue protrusion, head and trunk swaying, facial grimacing, and chorea.

However, this constellation of motor phenomena seems to be transient, with the age of disease onset and disease duration both inversely related to motor composite scores, according to Dr. Giuseppe Plazzi and colleagues (*Brain* 2011; 134:3480-92).

"Our description is of a new clinical picture of childhood narcolepsy with cataplexy close to disease onset," Dr. Plazzi wrote in an e-mail interview.

"The clinical picture [of narcolepsy] is easily misunderstood for a movement disorder, muscle disease, epilepsy, malingering, or a psychiatric disorder. We hope that our description will help specialists to consider the potential role of sleepiness symptoms in the evaluation of such cases, thus adding … narcolepsy with cataplexy to their differential diagnosis," he added.

Dr. Plazzi, a professor of neurology at the University of Bologna, Italy, made video recordings of 39 patients (19 girls) aged younger than 18 years who were newly diagnosed with narcolepsy with cataplexy. These videos were then compared with videos of 25 matched, healthy controls. The recordings included several minutes of "baseline recording" and then up to 30 minutes of the patient watching a funny video.

NARCOLEPSY IS EASILY MISTAKEN FOR A MOVEMENT DISORDER, MUSCLE DISEASE, MALINGERING, EPILEPSY, OR PSYCHIATRIC DISORDER.

Two neurologists independently reviewed the recordings and noted the subjects' movements, classifying them as either "active" or "negative" in nature, and noting whether they occurred at baseline or only in response to emotional stimuli (in this case, the funny video).

"Negative" motor phenomena were classified as paroxysmal head drops and falls, persistent eyelid narrowing and tongue protrusion, persistent facial hypotonia, and persistent generalized hypotonia.

"Active" movements included eyebrow raising, perioral and tongue movements, facial grimaces; head and/or trunk swaying, stereotyped motor behavior, and dyskinetic or dystonic movements.

The patients' mean age was 11.5 years, and the mean age of symptom onset was 9.3 years. There was a mean diagnostic delay of 1.8 years, ranging up to 9 years.

'The age of disease onset and disease duration [are] inversely related to motor composite scores.'

DR. PLAZZI

"All 'negative' motor phenomena and the composite score evaluated at baseline and during emotional stimuli were significantly more common in the patients," the authors wrote.

Patients and controls obtained a mean score greater than or equal to 1 in the following percentages at baseline and during emotional stimuli, respectively: head drops and falls, 18% (baseline) and 82% (emotional stimuli) for patients vs. 0% and 4% for controls; ptosis and tongue protrusion, 51% (baseline) and 82% (stimuli) for patients vs. 0% and 0% for controls; facial hypotonia, 39% (baseline) and 71% (stimuli) for patients vs. 0% and 0% for controls.

Similarly, all "active" phenomena except facial grimacing were significantly more prevalent in patients.

Patients and controls had a mean score greater than or equal to 1 in the following: eyebrow raising, 23% (baseline) and 76% (stimuli) in patients vs. 0% and 36% for controls; facial grimaces, 10% (baseline) and 82% (stimuli) for patients vs. 0% and 36% for controls; and dyskinetic-dystonic movements, 10% (baseline) and 55% (stimuli) for patients vs. 0% and 8% among controls.

"Two additional abnormal complex behaviors could not be simply classified as 'active' or 'negative' motor phenomena," the authors wrote. One was a "neck extension viewing" posture (characterized by neck extension and eyelid ptosis with eyebrow raising while the patient watched videos), which was observed exclusively in nine patients (24%). The other was puppet-like movement (characterized by a rapid and rhapsodic set of choreic movements of the whole body, and limbs with hypotonia), which was observed exclusively in five patients (13%).

Dr. Plazzi and his associates then sought to determine which clinical and demographic factors were associated with the observed motor phenomena.

"We found that the age at narcolepsy with cataplexy onset was inversely related to 'negative' composite scores, and that disease duration was inversely related to both 'negative' and 'active' composite scores, the latter reaching statistical significance only during emotional stimulation," the investigators wrote.

DOPAMINERGIC ABNORMALITIES AND THE TRANSIENT IMBALANCE OF BASAL GANGLIA AND CORTICAL NETWORKS MAY GIVE RISE TO THE DISORDER.

They did not find any correlations between sleep latency and sleep-onset REM (rapid eye movement) periods on the Multiple Sleep Latency Test, or with baseline hypocretin-1 levels.

Finally, the authors assessed whether prior streptococcal infection had any relation to the observed movements.

A total of 26 patients with elevated antistreptolysin-O titers scored "particularly high in subscales involving facial muscles" at baseline as well as during emotional stimulation in comparison with 13 patients who had normal baseline titers.

Negative motor features showed no such correlation, nor did overall composite scores.

The researchers were unable to offer a definitive rationale for why the observed motor phenomena seemed to fade over time from diagnosis.

"It is … possible that the complex movement disorder we have described in childhood narcolepsy with cataplexy close to disease onset results from increased dopaminergic transmission and the transient imbalance of basal ganglia and cortical networks. Altered emotional processing engaging cortico-subcortical networks may also be involved in the transition to clear-cut cataplexy," they wrote.

Commenting on the fact that some of the clinical features were reminiscent of chorea and that some patients had high antistreptolysin-O titers, the authors concluded that the movement abnormalities "seem transient, and the clinical phenotype may rapidly evolve into a more characteristic picture that includes typical cataplexy. The rapid loss of hypocretin neurons is likely to be involved in the pathophysiology of the movement disorder, with the possible involvement of secondary dopaminergic abnormalities." ■

VITALS

Major Finding: Children with new-onset narcolepsy with cataplexy had significantly more negative motor phenomena (falls, head drops, ptosis, tongue protrusion, and facial hypotonia) and positive motions (eyebrow raising, facial grimaces, and dyskinetic-dystonic movements) during emotional stimuli than did healthy control children, but the movement disorder faded over time from diagnosis.

Data Source: A prospective study of 39 children who were newly diagnosed with narcolepsy with cataplexy.

Disclosures: The study was funded by a grant from nEUroped. The authors stated that they had no conflicts to disclose in relation to this study.

COMMENTARY

The active movements described by Dr. Plazzi and his colleagues "cast a new light on the pathogenesis of the disease and on the interaction between increasing hypocretin deficiency and dopaminergic mechanisms. In spite of their temporary character, the description adds to our knowledge of cataplectic attacks in young kids, thus helping us to diagnose new cases," Dr. Sona Nevšímalová wrote in an e-mail interview.

She praised her colleagues' work in offering up new clues to a correct diagnosis in the setting of childhood narcolepsy with cataplexy.

"Narcolepsy is a frequently underdiagnosed disease, particularly in children," she wrote, adding that a diagnostic delay can extend until adulthood in some cases.

"Therefore, a clinical description of childhood symptoms is extremely important, and so is awareness of the disease, both in the medical profession as well as in the general population.

"Since 2009, European Narcolepsy Day has been celebrated in many countries with a huge media campaign to draw attention to this morbidity. The third European Narcolepsy Day will be held this year in Bologna, Italy, on March 17 under the auspices of the European Narcolepsy Network."

DR. NEVŠÍMALOVÁ *is a neurologist at Charles University I, Prague. She wrote that she has no conflicts to disclose in relation to her comments or this study.*

BOOK REVIEW

An Exploration of the Neuropsychological Borderland

The Shaking Woman or A History of My Nerves

By Siri Hustvedt
Henry Holt and Co., New York, 2010

From time to time, what I need as a physician is not a picture but a thousand words. There are few materials that are both factual and reassuring, insightful, and practical that one can draw on to educate medical students or help patients feel less alone. As a third-year medical student, I spent 6 weeks at a tiny psychiatric hospital on an island off the coast of Georgia. When I arrived, the enigmatic psychiatrist immediately handed me a copy of *An Unquiet Mind*, psychiatrist Kay Redfield Jamison's account of living with bipolar disorder. Over the next couple of hours I saw him reach into a box and hand another copy to a patient, newly diagnosed with bipolar disorder. He would also sometimes give out Dale Carnegie's *How to Win Friends and Influence People* to the adolescent inpatients. Everyone had a book; reading was therapy and education at once, for students and patients alike.

Neurologists too love a good story, and our patients make for bestsellers via Oliver Sacks and Vilayanur S. Ramachandran. At the borderland of neurology and psychiatry, patients with psychogenic or conversion disorder are seemingly underrepresented in these collections. The paucity of narratives for the lay public describing conversion is particularly unfair given that these are the same patients in whom the story is so critically important. They come with stacks of documents, often meticulous self-written accounts of lab data and clinical details, are endlessly frustrated with the limits of the 45-minute appointment,

BY SARAH M. KRANICK, MD

Dr. Kranick is chief of the Neurology Consult Service, Assistant Clinical Director, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Md., USA.

and can be remarkably improved, if not cured, through psychotherapy, by learning how to retell their personal story.

In Siri Hustvedt's *The Shaking Woman or A History of My Nerves*, the novelist describes her personal experience with the neuropsychological borderland. Two years after her father died, while giving a talk in his honor at St. Olaf College in Northfield, Minn., USA, where he had been a professor, she experienced uncontrollable shaking from the neck down but was able to finish the speech. These violent tremors recurred on multiple other occasions, usually when speaking publicly, casting a new perspective on previous symptoms such as febrile seizures as an infant and lifelong migraines with aura. As someone who was already deeply interested in the brain, to the point of taking practice tests for the psychiatry boards as research for a novel, she documents her search for a diagnosis through contact with psychotherapy, psychiatry, neurology, and psychoanalysis. She senses keenly the divide between neurology and psychiatry and the artificial duality of brain and mind. She describes the gray areas between migraine and epilepsy, the similarities between patients with neglect and conversion, phenomena that keep us from being able to draw strict borders around diagnoses.

Hustvedt's book is not entirely sure what it wants to be, perhaps reflecting the very ambiguity that haunts this subject matter. Part source book for a course on the history of hysteria and (a much smaller) part memoir, most of the customer reviews on Amazon would indicate that the lay public wants to hear more from her and less about history. It would most certainly benefit from chapter delineations. The story channels the patient's frustration at not having a clear diagnosis, but will also provoke the physician's frustration as we read with horror when, after beginning to acclimate to the idea of conversion disorder, a new psychiatrist tells her that this has to be something neurological after all and puts her on the path toward more tests. All of these experiences will ring true with many conversion patients as well as the neurologists who treat them.

The Shaking Woman works as a primer on how hysteria became conversion and a view into the patient's experience of this diagnosis. There are transformative moments in Hustvedt's lovely prose ("blurring borders create abiding conundrums") in which, always a reader, she attempts to make sense out of her shaking by reading and re-reading the experience in different contexts: "The search for the shaking woman takes me round and round. … My only certainty is that I cannot be satisfied with looking at her through a single window." This is the kind of self-reflection that, although not curative (this book is proof that insight alone is not enough to halt conversion symptoms for most patients), is certainly less harmful than the search for more invasive medical procedures to discover why conversion happens. Her memoir illuminates one particular illness experience that is too often left undescribed. ■

Cortical Demyelination, Inflammation Found in Early MS

BY MARY ANN MOON
Elsevier Global Medical News

Cortical demyelination is common early in the course of multiple sclerosis and is inflammatory in nature, according to an analysis of brain biopsy samples containing cortical tissue.

VITALS

Major Finding: A total of 53 (38%) of 138 biopsy samples of cortical tissue showed demyelination, with a high prevalence of inflammation.

Data Source: An analysis of brain biopsy samples containing cortical tissue from 138 patients early in the course of MS, often before the disease was diagnosed.

Disclosures: This study was supported by the National Multiple Sclerosis Society and the National Institutes of Health. Dr. Lucchinetti's associates reported ties to numerous companies that market and develop drugs for MS, as well as receiving research funding or travel awards from research institutions or patient advocacy organizations.

"These findings do not support a primary (noninflammatory) neurodegenerative process during early-stage multiple sclerosis," wrote Dr. Claudia F. Lucchinetti of the Mayo Clinic, Rochester, Minn., and her associates. Most previous studies of cortical lesions have focused on autopsy findings in patients with longstanding multiple sclerosis and "have suggested that neurodegeneration proceeds independently of parenchymal inflammation," they noted.

They chose instead to study the prevalence and histopathologic features of cortical demyelination in brain biopsy samples from 563 patients who underwent the procedure to rule out other possible causes of their neurological symptoms, such as brain tumors. The cortical matter was obtained "in passing," in samples that were targeting white-matter lesions. The samples were obtained within a median of 27 days from the onset of symptoms.

A total of 138 patients' samples contained a sufficient amount of cortex for analysis. Of those patients, 77 had clinical follow-up for a median of 3.5 years. MS was diagnosed in 58 (75%), and a clinically isolated syndrome was diagnosed in the remaining 19 (25%).

In all, 53 of the 138 samples (38%) showed cortical demyelination, the researchers reported (N. Engl. J. Med. 2011;365:2188-97). The lesions were highly inflammatory and had a high prevalence of CD3-positive and CD8-positive T-cell infiltrates as well as myelin-laden macrophages.

In addition, among patients who had sufficient meningeal tissue for analysis, meningeal inflammation was topographically adjacent to the cortical demyelination.

The researchers also found concurrent subpial and leukocortical lesions within individual tissue sections, "suggesting that superficial demyelinating disease may contribute to the generation of deeper lesions by means of cytokine diffusion."

In addition, "our findings of microglial activation, neuritic injury, pyknotic neurons, and reduced oligodendrocyte density ... are consonant with the findings in patients with progressive MS, underscoring the potential of cortical demyelination to cause irreversible injury, although inflammation may resolve rapidly."

They speculated that the mechanism of MS progression might involve "myelin-laden macrophages leaving the cortex, entering the cerebrospinal fluid, and gaining access to deep cervical lymph nodes to promote epitope spreading." ■

COMMENTARY

The "provocative" findings of Dr. Lucchinetti and her colleagues "provide definitive evidence that inflammatory disease of the gray matter commences early in the pathogenesis of some cases of multiple sclerosis," wrote Dr. Peter A. Calabresi.

Before now, macrophages laden with myelin – the hallmark of an active plaque – have not been seen in cortical tissue, and gray-matter lesions have been "routinely underestimated" because conventional MRI doesn't pick up MS plaques in the cortical and deep gray structures, he said.

This study suggests that cortical neuronal loss "is directly associated with inflammatory demyelination, and therefore early therapeutic efforts to suppress inflammation may be neuroprotective in both gray-matter and white-matter compartments," Dr. Calabresi added.

DR. CALABRESI *is in the department of neurology at Johns Hopkins Hospital, Baltimore. He reported ties to numerous companies that market and develop drugs for MS. These remarks were adapted from his editorial comment accompanying Dr. Lucchinetti's report*

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