

# WORLD NEUROLOGY

THE OFFICIAL NEWSLETTER OF THE WORLD FEDERATION OF NEUROLOGY

## Broadening Our Horizons

### WFN: 2010-2013

BY VLADIMIR HACHINSKI

Missions set goals and guide actions. The greatest change that took place in the past four years was an expansion of the WFN mission to “foster quality neurology and brain health worldwide.” To accomplish this required partners, so we invited representatives from all of the major brain organizations for a meeting in Geneva on March 30, 2011, that resulted in the World Brain Alliance composed of:

- European Brain Council (EBC)
- International Brain Research Organization (IBRO)
- World Federation of Neurology (WFN)
- World Federation of Neurosurgeons (WFNS)
- World Federation of Neurorehabilitation (WFNR)
- World Psychiatry Association (WPA)
- International Child Neurology Association (ICNA)
- International League Against Epilepsy (ILAE)
- World Stroke Organization (WSO)
- Alzheimer’s Disease International (ADI)

The World Brain Alliance activities can be summarized as an ABC.

- A = Advocacy**
- B = Brain Year**
- C = Cooperation**

I took part in a high ministerial meeting in Moscow in April 2011, then a consultation with the president of the United Nations General Assembly in June in New York and then a session of the General Assembly that adopted the Non-Communicable Diseases resolution in September 2011. Subsequently, I continued to be involved with the WHO, including participating in meetings of the Executive Committee.

In addition to my own activities with the WHO, Raad Shakir has chaired and Donna Bergen has participated in the expert panel advising on the revision of the International Classification of Diseases 10 (ICD10) regarding brain disorders. A

major achievement has been the acceptance by the WHO of the recommendation of the subcommittee on cerebrovascular disorders chaired by Bo Norrving, of which I was a part, that stroke cease to be part of cardiovascular disorders and be classified under brain disorders in the ICD-11.

The Brain Year is a project of the



Vladimir Hachinski

European Brain Council, led ably by Mary Baker. The intent is to proclaim a World Brain Year Europe 2014 at the European Parliament in Brussels. It is hoped that it will be followed by the World Brain Year Americas 2015, World Brain Year Asia 2016, and so on.

In terms of cooperation, the major initiative has been in the neurospecialty network founded and led by Werner Hacke, and now headed by William Carroll. This aims to bring together all of the specialties related to the brain. This complements the work done by Donna Bergen, chair of the Applied Research Committee, rationalizing research groups within the WFN whereby some have become largely irrelevant and have been dissolved while others have grown to become major organizations that now are reconnecting with the WFN.

A tangible proof of the new cooperative spirit is that several of the sessions of the World Congress of Neurology were co-sponsored by the Movement Disorders Society, the World Stroke Organization, the International League Against Epilepsy, the International Child Neurology and a session with the WHO.

### Grassroots

We initiated a process whereby we offer modest amounts of money to individual neurologists who had ideas for

projects that meet the criteria of value, viability, synergy and evaluation. The first year all of the projects were funded by the WFN. The second year, we asked leaders of other brain organizations to be part of the review process. This resulted in leadership of the different organizations learning about what each was doing, allowing for cooperation and avoiding overlap. Last year, there were 10 Grants-in-Aid, half of them were co-funded and half of them were in Africa. This year, the total value of the 11 grants was \$419,000, five co-funded and seven in Africa.

The geographic location of the Grants-in-Aid was based on the criteria alone so that it is encouraging that the largest number ended up being in the area of the greatest need, namely in Africa. The high quality of the projects makes it likely that some of them will

see WFN, page 14

## INSIDE

### FEATURES

#### Delegate Vote and Election Results

Almost 80 delegates and representatives assembled Sept. 22, 2013, in Vienna, for the Annual General Meeting of the Council of Delegates.

PAGE 3

#### 100 Years of Expanding Networks in Neurology

PAGE 4

#### Global, Interdisciplinary, Integrative

PAGE 7

#### Nano-Neuromedicine

PAGE 12

#### Our Brains, Our Future

Young students and minds are highly interested in knowing how the brain works and how can we make it work better.

PAGE 12

## WCN 2013 Report

BY DONNA BERGEN, MD

CO-CHAIR, SCIENTIFIC PROGRAM COMMITTEE

The 21st WFN World Congress of Neurology was held Sept. 21-26 in Vienna, with more than 6,300 attending from 135 countries. It was the joint meeting with the European Federation of Neurological Societies, and constituted the EFNS’ annual meeting for 2013. The Austrian Society of Neurology was the local host, with its president Eduard Auff, MD, presiding.

The joint production made for a particularly diverse, stimulating and memorable congress. More than 350 of the world’s leading neuroscientists and educators provided more than 75 scientific sessions on virtually all aspects of neurology, and led over 60 teaching courses and workshops.

Few other conferences provide a venue for neurologists from all subspecialties to meet and learn, and for young neurologists and trainees to listen to and to talk with leading scientists who may otherwise be just names in textbooks and journals. Accessibility was a major goal of the organizers, with a sliding conference fee scale designed to make it easier for those from countries with limited resources, young neurologists and trainees to attend. The WFN also provided travel bursaries enabling 150 junior neurologists from low resource countries to attend the Congress.

One of the highlights of the meeting was the opening plenary session, when Nobel Laureate Eric Kandel gave a remarkable talk on three innovative

see REPORT, page 12



**WORLD FEDERATION OF NEUROLOGY**

**Editor in Chief**  
Donald H. Silberberg

**Assistant Editor**  
Keith Newton

**WFN OFFICERS**

**President** Raad Shakir (United Kingdom)  
**First Vice President** William Carroll (Australia)  
**Secretary-Treasurer General** Wolfgang Grisold (Austria)

**ELECTED TRUSTEES**

Gallo Diop (Senegal)  
Gustavo Roman (USA)

**REGIONAL DIRECTORS**

Mohamed S. El-Tamawy (Pan Arab)  
Timothy Pedley (North America)  
Richard Hughes (Europe)  
Riadh Gouider (Pan Africa)  
Marco Tulio Medina (Latin America)  
Man Mohan Mehndiratta (Asia-Oceania)

**EXECUTIVE DIRECTOR**

**Keith Newton**  
1 Lyric Square  
Hammersmith, London W6 0NB, UK  
Tel: +44 (0) 203 542 7857/8  
Fax: +44 (0) 203 008 6161  
keith@wfneurology.org

**EDITOR OF THE JOURNAL OF THE NEUROLOGICAL SCIENCES**  
John England (USA)



**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 Ascend Integrated Media.

**Disclaimer:** The ideas and opinions expressed in *World Neurology* do not necessarily reflect those of the World Federation of Neurology or the publisher. The World Federation of Neurology and Ascend Integrated Media will not assume responsibility for damages, loss or claims of any kind arising from or related to the information contained in this publication, including any claims related to the products, drugs or services mentioned herein.

**Editorial Correspondence:** Send editorial correspondence to *World Neurology*, Dr. Donald H. Silberberg at [silberbe@mail.med.upenn.edu](mailto:silberbe@mail.med.upenn.edu).

*World Neurology*, ISSN: 0899-9465, is published bimonthly by Ascend Integrated Media, 7015 College Blvd., Suite 600, Overland Park, KS, 66211. Phone +1-913-344-1300 Fax: +1-913-344-1497.

©2014 World Federation of Neurology



**PUBLISHING PARTNER**

Ascend Integrated Media

**President and CEO**  
Cameron Bishop

**Vice President of Content**  
Rhonda Wickham

**Vice President of eMedia**  
Scott Harold

**Vice President of Sales**  
Donna Sanford

**Project Manager**  
Amanda Marriott

**Art Directors**  
Lorel Brown  
Lindsey Haynes

**Editorial Offices**  
7015 College Blvd., Suite 600  
Overland Park, KS 66211  
+1-913-469-1110

# Theodore L. Munsat (1930-2013)

## An Outstanding Legacy with the WFN

BY MARCO T. MEDINA, DEAN OF THE NATIONAL AUTONOMOUS UNIVERSITY OF HONDURAS

The World Federation of Neurology (WFN) lost an outstanding leader on Nov. 22, 2013, with the death of Professor Theodore Leon Munsat ("Ted"), in Waltham, Mass., U.S., at age 83.

Munsat was Emeritus professor of Neurology at Tufts University School of Medicine and served the WFN in several capacities as trustee, chairman of the WFN Education and Research Committees, chairman of the WFN ALS Research Group and founding director of the WFN Seminars in Clinical Neurology. He was president of the American Academy of Neurology (AAN) 1989-1991, chairman of the Continuing Educational Committee of the AAN and founding director of AAN's premier continuing medical education journal *Continuum: Lifelong Learning in Neurology*<sup>1,2</sup>.

Munsat was born in Portland, Maine, in 1930, to Leo and Ethel Munsat. When he was a child, the Munsat family moved



Marco T. Medina

to Rutland, Vt. He graduated from Rutland High School in 1948. He received his BA degree in chemistry at the University of Michigan, and in 1957, his MD degree from the University of Vermont, and then completed an internship at Mt. Sinai Hospital in New York, followed by a neurology residency with Houston Merritt at the New York Neurological Institute, Columbia Presbyterian Medical Center. He completed his training with Augustus S. Rose at the University of California in Los Angeles (UCLA). After serving in the Navy for two years, he returned to UCLA in 1963 as assistant professor of Neurology and director of the Muscular Dystrophy Clinic where he worked with Carl Pearson. In 1970, he moved to the University of Southern California, first as associate professor, and then, in 1973, as professor of Neurology. In 1975, he took a 12-month sabbatical in Newcastle upon Tyne, U.K, with Lord Walton. In 1976, he became chairman of Neurology at Tufts University and the New England Medical Center<sup>1</sup>.

He was a worldwide leader in ALS research and as chairman of the WFN ALS Research Group that published important international diagnostic guidelines. He authored more than 200 scientific articles and books, including classic texts as *Amyotrophic Lateral Sclerosis: A Guide for Patients and Families*,



Ted Munsat

Post-Polio Syndrome and Quantification of Neurological Deficits. He received many honors during his long career, including the A.B. Baker Award for Education of the AAM, the Sheila Essey Award for ALS Research, the Lifetime Achievement Award of the WFN Research Group on Neuromuscular Diseases and the degree of Doctor of Medicine, Honoris Causa, by the University of Marseilles<sup>1</sup>.

Munsat as the WFN chairman of the Education Committee developed a number of successful educational programs around the world:

1. A continuing medical education (CME) program using the journal *Continuum*, generously donated by the American Academy of Neurology, and the WFN Seminars in Clinical Neurology. More than 42 develop-

### IN MEMORIAM

## Ted Munsat

BY JOHN WALTON (LORD WALTON OF DETCHANT) KT, TD, MA, MD, DSC, FRCP, FMedSci

Ted Munsat was a close and much-valued friend whom I admired as a man, as a neurologist, as a teacher, and as an administrator and lifelong supporter of the World Federation of Neurology. I first met him many years ago (more years than I can remember with accuracy) when we both attended a conference in the United States on neuromuscular disease. I recognized at once that here was a man of outstanding ability and exceptional merit. Subsequently, we



John Walton

corresponded, and I think we even wrote one short paper together.

But perhaps my memory is sharpest of the time that he came to spend a year in my department in Newcastle. During that time, working with Peter Hudgson and others, he did some important original work leading to the publication of a number of papers, and he was widely respected and admired by the junior staff and by those working in research in the Muscular Dystrophy laboratories.

He was an immensely approachable man, full of advice and sensible comments. His contributions to the department's work were exceptional, and I remember how proud he was when his young son took up soccer at a Newcastle school and ended up playing for the junior first team, where he was regarded as one of its stars.

Subsequently, I kept in close touch with him when he became head of department in Boston, and I forgave him, eventually, for stealing Walter Bradley from Newcastle to work with him, before Bradley went off to independent chairs, first in New Hampshire and later in Miami.

We continued to keep in close touch,

and I was impressed with the work that he did on various WFN committees, and above all his contributions to continu-

**He was an immensely approachable man, full of advice and sensible comments.**

ing education in neurology through the publication of *Continuum*.

His wife Carla was a great charmer with a wonderful, twinkling attitude about life. They loved the social life in Newcastle, and later still, I met them both on many occasions at international meetings, and shared not only reminiscences but also their joint views about the future of neurology on a worldwide scale. Munsat has left a mark on international neurology that can never be erased, and he will be remembered by all who knew him with respect, pleasure and affection. •

ing countries participated in this program, including Argentina, Bangladesh, Brazil, Bulgaria, Cameroon, Chile, Columbia, Congo, Croatia, Cuba, Cypress, Czech Republic, Egypt, Ethiopia, Guatemala, Honduras, Hungary, India, Iraq, Jordan, Kenya, Lebanon, Lithuania, Macedonia, Mexico, Mongolia, Nigeria, Panama, Peru, Romania, Russia, Serbia, Slovenia, Sri Lanka, Syria, Tunisia, Uganda, Uruguay, Vietnam, Venezuela, Yemen, and Zambia with an extraordinary local impact<sup>3,7</sup>.

2. Support for Neurologic Training program and WFN Certification: Munsat founded programs for the WFN to provide assistance in establishing neurology training programs where there were none, helping further develop existing programs and providing a certification process for programs that wished to have an external review. He worked with programs in Ethiopia, Honduras, Guatemala, Mexico, Peru, etc.<sup>3,5,8</sup>.

The first pilot program was the Honduras Neurology Training (HNT) Program. Munsat and Professor Alberto Portera Sanchez from the WFN Education Committee visited Honduras in July 1998 for the first time, and after an evaluation, they concluded: "It is our recommendation that a training program in neurology should be established at the Hospital Escuela. We believe that there is a pressing need for more neurologists to address the unmet health needs of the people of Honduras. The relevant members of the medical school faculty have expressed their strong support of such

a program. More than adequate human and structural facilities are currently available. There is no reason why this program could not be a program of unqualified excellence and effectiveness."

After the initial visit, the National

Autonomous University of Honduras established the country's first Neurology Training Program in 1998.

This program was established using a problem- and epidemiological-oriented methodology with oversight by an external WFN review board. By 2013, the program resulted in a 50 percent increase in the national neurologist ratio per inhabitant, significantly improving the quality of patient care and promoted research in the neurosciences. During 10 years, Munsat and Sanchez have visited and evaluated annually the HNT program. The legacy of Munsat in our program and country is invaluable<sup>5,8</sup>.

3. Neurologic care where there is no neurologist. With Gretchen Birbeck, he supported the development of training materials for nonphysician health care providers and established a program for non-physician neurologist clinical officers in Zambia and Malawi<sup>3,9</sup>.

4. The WFN Africa Initiative.

Munsat, Johan Aarli, Gretchen Birbeck, Gallo Diopp and others started this initiative. Six sub-Saharan countries started their participation in the WFN Continuing Education program: Camer-

oon, Uganda, Zambia, Nigeria, Ethiopia, and Kenya. He helped on the development of the Ethiopia Neurology training program<sup>3</sup>.

5. London WFN Education Committee meetings: Since 2003 Munsat organized successful planning meetings in London with members representing WFN regions around

the world.

6. WFN Seminars in Clinical Neurology. Munsat founded the Seminars in Clinical Neurology because of the lack of educational material specifically designed and directed to neurology health care givers practicing in low resource environments<sup>3</sup>.

It was a great privilege and honor for me to have met and worked with Munsat. He was gentle, gracious mentor with a warm and sincere personality, who loved helping others every chance he had. He inspired me as well several generations of residents and neurologists all around the world, and he left an outstanding legacy with the WFN.

Munsat is survived by his wife, Carla Munsat; his daughter, Amy Munsat, his son, Peter Munsat and six grandchildren. •

It was a great privilege  
and honor for me to  
have met and worked  
with Munsat.

## References

1. Rowland TL. Theodore L. Munsat MD: President American Academy of Neurology. *Neurology* 1987;37:548-9
2. Munsat TL, Mancall EL, DesLauriers MP. The AAN launches a new education program: CONTINUUM lifelong learning in neurology. *Neurology* 1994;44:771-2.
3. Munsat T, Aarli J, Medina M, Birbeck G, Weiss A. International Issues: educational programs of the World Federation of Neurology. *Neurology*. 2009;10;72(10):e46-9.
4. Gusev EI, Konovalov AN, Volodin NN, Munsat T, Fedin AI, Khaass A, Gekht AB, Diankina MS, Martynov Mlu, Kamchatnov PR, Beliaeva IA, Lebedeva AV, Kovaleva Ilu. [Continuing medical education in Russian neurology and neurosurgery]. *Zh Nevrol Psikhiatr Im S S Korsakova*. 2009;109(5):5-9.
5. Medina MT, Munsat T. Neurology education in Latin America and the World Federation of Neurology. *J Neurol Sci*. 2010; 15;298:17-20.
6. Medina MT, Munsat T. Continuing medical education in developing countries. *J Neurol Sci*. 200; 15;190:1-2.
7. Corrales J, Allegri RF, Pelli-Noble RF. Background of the Sociedad Neurologica Argentina: current state and concerns about neurologic education. *Neurology*. 2013;80:1978-80
8. Medina MT, Munsat T, Portera-Sánchez A, Durón RM, Becker CA, Holden KR; WFN Education Committee. Developing a neurology training program in Honduras: a joint project of neurologists in Honduras and the World Federation of Neurology. *J Neurol Sci*. 2007;253:7-17.
9. Birbeck GL, Munsat T. Neurologic services in sub-Saharan Africa: a case study among Zambian primary healthcare workers. *J Neurol Sci*. 2002;200:75-8.

## PRESIDENT'S COLUMN

# The Way Ahead

BY RAAD SHAKIR

It is an honor to write to you as the 10th president of the WFN. I follow a long and distinguished line of presidents over the past 56 years. Each president has complemented and strengthened the work of his predecessor and added his own touch to maintain the upward curve of our federation and carry on the torch of neurology. Our history is indeed illustrious and glorious thanks to their achievements. It was a great opportunity to have four previous presidents join me in Vienna. (See photo on page 14.) Unfortunately, James Toole was unable to join us. The contributions and wisdom of all of our presidents will be our guide for the future.

Our predecessors have laid out the path. As president, I will move full speed ahead with determination to carry out the tasks entrusted to me and to all the trustees. The newly elected officers — William Carroll (Australia) as first vice president and Wolfgang Grisold (Austria) secretary-treasurer general — have vast experience and the zeal to work. Gallo Diop (Senegal) is the first sub-Saharan African trustee, and he will add another dimension to the group.

Since my first involvement with the WFN over 33 years ago, I have learned that the way to make progress is to bring neurologists together, and to respond to their requests to be put in touch with



RAAD SHAKIR

colleagues. In an electronic world, communication is instantaneous and those with ideas may be anywhere in that world. To provide access to others with similar interests but who perhaps live in communities where the technology and financial support is different is what the WFN is all about.

My task and that of my fellow trustees is huge and daunting. As I said in my election statement, my plan is to involve all societies and their members in our activities. This will need openness and transparency to achieve inclusivity and collaboration. Transparency of our decisions is vital and will be adhered to in the years to come. As new trustees, our plan of action will be formulated in the first year of office, and we will fulfill our responsibilities with the diligence that the Council of Delegates expects of us. At least for me, and I hope for the WFN, the elections in Vienna were a turning point toward Global Involvement Through Regional Empowerment. This in my opinion is crucial for the future success of the WFN.

We now live in a world of change both

in our scientific understanding of our speciality and the need for cooperation between all our six regions. Many will need to interact closely with each other for advancement of their scientific progress, education, training and provision of care to patients. This needs an organizer, a go-between, a fixer, and the WFN can and should be all of that.

Collaboration through WFN member societies is possible because we all have the ability to help each other and strong reasons to do so. Moreover, our neurology specialty associations are also strong and willing to participate. This is the way forward.

The newly elected trustees started work in earnest in January by holding a first meeting at the headquarters in London. It brought together the regional directors and chairs of initiatives, and will culminate in the reconfiguration of our committees. The work will begin immediately. I think that the outcome will determine our future for the next four years. I am under no illusion about the seriousness of the task ahead but

# Delegate Vote and Election Results

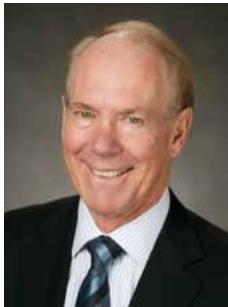
BY KEITH NEWTON, WFN EXECUTIVE DIRECTOR

Almost 80 delegates and representatives assembled Sept. 22, 2013, in Vienna, for the Annual General Meeting of the Council of Delegates. They arrived for registration to be greeted by a colorful oriental display from the three cities bidding to host the 2017 World Congress of Neurology — Hong Kong, Kyoto and Seoul.



Raad Shakir

The importance of the occasion was evident to everyone, even more so because, in addition to the selection of the WCN 2017 venue, delegates were asked to choose three new officers and one new elected trustee.



William Carroll

As well as presentations from the three member societies, delegates heard an assessment from the Federation's Professional Congress Organizer (PCO) and received reports from members of the site visit team to help them make up their minds. It was a difficult choice, but eventually Kyoto won the day.



Wolfgang Grisold

Just as keenly contested were the elections for officers and trustee, where 11 highly qualified candidates from across the globe stood for President, First Vice President, Secretary-Treasurer General and Elected Trustee. All of them addressed the assembly to present their vision and goals if elected. Ballot papers were collected and counted outside the meeting by WFN Executive Director Keith Newton with assistance from Austrian Society Executive Secretary Tanja



Amadou Gallo Diop

Weinhart, under the close supervision of WFN Past President Johan Aarli and EFNS Vice President Marianne de Visser. The results, announced at the close of the meeting, were:

- WFN President, Raad Shakir (UK)
- WFN First Vice President, William Carroll (Australia)
- WFN Secretary-Treasurer General, Wolfgang Grisold (Austria)
- WFN Elected Trustee, Amadou Gallo Diop (Senegal)

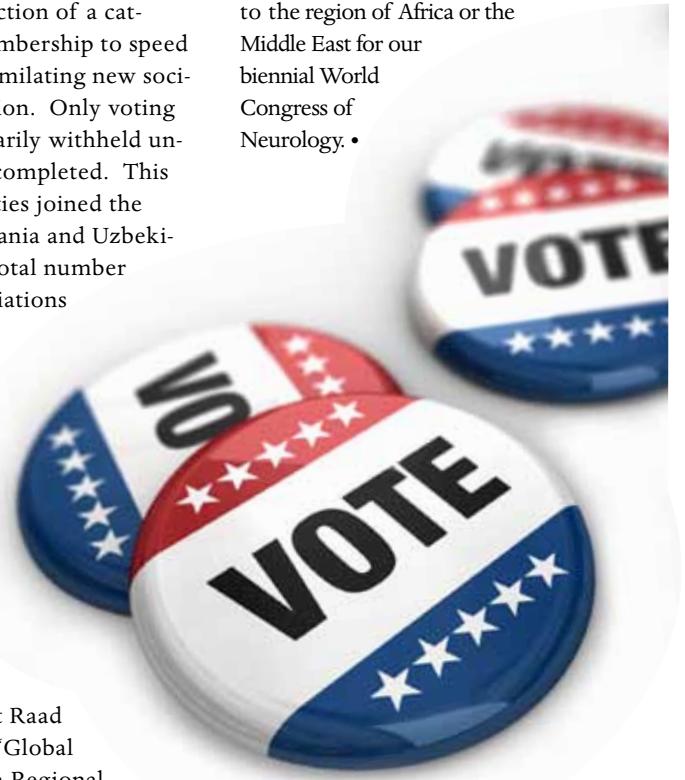
Delegates also received reports from officers and committee chairs, including chairs and co-chairs of the Education and Applied Research Committees. The former gave a PowerPoint presentation of the activities of the Education Committee, including the development of standard operating procedures for committee activities, such as the monitoring of educational grants, departmental visit programs, and teaching center accreditation. Donna Bergen, chair of the Applied Research Committee, reported that new Applied Research Groups have been established on coma, neuro-oncology

and neuro-infectious diseases.

The Membership Committee has proposed the introduction of a category of Pending Membership to speed up the process of assimilating new societies into the Federation. Only voting rights will be temporarily withheld until all formalities are completed. This year, three new societies joined the WFN — Oman, Tanzania and Uzbekistan — bringing the total number of neurological associations in the organization to 117.

Regional Initiatives in Africa, Asia and Latin America have already begun to lay the foundations for the future and look set to build on them under the next administration now that Raad Shakir has promised "Global Involvement Through Regional Empowerment."

By common consent, the Vienna Congress was a resounding success. Planning for Chile 2015 has already begun; Kyoto, Japan is our destination in 2017; and members are now urged to think ahead to 2019, when we return to the region of Africa or the Middle East for our biennial World Congress of Neurology. •



## Featured Articles from JNS

BY JOHN D. ENGLAND, MD

Beginning with this issue of World Neurology, we will feature an "Editor's Selection" of articles from the *Journal of the Neurological Sciences* (JNS). Elsevier, the publisher of JNS, has agreed to provide free access to these articles in PDF format to the members of the World Federation of Neurology. Simply click on the PDF of the article to access it.



John D. England

For this issue, we will feature two recent articles:

- Andreas Steck and members of the Education Committee of the World Federation of Neurology (WFN) provide the results of a survey, which examined the current global state of training in neurology. These results were compared with a previous survey done in 2006. The paper outlines the areas where advances have occurred and also indicates areas where improvements are needed. The findings provide important data which should be helpful in guiding the future training of neurologists around the world.

The major disappointing aspect of the survey was that only 39 out of the 113 WFN member organizations provided answers to the survey. Most respondents were from Europe and Asia. Notable non-responders were Canada, France, India, Italy, Japan, United Kingdom and The United States. **Manuscript # JNS-D-13-00728**

- Maria Nagel and others from the University of Colorado, U.S. present a remarkable case of a patient suspected of having giant cell arteritis (GCA) whose temporal artery biopsy was initially negative for GCA. Further analysis demonstrated varicella zoster virus (VZV) antigen and VZV DNA in the temporal artery and adjacent skeletal muscle. More extensive pathological analysis of temporal artery sections adjacent to those containing VZV antigen

showed classic features of GCA. These findings build upon the previous research from this group, which detected VZV in the temporal arteries of 5/24 patients with clinically suspected GCA. Taken together, these findings raise important questions about the role of VZV in both suspected and proven GCA. **Manuscript # JNS-D-13-01090R1**

We hope that this new feature of highlighted articles from JNS will be a useful addition for readers of World Neurology. •

England is Editor-in-Chief, *Journal of the Neurological Sciences*.



# 100 Years of Expanding Networks in Neurology

PETER J. KOEHLER, MD, PHD, FAAN

Since we started this history column in 2010, we have paid attention to international relationships in the neurosciences, in particular the exchange of students and neurologists among institutes. In this essay, I will describe another way of international cooperation that coincided with the evolution of the specialization of neurology.

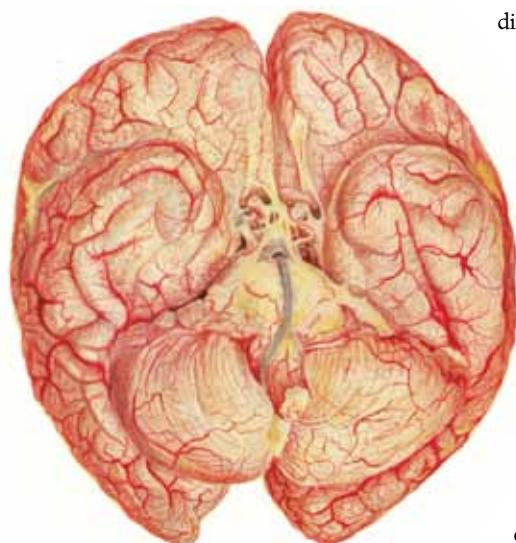


Peter J. Koehler

In general, specialization in medicine is considered to have started in the second half of the 19th century. It was accompanied by the establishment of journals, societies, university chairs, the invention and application of new instruments (ophthalmoscope, reflex hammers, etc., for neurology), and the publication of comprehensive textbooks.

During the 19th century, neurological textbooks appeared in several countries, usually written by one person. Examples are *John Cooke's Treatise of Nervous Diseases* (1820), *Moritz Romberg's Lehrbuch der Nervenkrankheiten* (1840), *William Hammond's Treatise on Diseases of the Nervous System* (1871), *Joseph Grasset's Traité Pratique des Maladies du Système Nerveux* (1878), and *Alexey Kozhevnikov's Rukovodstvo k Nervnym Boleznyam i Psichiatrii* [Treatise of Nervous Diseases and Psychiatry; 1883].

During this period, however, multi-volume, multi-authored books of general medicine started to appear (Reynolds *System* in five volumes, 1866-79; Albutt's *System* in eight volumes, 1896-9, Ziemssen's *Handbuch*). Although Dercum's 1895 *Textbook of Nervous Diseases* was multi-authored



From volume 10 of Bumke's and Foerster's *Handbuch*: pneumococcal meningitis.

(24), it comprised one volume. Hermann Nothnagel's *Specielle Pathologie und Therapie* (1895-1915) was on general medicine, but possibly because of his interest in neurology, 17 of the 41 volumes were on neurological subjects, including well-known books by



Editorial advisory board of Vinken and Bruyn in the 1960s: (L-R) M. Critchley, A. Biemond, R. Garcin, K.J. Zülch, S. Refsum, P.J. Vinken, E. van Tongeren and G.W. Bruyn.

Freud, Hitzig, Möbius, Monakow and Oppenheim. With respect to neurology, it may be considered a kind of transitional book.

This year is the centenary of the completion of the first multi-authored and multivolume "handbook" devoted entirely to neurological subjects: *Handbuch der Neurologie* (1910-4). It was edited by the Berlin neurologist Max Lewandowsky (1876-1918). In the preface, he stated that "Until today, the field of neurology has not been mapped out by means of a student handbook. By such a treatment in handbook form, I mean a publication approach that circumscribes and integrates the whole field, with a uniform thoroughness and professionalism and which, in distinction with a shorter textbook, is based on an extensive presentation of the available literature in a documentary style."

The handbook appeared in six volumes and was written by 81 authors, including 21 foreign authors. Due to Lewandowsky's untimely death, supplements were edited by Oswald Bumke and Otfried Foerster. Interestingly, the second supplementary volume contained almost entirely observations from war injuries of the peripheral nerves and spinal cord and was written by Foerster himself (altogether 1,152 pages). The same Bumke and Foerster continued the project with a new series of 18 volumes, published between 1935 and 1937. It is clear that the area of neurology had expanded and knowledge increased, but also became a more international undertaking with no less than 133 authors, of whom 45 were from 14 non-German countries.

After World War II, a new project was started in the 1960s, when the Dutch neurosurgeon Pierre Vinken and neurologist George Bruyn launched the *Handbook of Clinical Neurology*. This project became even more comprehensive than Bumke's and Foerster's *Handbuch*. It was clear for them that the new series should be published in English (like *Excerpta Medica* that inspired them, for which they both worked and that was started in the late 1940s). They were able to engage a large international network of authors. The number of authors of the 78 volumes that Vinken and Bruyn edited (between 1968 and 2002) was 2,799 of which 48 percent was American.

Considering the publication of these three 20th century multivolume neurological textbooks, several changes in the field of neurology may be distinguished. Obviously, knowledge increased and more space was needed to describe it. Subspecialization within neurology is becoming evident in the course of publication of these volumes. Language now changed from German to English, reflecting the ever-changing teaching centers of medicine through the ages.

While Paris, after Leiden and Edinburgh in the 18th century, had played an important role as the major center of medical teaching in the first part of the 19th century — resulting in a change from Latin to English and French — this gradually shifted to Austria and Germany in the 1860s. Following the two World Wars, English became the major language in (medical) science. Although basic neurological knowledge was spread throughout the pre-WWII German handbooks, Vinken and Bruyn emphasized the clinical aspect. Today, the three handbooks may be considered important sources for the history of neurology, reflecting the emergence of the specialty of neurology as



From volume 3 of Lewandowsky's *Handbuch*: chapter on paralysis agitans by Foerster and Lewy.

a scientific and clinical entity. Moreover, it shows the increasing international cooperation throughout the 20th century. •

Koehler is neurologist at Atrium Medical Center, Heerlen, The Netherlands. Visit his website at <http://www.neurohistory.nl>.

## References

- Koehler PJ, Jennekens FGI. Vinken and Bruyn's *Handbook of Clinical Neurology*: A witness of late 20th century neurological progress. *J Hist Neurosci* 2008;17:46-55.
- Stahnisch FW, Koehler PJ. Three 20th-century multi-authored handbooks serving as vital catalyzers of an emerging specialization: a case study from the history of neurology and psychiatry. *J Nerv Ment Dis*. 2012;200:1067-75
- Koehler PJ, Stahnisch FW. Three Twentieth-Century Multiauthored Neurological Handbooks - A Historical Analysis and Bibliometric Comparison. *J Hist Neurosci*. 2013 Oct 1. [Epub ahead of print]

## FROM THE EDITOR-IN-CHIEF

# In This Issue

**W**orld Neurology now has a superb Editorial Advisory Board, representing every region, and equally important, representing the WFN's website and *Journal of Neurological Sciences*. In “@WFNeurology” on page 9, Walter Struhal and Peter Engel discuss the advantages of these linkages.



**DONALD H.  
SILBERBERG**

Also in this issue, for the first time, you can see a list of some of the current articles in the *JNS*, with hyperlinks to the PDFs of selected articles. Similarly, when I receive announcements that require immediate display, I forward them to Engel for posting on the WFN website.

This issue is the fifth online, with subsequent issues to come every two months. This is a good time to remind you that the content of *World Neurology* is entirely what you wish to make it. Please send me reports from your region, historical or personal reflections, notices of future events, letters to the editor, and of course, original articles on a topic

that interests you. When you publish work that will later be submitted to a peer-reviewed journal, you don't need to worry about copyright issues on the part of *World Neurology* or the WFN.

You can help with our distribution list. Because many national societies are reluctant to release email addresses due to privacy concerns, our list serve is incomplete.

Please ask your colleagues if they are receiving communications from *World Neurology*. If not, please advise them to send their address to me or to Keith Newton, assistant editor, at [keith@wfneurology.org](mailto:keith@wfneurology.org), in order to become a subscriber. If your national society can provide a list, please ask that it be sent to us.

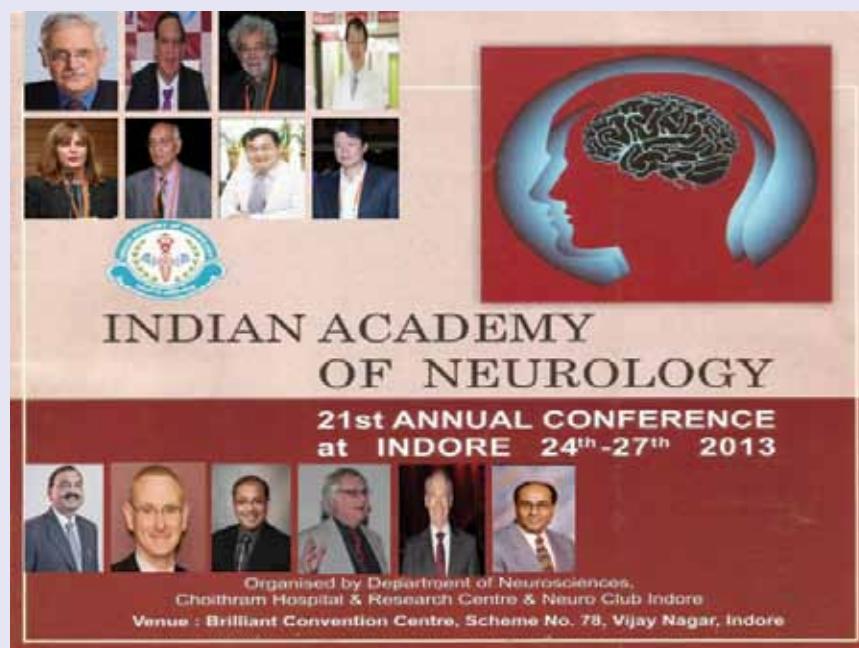
Finally, a wish for a happy, productive and healthy 2014 to all. •

## Enhanced Academic and Outreach Services of the Indian Academy of Neurology

BY MAN MOHAN MEHNDIRATTA, MD, DM (NEUROLOGY), FAMS, FRCP

**T**he Indian Academy of Neurology (IAN), with its primary objective of imparting education, coordinates various activities that support and supplement formal neurology education. It has been instrumental in organizing various national and international conferences, workshops and Continuing Medical Education (CME) programs with national and international outreach programs<sup>1</sup>.

Professor Marco T. Medina, professor of Neurology from Honduras was one of the faculty invited as part of this outreach program. Other invited international faculty members were Beom S. Jeon, vice president of the Asian Oceanian Association of Neurology; William Carroll, vice president of the World Federation of Neurology; Robert H. Brown, president of the American Neurological Association; Shri K. Mishra; Bhupendra O. Khatri; Neeraj Kumar and Page Pennel; J. D. Khandekar (USA); Barry Snow; Olivier Dulac and Martin Brodie. (See Figure 1.) These academic outreach programs foster critical and analytical thinking, professional and experiential learning and promotes research<sup>2,3</sup>. It has an advocacy subsection convened by Man Mohan Mehndiratta and ably assisted by other committed members of IAN — Apoorva Pauranik and Lakshmi Narsimhan. It had been their sincere endeavor to improve the status of public awareness, education and care in India. This subsection organizes workshops to train the members in skills, organizes the neurology quiz, neurology education courses, public awareness and edu-



**Figure 1. International speakers on the occasion of IAN Conference Oct. 24-27, 2013:** Upper panel from left to right are Robert H. Brown (USA), Marco T. Medina (Honduras), Olivier Dulac (France), Shuu Jiun Wang (Taiwan), Page B. Pennell (U.S.), Shri K. Mishra (U.S.), Beom S. Jeon (South Korea) and Keun Hwa Jung (South Korea). Lower panel from left to right are Vijay Sharma (Singapore), Barry Snow (New Zealand), Neeraj Kumar (U.S.), Martin J. Brodie (Scotland), William Carroll (Australia) and Bhupendra O. Khatri (U.S.).

cation series, CMEs and camps. Hence, it streamlines and disseminates authentic and comprehensive outreach public health education.

Like every year, the 21st Annual Conference of Indian Academy of Neurology, the IANCON2013, was held at Indore Oct. 24-27, 2013. It was hosted and organized by the Department of Neurosciences, Choithram Hospital and Research Centre and Neuro Club Indore. The conference featured the major breakthroughs and developments in the field of neurology — from clinical practice to research and technology and was attended by renowned national and international faculty

and approximately 1,000 delegates. It included a highly informative and interesting scientific program starting with CME on neurological manifestations of systemic diseases, which addressed a wide range of conditions such as nutritional deficiencies, SLE and antiphospholipid antibody syndrome, liver disease, pregnancy, lymphoma and leukemia and small vessel disease. This was followed by symposia and seminars. The theme of one of the symposia was neurotechnology and e-learning, which was chaired by Mehndiratta and

see **INDIAN ACADEMY**, page 14

## Mark Your Calendars 2014

### The 2nd International Conference on Heart & Brain (ICHB 2014)

Feb. 27-March 1

Paris

<http://www2.kenes.com/ichb/Pages/Home.aspx>

### 14th Asian & Oceanian Congress of Neurology (AOCN 2014)

March 2-5

Macao, China

<http://www.aocn2014.org/index.html>

### Eighth Symposium on Neuroprotection and Neurorepair — 2014

April 9-12

Magdeburg, Germany

<http://www.neurorepair-2014.de/>

### Alzheimer's Disease International Annual Conference 2014

May 1-4

San Juan, Puerto Rico

<http://www.adi2014.org/>

### International Child Neurology Congress 2014

May 4-9

Igazu Falls, Brazil

<http://www.icnapedia.org/>

### Third International Conference & Course on Neuromuscular Ultrasound

May 22-24

Vienna

<http://www.ispni.org/>

### EFNS-ENS Joint Congress, Istanbul 2014

May 31-June 3

Istanbul

<http://www.efns.org/EFNS-ENS-Joint-Congress-Istanbul-2014.877.0.html>

### Movement Disorder Society Annual Congress 2014

June 8-12

Stockholm

[http://www.movementdisorders.org/congress/past\\_and\\_future.php](http://www.movementdisorders.org/congress/past_and_future.php)

### Congress of the European Committee for Treatment and Research in Multiple Sclerosis 2014

Sept. 10-13

Boston, U.S.

<http://www.ectrims.eu/conferences-and-meetings>

### Ninth World Stroke Congress

Oct. 22-25

Istanbul

<http://www.world-stroke.org/meetings/world-stroke-congress>

### 10th International Congress on Non-Motor Dysfunctions in Parkinson's Disease and Related Disorders

Dec. 4-7

Nice, France

<http://www.kenes.com/nmdpd>

# Teaching Center Update

BY WOLFGANG GRISOLD AND RAAD SHAKIR

The WFN mission is to foster quality neurology and brain health worldwide. One of the cornerstones of this mission is to sponsor and support worldwide concepts of education. This is the function of the WFN Education Committee. In addition to other valuable tools as congresses, symposia, departmental visits and traveling fellowships.

The WFN has developed the concept of worldwide approved teaching centers. These centers should fulfill standards defined by the WFN in order to fulfill the role for training neurologists and perform this in a standardized internationally recognized manner. Moreover, these centers will be able to train neurologists from low income countries to further their education and improve their clinical and research abilities.

Once these centers are approved, they can offer training fellowships, in a neurological subspecialty as well as a full training program to produce neurologists who will go back and serve in their own countries. The WFN approval will therefore carry the stamp of international recognition on the status and performance of a training program.

The department visit process has been adapted from the UEMS (UEMS.net) department visitation process. This process assesses training centers, their hospital resources and equipment, and the training facilities, and has a system of assessing the opinions of all persons involved in the training process using standardized questionnaires. In addition to structured personal interviews, a randomly selected person from all groups is involved in the process. The analysis of the questionnaires and of the structured interviews are all part of the report, which also includes the activities of the hospital, access to other related fields (e.g., neurosurgery) and the completeness of the training program. The report concludes on the status of the present situation and also gives recommendations for further improvement and development.

The WFN Education Committee (Chair Steven Sergay and Co-Chair Wolfgang Grisold) has developed a structured and a well-organized questionnaire, which

covers all aspects of a neurological training center. Prior to any visit, the size, structure as well as the personnel are to be explored. In addition, residents, trainers and hospital staff will be asked to answer standardized questionnaires, aimed at various educational aspects.

The Neurology Center in Rabat was the first neurological center worldwide to apply for this status.

The WFN committee consisted of Wolfgang Grisold (trustee, co-chair of the Education Committee), Raad Shakir (then WFN secretary-treasurer general) and Riadh Gouider (president of the Pan African Association of Neurosciences Societies). The visitors were welcomed by the faculty of the hospital and academic members of Rabat University. All information and facts about the hospital and the Moroccan neurology training system were presented.

The Rabat neurological department consists of several sections: an outpatient's service which is closely associated with neurosurgery, neuroradiology, neuropathology and with the national center of rehabilitation and neurosciences.

The practical visit was guided through the neurological departments, as well as the laboratories, including histopathology, chemistry and genetics. During the visit, patients and trainees, as well as post-graduate and undergraduate students, were met and some questions and discussion were carried out.

The visit also included the electrophysiology laboratories, where practical teaching was observed. The associated departments of neurosurgery and neuroradiology were well equipped, modern CT, MRI, angiography suites and gamma knife were all observed. There is also a newly adapted rehabilitation unit. The outpatient and emergency as well as the consultation system of the hospital were looked at in detail. The academic research unit of the university provides laboratories including an animal house with space for scientific cooperation, which are open to projects from the neurological department.

The structure of the visit was supplemented by interviews with residents, teaching professors and hospital staff. These interviews were performed in a standardized written format, which was distributed prior to the visit to faculty and current residents. In addition, three teachers and four residents were randomly selected and attended personal interviews. They were asked standardized questions. Also the director of the hospital was personally interviewed. The visiting WFN committee carried out the confidential interviews. A résumé was contained in the report.

Based on the visit, including discussions, there were presentations of the faculty, and detailed analysis of the various aspects of the department. The

visiting committee was fully satisfied that the Hospital Center Ibnou Sina, Rabat, is fully compliant with all aspects of a WFN training center. It will be able and willing to train not only its own national neurologists, but neurologists from Africa and elsewhere and will be providing one year fellowships, as well as a full four year training programs.

The concept of WFN teaching centers will be further developed, and the WFN

website will provide a detailed definition of teaching centers, as well as the requirements, questionnaires and application details. Being a WFN teaching center is a sign of excellence and clearly conveys international recognition of the teaching center in that it fulfills all of the criteria in its structure, equipment and the teaching facilities needed to participate in the important role of neurology education in the future. •



Wolfgang Grisold



Raad Shakir

## Join us for AOCN 2014

Please join us for the 14th Asian and Oceanian Congress of Neurology (AOCN) March 2-5 at the Convention and Exhibition Centre of The Venetian® Macao.

AOCN will become a biennial conference starting in 2014. The Hong Kong Neurological Society (HKNS) is honored to host AOCN 2014 and will bring this special occasion to Macao, which is only 60 km from Hong Kong. There are direct

AOCN 2014

March 2-5

[www.aocn2014.org](http://www.aocn2014.org)

flights between Macao and the cities in Mainland China, Taiwan, Korea, Japan, Singapore, Malaysia, Thailand, The Philippines, Indonesia, Europe and the United States. Also, there is frequent ferry service between Hong Kong and Macao Ferry Terminal.

Hong Kong and Macao are at the center of Asia with easy access to Asian neurologists. Macao is an interesting place with perfect blending of East and West.

Following the footsteps of the previous successful congresses, the Organizing Committee has been working closely with AOAN to provide you with a valuable opportunity to learn new advances in the field of neurology, an interactive platform for exchange of experiences and a warm atmosphere for establishing collaboration networks.

AOCN 2014 will cover the latest in the speciality of neurology as well as in the allied subspecialties. The Scientific Program Committee has prepared an academically rich scientific program with the regional specialty societies, including The Asian Pacific Stroke Organization (APSO), The Asian Society Against Dementia (ASAD), Commission for Asian Oceanian Affairs (CAOA) of The International League Against Epilepsy (ILAE), Asian and Oceanian Chapter International Federation of Clinical Neuro-

physiology (IFCN), Asian Regional Committee for Headache of International Headache Society (IHS), The Movement Disorder Society (MDS), The Pan-Asian Committee on Treatment and Research of Multiple Sclerosis (PACTRIMS) and The World Federation for NeuroRehabilitation (WFNR). Besides these societies, we acknowledge The Chinese Society of Neurology under the Chinese Medical Association to be one of the supporting organizations of the congress.

Lectures in a wide range of topics in multiple sclerosis, epilepsy, infection, headache and pain, dementia, movement disorder, stroke, neurogenetics, neurorehabilitation, neuromuscular diseases and neurophysiology as well as the pre-congress workshops have been organized. Renowned speakers from all around the world as well as local experts from the Asia-Pacific are invited to share their experience and expertise with more than 1,500 neurologists, researchers and other health care professionals from related medical disciplines. An exhibition also will be held concurrently to show you the latest products and services offered by the health care industry.

To promote the development of neurology in the region, the Scientific Program Committee of the AOCN 2014 will be presenting oral and poster presentations from neurologists and neurology trainees at the congress.

**Plan to attend this important neurology event, and register online now.** We look forward to seeing you at AOCN 2014!

For more information, visit [www.aocn2014.org](http://www.aocn2014.org). •



# Global, Interdisciplinary, Integrative

BY THOMAS H. BAK AND FACUNDO MANES

The WFN Research Group on Aphasia, Dementia and Cognitive Disorders (RG ADCD) goes back to the Problem Commission on Aphasiology, founded in Varenna on Lago di Como in 1966, as one of the first “problem commissions” (as the research groups were initially called) of the WFN.

From early on, the group’s activities have been strongly influenced by two complementary developments. The first one is the continuous move toward a broader, interdisciplinary, collaborative and integrative approach. Early in its history, the group recognized the close connection between aphasia and other aspects of cognition.

Cognitive symptoms can occur in a wide range of neurological diseases, such as stroke, neurodegeneration, inflammation, neoplasms, trauma, epilepsy or even migraine. Accordingly, our group has always been keen to establish collaborations with other research groups. The most lasting and fruitful one has been the collaboration with the WFN Research Group on Motor Diseases (RG MD). It has been given a strong impetus by recent advances in clinical studies as well as in basic sciences, such as the discovery of the C9ORF72 gene, which can cause both Motor Neuron Disease (MND) as well as Frontotemporal Dementia (FTD).

Within a few years, MND changed from a classical prototype of a purely motor disorder to a prime example of the overlap between movement and cognition. The collaboration between RG ADCD and RG MD kept up with these developments. We have organized joint symposia and teaching courses across the world and the official journal of the RG MD, *Amyotrophic Lateral Sclerosis*, has been renamed to *Amyo-*

*trophic Lateral Sclerosis and Frontotemporal Degenerations* and is now also endorsed by our group.

The second development, which has defined our activities in the last decades, is a move to an increasingly global perspective. Originally, the biennial meetings of the group alternated between North America and Western Europe. From the late 20th century, they expanded to encompass Central/Eastern Europe (Prague), South America (Praia do Forte, Buenos Aires) and Asia (Istanbul, Hyderabad) with the next meeting due to take place in Hong Kong this year.

This has led with time to an increasingly diverse, international membership as well as to a more global focus of our meetings. Thanks to the Cognitive Clinics Worldwide grant from the WFN, our group has been able to organize teaching courses in cognitive neurology in Hyderabad, Kolkata and Bangalore in India, as well as in Beijing, Ulan Bator, Havana and Cartagena.

We are in process of establishing local networks of expertise throughout the world as well as websites containing relevant information about cognitive tests available in different countries and languages. This will provide valuable information to practitioners wishing to establish cognitive clinics in their countries.

An important part of our strategy to be globally inclusive is to make sure that our meetings and courses are affordable to everyone interested. This is particularly relevant for the young neurologists, who we welcome into our group as members of Forum of Young Researchers (FYRE). At our last meeting in Hyderabad, the FYRE members were invited to stay free of charge with local families, a way of creating personal friendships as well as professional partnerships.

These activities belong to the very core of our mission. Our growing interaction with neurologists across the world made us increasingly aware of the importance of linguistic, cultural and social factors in the diagnosis and treatment of aphasia, dementia and cognitive disorders. The same disease, such as FTD, can present differently in different countries and cultures<sup>1</sup>—an observation that has to be taken into account when developing universally applicable diagnostic criteria. Likewise, cognitive tests cannot be applied across the world without being properly translated, adapted and validated. But



Attendees and participants in Hyderabad.

the challenge of a global approach to cognitive disorders also brings opportunities.

Studies extending beyond the Western world can avoid certain confounding variables and contribute to new insights, as illustrated by recent research on the relationship between bilingualism and dementia<sup>2</sup>. Our courses and meetings highlight such topics, raise the awareness and offer practical advice and help to researchers as well as

clinicians. We hope that in the future, while consolidating our programs in Asia and Latin America, we will be able to extend our activities further to encompass Africa.

The recent change in our name to the WFN Research Group on Aphasia, Dementia and Cognitive Disorders (RG ADCD) is the next, logical step in our group’s continuous development. The change was suggested at the World Congress of Neurology in Vienna and approved by the WFN Nov. 1, 2013.

The new name reflects changes, which have happened in the group gradually over the past decades. A large number of our members focus their research on different types of dementia, in particular FTD<sup>1,3</sup>,

as well as Alzheimer’s Disease and vascular dementia<sup>2</sup>. Our biennial meetings as well as our teaching courses cover many dementia-relevant topics, with a particular emphasis on cognitive assessment. Moreover, research on progressive aphasia,

reflected in the recent diagnostic criteria<sup>4</sup> brought together aphasias and dementias, highlighting clinical as well as biological connections between both disease groups.

We hope that the broader scope of our group will attract both scientists and clinicians from all over the world with an interest in research on aphasia, dementia or any other cognitive disorder.

If you are interested in joining the group or attending our biennial meeting in December 2014 in Hong Kong, contact thomas.bak@ed.ac.uk. •

Bak and Manes are the chair and co-chair, respectively, of the WFN Research Group on Aphasia, Dementia and Cognitive Disorders.

## References

1. Ghosh A, Dutt A, Ghosh M, Bhargava P, Rao S. Using the revised diagnostic criteria for Frontotemporal Dementia in India: Evidence of an advanced and florid disease. *PLoS one*. 2013;8(4):e60999.
2. Alladi S, Bak TH, Duggirala V, Surampudi B, Shailaja M, Shukla AK, et al. Bilingualism delays age at onset of dementia, independent of education and immigration status. *Neurology*. 2013;81(22):1938-44.
3. Rascovsky K, Hodges JR, Knopman D, Mendez MF, Kramer JH, Neuhaus J, et al. Sensitivity of revised diagnostic criteria for the behavioural variant of frontotemporal dementia. *Brain*. 2011;134:2456-2477.
4. Gorno-Tempini ML, Hillis AE, Weintraub S, Kertesz A, Mendez M, Cappa SF et al. Classification of primary progressive aphasia and its variants. *Neurology*. 2011;76(11):1006-14.

## WFN Online Services Reach Out to Gen-Y Young Neurologists

BY W. STRUHAL AND PROF. P. ENGEL

Young individuals born between 1981 and 1999 belong to Generation Y (Gen-Y). They are also called Digital Natives. In contrast to their parents belonging to the Baby Boomer generation, Gen-Y individuals are comfortable with the World Wide Web. They expect to find all information online, they rapidly adopt new online services and appreciate interacting digitally. Residents and young neurologists are mainly now recruiting from this new generation. Gen-Y neurologists do show fundamental different knowledge

acquisition strategies mainly focused on online resources, challenging not only online services, but also training and teaching<sup>1,2</sup>.

WFN has a fundamental interest in attracting these young neurologists to its organization and to including them in WFN’s activities and projects. In addition, WFN aims to support and foster active contributions of Gen-Y neurologists to the biannual world congresses of neurology (WCN).

To achieve this aim, the WFN Website Committee has extended its online footprint from website alone to social

media. There are distinct differences between the online service of a website and social media. A website provides one-directional information like other mass media (one sender-many recipients). In contrast, social media offers the opportunity to discuss a topic, add personal opinions or simply show that the topic is appealing by “liking” it (many senders-many recipients). While Baby Boomers appreciate the mass media approach of a website, Gen-Y’ers are used to social media and expect to have the chance to interact with information online rather than simply consume it. Another difference between websites and social media is that with websites users become aware of news published only if they revisit the website (the user comes to website content). On global organizations, users usually

see DIGITAL, page 14



# Neurology Training for Non-Neurologists in West Africa

Sept. 15-18, 2013

This course was jointly funded by the Movement Disorder Society (MDS) and the World Federation of Neurology. Additional co-sponsors were the Fondazione Grigioni per il Morbo di Parkinson (Italy) and the Society of Worldwide Medical Exchange (U.S.). This was the first neurology course designed for medical doctors who are not specialized in neurology. It was also open to neurologists interested in training in the field of movement disorders and dementia.

Participants were invited from throughout West Africa. Thirty-six participants attended the course, from Ghana (24), Nigeria (6), Sierra Leone (3), Gambia (2), and Cameroon (1).

The international faculty consisted of 16 international and local members, including neurologists, geriatricians, nurse specialists, a neuropsychologist, a physiotherapist, a nutrition specialist and a general practitioner from rural Ghana. The opening ceremony included guests such as the representative of the Minister of Health and of the nursing system in Ghana, the Italian Ambassador in Ghana, the chairman of Internal Medicine Department of the Teaching Hospital in Accra.

The course was run in English and

included slide presentations and practical sessions with assessment of patients. Slide sessions focused on Parkinson's disease (PD), dementia and other neurodegenerative disorders, covering epidemiology, diagnosis, pharmacological and non-pharmacological therapy. For the practical sessions with patients, participants were divided into small groups of five to six each, under the guid-

## Course Organizers

**Roberto Cilia (Italy)**

roberto.cilia@gmail.com;

roberto.cilia@icp.mi.it

**Albert Akpalu (Ghana)**

a\_akpalu@yahoo.com.

ance of a faculty member, aiming to teach how to perform a neurological examination, neuropsychological scales screening for global and frontal-lobe cognitive functions and examples of physical therapy focused on gait and balance. Twelve patients attended these sessions, including PD, Lewy body dementia, Alzheimer's disease and spino-cerebellar ataxia. In a session titled "Bring Your Own Patient," participants presented a patient from their own clinic and discussed with

faculties the most relevant diagnostic and management challenges.

There were joint sessions with the PD Nurse Specialist Course, organized by Richard Walker (chair of the MDS Task Force on Africa).

Doctors and nurses had the opportunity to interact and share experiences about caring for patients. In particular, we included a Beyond the Neurologist session, dealing with the importance of a multi-disciplinary approach to patients, especially in settings where medications are limited.

Educational material has been prepared and released for this course, including basic information about motor and non-motor features of PD and/or dementia. These booklets were drafted by different health care professionals (nurses, nutrition specialist, physiotherapists, neuropsychologists) and were full of pictures and photographs to be suitable for patients and caregivers with low education.

The course was a great success and participants' feedback was positive in large part due to the practical sessions with patients and the interactive sessions. Each participant was given a DVD including all the slide presentations of the course, the UPDRS and the



Organizers of the neurology training: Albert Akpalu (left), Korle Bu Teaching Hospital in Accra, Ghana, and Roberto Cilia, Parkinson Institute, Milan, Italy.

cognitive screening scales, the two educational booklets and photographs of the course. An email list was created including all the participants as well as the Italian and Ghanaian faculty, to share information and help in challenges of everyday clinical practice.

One of our aims was to make this course an opportunity to boost the education in the field of neurodegenerative disorders in developing countries. We promoted two initiatives:

- The entire course was professionally videotaped to make it available online.
- We provided two travel grants for the MDS events in 2014, the International Congress in Stockholm and the MDS summer school. •

# Paroxysmal Diseases and PRRT2 Mutations

BY MARK HALLETT, MD, NINDS, BETHESDA

The paroxysmal dyskinesias are rare familial disorders, but very dramatic. There are three main types: paroxysmal kinesigenic dyskinesia (PKD), paroxysmal non-kinesigenic dyskinesia (PNKD) and paroxysmal exertional dyskinesia (PED).

PKD is typically precipitated by a quick movement, PNKD is precipitated by stressors such as coffee, tea and alcohol, and PED is produced after long periods of exercise. In the past few years, the main mutations responsible for all three have been determined. The gene for PNKD is myofibrillogenesis regulator 1, now called PNKD gene, and the gene from PED is the SLC2A1 gene that leads to GLUT-1 deficiency. Only recently has the gene for PKD been found to be PRRT2. As is often the case, when a gene has been found, some surprises emerge.

On Oct. 24, 2013, the Xiangya Hospital of Central South University in Changsha, China, held its Fifth Xiangya International Congress on the Clinical and Basic Research of Neurodegenerative Disorders focused on PRRT2 related diseases. The basic phenotype of typical PKD cases had been refined by Louis Ptacek's group in 2004, and this certainly helped in narrowing the gene search. Already at that time, it became clear that there was a significant overlap between PKD and infantile convulsions. At about the same time,

two years ago, Bei-Sha Tang's group from Central South University and Ptacek's group from University of California, San Francisco, identified PRRT2 as the relevant gene. Tang and his group as well as Ptacek came to the meeting.



Faculty at Changsha meeting.

Clinically, the PRRT2 mutation brings PKD and Benign Familial Infantile Convulsions (BFIC) together. Lu Shen, also from Xiangya Hospital, discussed the clinical aspects of the BFIC cases. Another significant phenotype is hemiplegic migraine, as discussed by Pierre Szepietowski from Marseille. Zhi-Ying Wu from Fudan

Hospital, Shanghai, widened the spectrum further by pointing out that PRRT2 mutations also have been seen in some cases of paroxysmal torticollis, episodic ataxia, childhood-absence epilepsy, febrile seizures, and both surprisingly and confus-

ingly, in cases of PED and PNKD. Hence, while there is a most typical phenotype of PRRT2, it appears to be able to cause a variety of paroxysmal disorders, mostly in young persons.

Qing Liu from Peking Union Hospital, Beijing, speaking for Li-ying Cui, reported on SPECT neuroimaging in ictal attacks of

PKD. There have only been a few cases and findings are not completely concordant, but it appears that there is hypermetabolism of the basal ganglia or thalamus during an attack. This confirms the general suspicion that the basal ganglia are the site of origin of PKD, but the nature of the abnormal activity is still unclear. There was discussion as to whether this might be a subcortical seizure, but clearly more data would be needed to determine this.

Ptacek led the discussion about the basic cellular mechanism of PRRT2. It is a novel protein and its role is not yet clear, but it interacts with SNAP-25. SNAP-25 is a SNARE protein that plays a critical role in synaptic release mechanisms, and is well known by neurologists as the target for botulinum toxin type A. He speculated that PKD might be a type of synaptopathy, a new general mechanism for paroxysmal disease, distinct from channelopathies, which cause other types of paroxysmal disorders. He noted that the PNKD protein also plays a role in exocytosis at the synapse.

Thus, PRRT2 mutations can lead to a variety of paroxysmal diseases that at the meeting were referred to as the PRRT2-related paroxysmal diseases (PRPDs). Taken all together, this class is not as rare as it might first appear. Moreover, knowledge of the gene function is leading to a new general mechanism for paroxysmal disorders.

The meeting, organized by Hong Jiang of Xiangya Hospital, provided a worthwhile current synthesis of this field, which certainly will have more surprises coming. •

# Parkinson's Disease: Web-Based Education Program for Health Providers in Cameroon

## Coordinator

Esther Cubo MD, PhD

## Academic Collaborators

Jacques Doumbe, MD; Erero Njiengwe, PhD; Sixto Cubo, PhD

## Computer Engineers Team

Centro Servicios Avanzados (CSA), Burgos (Spain), Paul Onana, Computer Engineer, Douala (Cameroon)

## Faculty Members

Ray Dorsey, MD; Christopher G. Goetz, MD; Katie Kompoliti, MD; Leo Verhagen, MD, PhD; Ellan Louis, MD; Richard Walker, MD; German Moris; Maria José Catalan, MD, PhD; Emily Wang, PhD; Meg Morris, PhD; Victor McConvey, RN; Antonio Campolungo, RN; Marie Cahill; Patrick Browne, RN; Jose Maria Trejo Gabriel y Galán MD, PhD

## Sponsor

International Parkinson's disease and Movement Disorder Society, through the Telemedicine Task Force

Due to rapid demographic changes, the prevalence of Parkinson's disease (PD) is increasing in sub-Saharan (SS) countries.<sup>1</sup> In contrast to developed countries, evidence suggests that most patients with PD are underdiagnosed and untreated, with markedly increased mortality and shortage of qualified personnel.<sup>2</sup> In the last years, there has been renewed interest from the World Health Organization, telecommunications companies and medical associations about the use of telemedicine in Africa.<sup>3</sup>

To help increase access to care and to train providers around the world using technology, the International Parkinson's disease and Movement Disorder Society (MDS) has sponsored pilot projects in care and education that can lay the foundation for reaching the majority of people with

PD. In this regard, a telemedicine program for health providers has been developed at Hospital Laquintinie in Douala, a 3 million inhabitants city of Cameroon.

The course is a web-based program that will provide participants with access to specialized education in the field of movement disorders, which is currently unavailable in their region. Local neurologists and professors at the University of Douala, including Jacques Doumbe, MD, chairman of the Department of Neurology (Hospital Laquintinie), and Erero Njiengwe, PhD (University of Douala) have significantly contributed to the implementation of this course at Hospital Laquintinie in Douala, Cameroon.

The course consists of 12 lectures over the course of a year, which will connect participants with experts in the field of

movement disorders using live video, slides, chat and audioconferencing. The participants will have the opportunity to receive MDS membership and its benefits, including special education to certify them to use the MDS rating scales. Two courses have been launched — one designed for doctors (neurologists, neurology residents, primary care and internists) and another one for other health professionals (nurses, physiotherapists and psychologists).

The course will be taught by professors from Hospital Universitario de Burgos, Hospital 12 de Octubre, Hospital Clinico San Carlos, Hospital Sant Pau and Hospital Central de Asturias all from Spain; Rush University Medical Center, Columbia University, Rochester University, all in the United States, Parkinson Victoria Association, Health Sciences University all in Australia, Hospital Universitario Asturias, Spain, North Tyneside General Hospital in Great Britain and Hospital Galway and Parkinson Galway Association in Ireland.

The main objectives of this pilot telemedicine education program will be to analyze the feasibility and adherence from participants, as well as satisfaction of users.

However, telemedicine for PD strategy development in Africa is challenging. It is still expensive, and most of the SS countries have inadequate and communication technologies infrastructure, which creates difficult implementation and little access to the population. Telemedicine also needs to demonstrate success and sustainability, and

this type of initiative has to survive beyond the end of the initial funding period.

Therefore, networking provides opportunities to spread the cost of infrastructure of telemedicine development between the local governments, business, foreign education providers and health sectors; therefore the cost burden should not be borne by just one sector. Telemedicine for PD should be recognized to remove or at least mitigate the barriers that society and physical geography imposes, especially rural areas in Africa, and to be culturally appropriate if they are to be adopted and sustained. •



Participants in the web-based program in Cameroon.

## References

1. Dotchin CL, Msuya O, Walker RW. The challenge of Parkinson's disease management in Africa. *Age Ageing* 2007;36:122-7.
2. Dotchin C, Walker R. The management of Parkinson's disease in sub-Saharan Africa. *Expert Rev Neurother*;12:661-6.
3. Scott RE, Mars M. Principles and framework for eHealth strategy development. *J Med Internet Res*. 2013 Jul 30;15(7):e155. doi: 10.2196/jmir.2250.

## Report of WFN CME

BY S. M. KATRAK, MD, DM, FRCPE

As president of the Indian Academy of Neurology (IAN) (2004-2005), I was disturbed by the fact that the WFN sponsored CME program had a weak presence in Asia, particularly India. This stimulated me to take over the reins as coordinator for this program in India. As per the advice and guidelines provided by Ted Munsat, I initially started the program in Mumbai. The first CME was held on July 17, 2005, on the topic of multiple sclerosis. From the feedback given by the postgraduate students, it was evident that they enjoyed the CME and found it to be unique and useful.

Considering the success of the program in Mumbai, I decided to "export" the program to other centers in India. I have received

enthusiastic support from my colleagues in nine centers all over India: R. S. Wadia (Pune); C. S. Meshram (Nagpur); S. Prabhakar (Chandigarh); J. S. Kathpal (Indore); S. K. Jabeen/Subhash Kaul (Hyderabad); Mutharasu (Chennai); P. C. Gilvaz (Thissur); Birinder Paul/Gagandeep Singh (Ludhiana) and P. S. Gorthi (New Delhi). I would like to thank them for their support in making this program a success in India.

In all these centers, the postgraduates, young and senior neurologists and internists attend these CMEs depending on the topic of discussion. Usually the postgraduates take up each chapter of the continuum highlighting the "take-home" messages. They are usually coupled with a consultant who highlights the salient points and gives the Indian perspective

because of the geographical differences in the pattern of neurological diseases.

It is difficult coordinating nine centers in India, but gentle reminders are sent to each coordinator at three- and six-month intervals about their "backlogs." What really works is a message that we owe the WFN and AAN a debt of gratitude for the gift of these issues of *Continuum*. Filling out the evaluations forms is just a small way of showing our appreciation. We have been able to get 659 evaluation forms for the year 2012 and 823 for the year 2013.

For the last two years, I got accreditation from the Maharashtra Medical Council (MMC), and they give two credit hours to every participant. This is an added incentive to attend at least in Mumbai and the other two centers in the state of Maharashtra (Pune and Nagpur).

No program can be sustained without some financial support. I was fortunate to

get a generous grant from the Australian Association of Neurologists for a sum of \$5,000 (Australia) in August 2005 and again in July 2006. We have used these funds frugally to send the evaluation forms to the U.K. and to courier the journals to the various centers in India. The balance funds are now low and soon we may need more funds.

We also are fortunate to get an unconditional educational grant from Intas Pharma, which has supported these CME session in many centers across India — particularly Mumbai. On behalf of the IAN, I would like to thank them for promoting neuro-education in India. I also would like to thank Satish V. Khadilkar who shares the responsibility of coordinator with me in Mumbai with the view of taking over as coordinator for India in the near future. •

Katrak is the national coordinator of WFN CME program in India.

# @WFNeurology

BY W. STRUHAL AND PROF. P. ENGEL

The World Federation of Neurology (WFN) is a huge and complex structure, representing neurologists worldwide. To achieve its aim, many international neurologists collaborate and work on WFN projects, represent the organization as officers or serve as editors or authors for WFN media. These initiatives play an important role in advocating the interests of neurologists on a global scale.

You can follow all of these activities and more at [www.wfneurology.org](http://www.wfneurology.org).

## Content

A major aim of WFN is supporting educational initiatives and encouraging global networking. The website provides a sound insight into WFN educational activities. These include WFN seminars in clinical neurology, which provide teaching and training materials and patient care guidelines. Exchange among

young neurologists is encouraged by WFN through programs such as the Turkish Department Visit, and available grants and awards for young neurologists interested in extending their training internationally. Reports are published on projects such as the Zambia Project, which aims to improve medical care in Zambia. Young neurologists are encouraged to participate in the WFN, and the website

lists representatives of young neurologists. A singularly interesting section is neurology for non-neurologists, which provides educational materials for areas where there is a severe shortage of neurologists.

Bringing worldwide science and patient care closer together is a strong objective of the WFN. At [www.wfneurology.org](http://www.wfneurology.org), you will find details on the World Brain Alliance, an umbrella group of international neurological organizations. WFN applied research groups organize scientific projects



and educational activities in neurology subspecialties, and publish their activities on the website on an annual basis.

Some additional important topics presented at [www.wfneurology.org](http://www.wfneurology.org):

- WFN initiatives (e.g. the WFN Africa Initiative)
- Candidates for 2013 election, including the president of WFN
- WFN officers, national WFN delegates, WFN regional directors

## Do you want to keep up to date?

The WFN website provides insights into our organization, but it offers more than that. Neurology news of major global importance is published in WFN's publication *World Neurology* ([www.worldneurologyonline.com](http://www.worldneurologyonline.com)). Because one aim of the WFN web strategy is to establish direct interaction with its users, social media channels are offered.

You may follow WFN updates and actively exchange your thoughts with WFN on Facebook ([www.facebook.com/wfneurology](http://www.facebook.com/wfneurology)), Twitter ([www.twitter.com/wfneurology](http://www.twitter.com/wfneurology)),

or the World Federation of Neurology LinkedIn group ([linkedin.com](http://linkedin.com)). You can use these social networks to interact and get to know other participants of the XXI World Congress of Neurology in Vienna – the first World Congress where social media channels were offered. For Twitter users, please follow our official hashtag (#) and don't hesitate to use it in your tweets: [#WCNeurology](https://twitter.com/WCNeurology).

## Aims and vision of the WFN website

The WFN website and WFN digital footprint comprise a platform for neurologists who advocate neurology through WFN initiatives and projects, and inform the public on activities of WFN. Social media platforms offer the prospect of increased online interactivity and the hope that neurologists worldwide will interconnect more. The future vision is that these digital resources

will help to build a strong network of neurologists worldwide and strengthen scientific collaboration in neurological research and services.

We warmly invite you to visit [www.wfneurology.org](http://www.wfneurology.org).



# Moroccan Foundation of Neurology



Representatives met in May 2012 to discuss a foundation dedicated to developing neurological

The World Congress of Neurology, organized by the Moroccan Society of Neurology in Marrakesh, November 2011, was a great success at both the scientific and organizational level. Moreover, the conference has generated substantial financial benefits for both the Moroccan Society of Neurology and the World Federation of Neurology, which will devote 20 percent of its profits to the development of neurology in Africa.

Moroccan neurologists met in May 2012 and unanimously decided to devote all profits obtained by the Moroccan Society of Neurology to the creation of a foundation dedicated to the development of neurological sciences and the fight against neurological diseases in Morocco.

Indeed, Morocco is experiencing a delay in neurology and care of neurological diseases even compared to countries of the same level of economic development. The number

of neurologists remains low: 170 (counting the neurologists in training) for a population of 32 million. Besides, there are few hospital beds dedicated to neurology, and CT scans are only available in large cities.

The country has worrying indicators in public health. Neonatal and perinatal morbidity, which remain high, are causing a large number of children to experience neurodevelopmental disorders responsible for motor and cognitive disabilities that require rehabilitation throughout their lives.

In addition, urbanization, changing lifestyles and increasing life expectancy have caused a rapid epidemiological transition that led to an increase in diseases related to aging. Thus, an epidemiological survey conducted in Rabat and Casablanca in 2009, showed that the prevalence of stroke in people aged 65 years and older was 25 per 1,000. This is almost equal to that found in industrialized countries. As for dementia, the report of the WHO in 2012 estimated the number to be 100,000 cases. Also, Morocco suffers from an unusually high number of road traffic accidents responsible for head injuries and neurological disorders.

Faced with this alarming situation, the foundation is focused on these objectives:

- To advocate for the increase of the number of neurologists and other caregivers in the neurological field
- To advocate for a policy of prevention of neurological diseases in both children and adults
- To promote a better understanding of neurological diseases among the general population
- To fight against the stigmatization of patients with neurological diseases
- To inform national policymakers of the urgency to implement a policy of neurological diseases in Morocco
- To support education and research in neurology
- To promote the highest standards of ethics and practice in neurological sciences

By its bylaws, the Moroccan Foundation of Neurology is a non-profit organization that can receive donations from persons, associations and governments to accomplish its objectives. The foundation also aims to develop cooperation with other similar institutions in Africa and in the Arab world to improve neurological care in these regions.

The Moroccan Foundation of Neurology, with active support from the World Federation of Neurology, the World Health Organization and other international institutions, will undoubtedly succeed in its mission to improve the lives of patients with neurological diseases.

## BOOK REVIEW

## Breaking Down Neurophobia

BY SARAH MATTESON KRANICK, MD

A recent study asked medical students and internal medicine residents to rate eight medical specialties with regards to the students' feelings of competency and perceived difficulty. The 150+ respondents identified neurology as the specialty in which they had least knowledge ( $p < 0.001$ ) and was most difficult ( $p < 0.001$ ). [Winchuk AV BMC Medical Education 2010]

Similar studies in Europe and elsewhere have led to much consternation in the medical education literature over an emerging epidemic of "neurophobia." The demand for neurologists is predicted by the Workforce Task Force of the AAN to overtake supply by 2020, making "neurophobia" not just a problem for academic neurologists, but for all of primary medical education. Primary care doctors will be increasingly called upon to triage, diagnose and treat neurological disorders at a time when subspecialization is increasingly common among neurologists. How do we prevent "neurophobia" and increase the number of neurophiles among all of our medical students and medicine resident rotators?

The new edition of "DeJong's The Neurological Examination," by William W. Campbell, will appeal to neurophiles. It has been modernized in many ways — the four-color edition is much easier on the eye, for one thing. There are more images accompanying the text, with clearer photographs and MRIs to supplement the clinical vignettes.

The text has been reorganized somewhat, but still follows the general neurological encounter as most of us practice it. This book is longer than the prior edition by almost 200 pages, but the expanded material is primarily clinical in nature, and the neuroscience underlying these observations remain mostly the same. Most of us in practice will appreciate the balance of anatomy and pathophysiology here, as we are typically consulting such texts when we have just seen a patient with bilateral cortical ptosis, for example, and we are trying to remember whether supranuclear control

of the levator muscles has a left or right predominance. This is the sort of question Campbell answers for us time and time again, with a concise description of the anatomy involved. The "voice" of this textbook will remind you of a favorite professor from residency, and makes me envious of Campbell's students at USUHS.



Sarah Matteson Kranick

Throughout this edition, links have been inserted to various videos of the neurological exam and clinical examples of abnormal neurological signs. Having the Kindle edition would certainly make these (hyper)links easier to use, although some reviewers on Amazon have noted that the Kindle edition makes viewing tables less ideal. Unfortunately, after typing in four examples of links from the print edition, I found non-working videos each time. Future editions would benefit from a webpage devoted to accompanying videos, or a DVD included in the print version.

Frequently DeJong's is described as a book for residents, fellows or practicing neurologists. I agree that the level of detail is likely too much

**DeJong's The Neurological Examination**

By William C. Campbell

830 pages

for medical students, and that basic neuroscience must be mastered before attempting to understand clinical neurology. This textbook, however, can play an important role in medical education at all levels.

For many of us neurophiles, it was the detection of some abnormal neurological sign in a patient we saw as medical students that started our lifelong interest in neurology. In the short span of a four-week clinical rotation, we cannot expect every student to have enough patient encounters to prevent neurophobia. Showing them how we practice the neurological exam, and what resources we use to put abnormal findings into context, like this text, may break down some of the intimidation that surrounds our specialty. •

Kranick is chief of Neurology Consult Service, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Md.

## REPORT

continued from page 1

Viennese artists of 1900: Gustav Klimt, Egon Schiele and Oskar Kokoschka. In his recently published book, *Vienna and the Age of Insight*, Kandel related their artistic choices to new theories of mind of Freud [another Viennese], and used 21st century discoveries in functional brain mapping to explain perceptual and aesthetic responses to viewing a painting. Other plenary sessions were an opportunity to hear masterful synopses of developments in neurogenetics by John Hardy, PhD, (UK), the neurology of aging by Ayrton Massaro, MD, (Brazil), and recanalization in acute stroke by Werner Hacke, MD, (Germany), among others.

For the first time, the main scientific sessions included joint sessions with member organizations of the World Brain Alliance such as the World Psychiatric Association and the World Federation of Neurological Societies. Members of the recently formed network of international neurological subspecialty organizations also convened main sessions in their areas, bringing together the world's top neuroscientists in nearly every aspect of neurology. Reflecting its growing relationship with the WFN, the World Health Organization presented a session summarizing current programs aimed at neurological disorders such as its Non-Communicative Disease Initiative, which includes stroke as an important global target for prevention and care in the coming years.

The teaching courses took place on each day of the congress, each day covering the main topic of the next day's scientific sessions. The courses were attended by more than 4,500 participants. Workshops on EMG, magnetic stimulation and ultrasound of nerve, muscle and intra- and extracranial arteries offered

hands-on experience and an opportunity to confer with experts in these fields. Although most of the courses were aimed at consultant neurologists, there was a course especially for young neurologists, and crucial issues such as advocacy, how to write a paper and palliative care were also covered. An analysis of attendance will help guide programming of the WCN 2015 in Chile.

The Tournament of the Minds is a traditional contest, testing the neurological knowledge of teams nominated by their national societies. The final round was fought between Australia/New Zealand, Chile, India and the United Kingdom. Twenty questions brought the finalists down to the UK and Australia/New Zealand, with the latter winning the contest, medals and a large trophy. The tournament will be repeated in Chile at WCN 2015.

The social program organized by the local host society included a concert at the stunning Wiener Musikverein Concert Hall. The conductor of the orchestra was Norbert Pfaffmeyer, a practicing neurologist, and the program included the premier of a waltz composed by Vladimir Hachinski, who just finished his term as president of the WFN. The Heurigen evening at a traditional wine bar gave attendees a taste of the latest Austrian vintage and the local cuisine, and of course the splendors and history of Vienna were there to enjoy every day.

Abstracts of the platform and poster presentations presented at WCN 2013 will be published in the *Journal of Neurological Sciences*, the WFN's affiliated journal.

The next World Congress will take place in Santiago, Chile, in two years. During WCN 2013, the WFN Council of Delegates chose Kyoto, Japan, to be the site of the following Congress in 2017. •

## PRESIDENT

continued from page 3

with widespread advice and participation, I am confident we will identify the priorities for the future.

The WFN is but one of the organizations necessary to achieve these goals. It will do its best to be the catalyst and listen to all stakeholders. We have inherited a wonderful set-up from all our predecessors, and we should rise to the challenge to harness our legacy and add as much as we can with everyone's support.

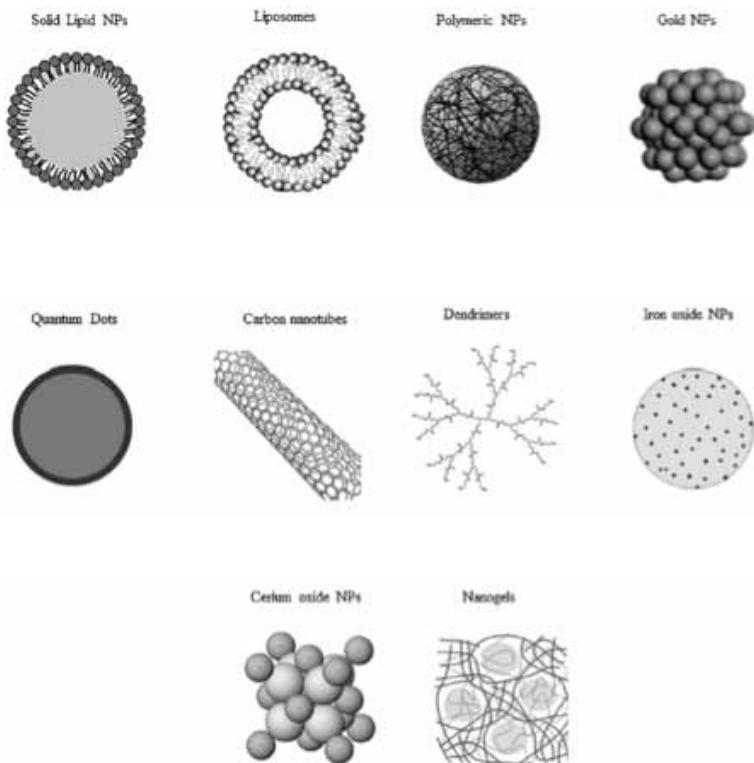
As secretary-treasurer general for the last seven years, I have learned that change is important and necessary, but in order to be implemented successfully it has to have relevance and be introduced with the agreement of the stakeholders. This will



Front Row (L-R): Jun Kimura (2002-2005); Lord Walton of Detchant (1990-1997); Johan Aarli (2006-2009) Back Row (L-R): Vladimir Hachinski (2010-2013); Raad Shakir (2014-2017)

be possible with the involvement of all our members. The new trustees have made clear commitments in their manifestos, which were clearly endorsed by the Council of Delegates. We will all work, consult, have our different points of view and then come to the appropriate collective conclusions. We will all work hard to justify the trust placed in us. •

# Nano-Neuromedicine



**Figure 1.** Different type of nanomaterials for biomedical use. Nanomaterials are commonly defined as objects with dimensions of 1-100 nm, which includes nanogels, nanofibers, nanotubes and nanoparticles (NP). In this illustration is represented the morphology of the most commonly used NP for therapy and diagnosis of neurodegenerative diseases (ND). (Ref. 3; reproduced with permission from Elsevier B.V. Ltd. © 2012.)

BY GIRISH MODI AND VINESH PILLAY

Nanotechnology employs engineered materials or devices (nanomaterials) with the smallest functional organization on the nanometer scale (1–100 nm) that are able to interact with biological systems at the molecular level<sup>1</sup>. They stimulate, respond to and interact with target sites to induce physiological responses while minimizing side effects<sup>1</sup>. By definition, nanomaterials are natural, incidental or manufactured materials containing particles (nanoparticles), in an unbound state or as an aggregate or as an agglomerate<sup>2</sup>. There are various methods of preparation of nanoparticles such as emulsion polymerization, interfacial –polymerization, –polycondensation, or –deposition, solvent –evaporation and –displacement, salting-out and emulsion/solvent diffusion, to name a few. There are several different types of nanostructures. These include polymeric nanoparticles, nanocapsules, nanospheres, nanogels, nanosuspensions, nanomicelles, nanoliposomes, carbon nanotubes and nanofibers<sup>3</sup> (See Figure 1.)

Nanoparticulate matter and related materials possess an inherent capability to efficiently and effectively cross the blood brain barrier (BBB) leading to an increased concentration of encapsulated bioactives and drugs in the cerebrospinal fluid (CSF). In addition to drug delivery, this BBB crossing ability of the nanoparticles can be employed to develop various real-time diagnostic tools.

Promising features of nanosystems in targeted CNS drug delivery are that

- their chemical properties can be easily modified to achieve organ-, tissue-, or cell-specific and selective drug delivery
- the delivery of the drugs can be controlled
- they increase the bioavailability and efficacy of incorporated drugs by masking the physicochemical characteristics and thus increase the transfer of drug across the BBB
- they protect incorporated drugs against enzymatic degradation
- they have fewer side effects<sup>1</sup>.

Taking these benefits into consideration, nanotechnology has immense potential such as in the field of neuro-molecular diagnostics, discovery of neurodegenerative markers, nano-enabled drug delivery and neuroactive discovery with implications reaching to the pre-

see NANO, page 16

## Our Brains, Our Future

BY MOHAMMAD WASAY MD, FRCP, FAAN

There are many days related to neurological diseases being celebrated by professional organizations in collaboration with the World Health Organization, national organizations and local health ministries, including World Stroke Day, Epilepsy Day and Rabies Day. These days have proved to be extremely helpful in promoting public awareness and generating advocacy throughout the globe including non-developed Asian and African countries.

For example, the World Stroke Organization announced a global competition for public awareness and advocacy campaign focusing on World Stroke Day. In 2012, Brazil, and in 2013, Sri Lanka won the competition creating a huge impact at the national level as well as the regional level. All of the days related to neurology are linked to neurological diseases.

A few years ago, Vladimir Hachinsky, then-WFN president, asked, “Why don’t we celebrate a day for the healthy brain?” The human brain is so fascinating and is

so closely linked to the health of the whole human being that we should promote healthy brains. The future of this universe is linked to our brains so we should start a global campaign with the slogan: “Our brains, our future.” This was suggested by the Public Awareness and Advocacy Committee.

Because the World Federation of Neurology was established on July 21, the Public Awareness and Advocacy Committee suggested that World Brain Day should be celebrated on the same date. This proposal was announced at the WCN Council of Delegates meeting in September, and the proposal was received with a warm welcome by delegates; Hachinsky; Raad Shakir, WFN president-elect; Werner Hacke, WFN vice president; and other officials. Our target audience is young brains throughout the world, and we want to promote healthy brain and brain health. Young

students and minds are highly interested in knowing how the brain works and how can we make it work better.

We should target to approach one billion people around globe to educate about the brain in 2014. Most activities will focus near World Brain Day but it is a year-long campaign. National societies should plan activities aimed at young school and college students, and with the help of social and electronic media, the information could go to millions of people. All societies should share their plans and activities, and organizations with the highest impact public awareness activities should be awarded.

We should especially focus efforts on Facebook and Twitter to connect with

**The human brain is so fascinating and is so closely linked to the health of the whole human being that we should promote healthy brains.**

millions of people. Our Young Neurologists Network on Facebook could be a great resource for this campaign. We should use multiple languages, especially Chinese, Spanish, French, Arabic, Hindi and German. We also could develop a 5-minute promotional

video with a brief introduction of WFN in multiple languages. This video could be shared by millions through YouTube and Facebook. We have more than 140 member societies. If we are able to organize a few hundred programs on July 21 in all of those countries, it is bound to create an impact.

Complexity of brain and neurological diseases often becomes a barrier for public awareness. “You should speak plain when you speak brain,” said Keith Newton of WFN. Our message should be simple and easily understandable for lay people. We could design a logo for this purpose which may be a simple global message. WFN and local organizations could start a poster or cartoon design competition to explain brain function and improve public awareness. Best posters, designs or cartoons could be awarded. We expect thousands of entries for this competition and some of these entries could become logos for our future campaigns.

There are many organizations working in this area, including the International Brain Council, the International Brain Research Organization, the American Academy of Neurology, the International League Against Epilepsy and the World Stroke Organization. We should work with them for this common agenda. Strong liaison and lobbying with WHO is important. If WHO adopts this day in the future, this could be a great success for WFN. •

Wasay is the chair of the Public Awareness and Advocacy Committee for the World Federation of Neurology.

## INDIAN ACADEMY

continued from page 6

Medina from Honduras. Both technical and clinical perspectives regarding the benefits, challenges and limiting factors of developing robotics in neurorehabilitation were discussed. The integration of e-learning in traditional learning was emphasized.

Four orations were presented and the Presidential Oration was delivered by Mehndiratta. His presentation was titled "My Journey Through Indian Academy of Neurology and Academy's Past, Present and Future." He portrayed the establishment of the IAN, his 14 years of journey in the academy, growth of IAN in terms of academic activities such as conferences, public education and awareness programs and official publications both online (website) and offline (newsletter, reviews in *Neurology, Journal- Annals of Indian Academy of Neurology*). According to his foresight, the way forward for IAN includes collaboration and synergy, young talent recognition and continental and intercontinental outreach.

William Carroll, vice president of World Federation of Neurology, also graced the occasion and presented his

oration on demyelinating diseases and challenges. Another interesting symposium focused on the diagnosis and management of cerebrovascular and neuromuscular diseases using point of care neurosonology.

For the first time in the history of IAN, an Asian and Oceanian Association of Neurology (AOAN) symposium was held in which one of the speakers was Beom S. Jeon, vice president of AOAN from South Korea. He provided valuable insight into how genetic disorders present in dystonia. He also participated in the workshop on videos in clinical neurology. To encourage young neurologists, a paper presentation competition was held, and first, second and third positions were awarded.

A high point of this conference like earlier years was clinicopathological conference (CPC) on a case of fever, rapidly progress altered sensorium, raised intracranial pressure and seizures. The clinical discussant suggested the possibility of Balamuthia granulomatous amebic encephalitis (GAE) and was confirmed as Balamuthia mandrillaris encephalitis on histopathology.

In the executive committee meeting, Robert H. Brown, president of the American Neurological Association (ANA) was



Man Mohan Mehndiratta

invited to discuss the logistics to foster collaboration of ANA and IAN, which would be really helpful in achieving inter-continental educational outreach.

Looking ahead, IAN will continue to support the neurologists through its key functions, mentor young neurologists and provide opportunities for research. It will continue to develop more outreach initiatives to prepare students and practicing neurologists for academic excellence'. •

Mehndiratta is the director, professor and department head, Department of Neurology, Janakpuri Superspeciality Hospital, New Delhi-110058. He may be contacted at mmehndi@hotmail.com

### References

1. Indian Academy of Neurology. Available at <http://www.ian.net.in/index.html>. Assessed on Nov. 8, 2013
2. O'Brien MA, Rogers S, Jamtvedt G, Oxman AD, Odgaard-Jensen J, Kristoffersen DT, Forsetlund L, Bainbridge D, Freemantle N, Davis DA, Haynes RB, Harvey EL. Educational outreach visits: effects on professional practice and health care outcomes. *Cochrane Database Syst Rev.* 2007 Oct 17;(4)
3. Forsetlund L, Bjørndal A, Rashidian A, Jamtvedt G, O'Brien MA, Wolf F, Davis D, Odgaard-Jensen J, Oxman AD. Continuing education meetings and workshops: effects on professional practice and health care outcomes. *Cochrane Database Syst Rev.* 2009 Apr 15;(2)

## WFN

continued from page 1

produce enough pilot data to allow for applications to larger funding agencies such as the Fogarty Foundation.

### Public Awareness and Action Committee

The Public Awareness and Action Committee headed by Mohamed Wasay is trying to establish a World Brain Day inspired by the highly successful World Stroke Day, that I proclaimed when I was vice president of the WFN in Cape Town on Oct. 29, 2006, along with a World Stroke Agenda to which all of the major organizations dealing with stroke contributed.

### Publications

During this administration at the recommendation of the Publications Committee, chaired by Christopher Kennard, a new editor was selected for the *Journal of Neurological Sciences*. Robert Lisak who served as editor for 15 years steadily increased the journal's impact factor and circulation for which the WFN is immensely grateful. He was succeeded by John England who has co-opted highly capable associate editors in the areas of global neurology, translation research, outcomes research and practice standards that will give the journal a distinctive personality and a higher profile.

World Neurology is now totally digital, being capably edited by Donald Silberberg. World Neurology is in dynamic interaction with the website that has been modernized, updated and made more useful under the editorship of Pete Engel and with the gifted technical capabilities of Chu Man. Wolfgang Grisold has been active in the website in close coordination with the activities of the Education Committee.

### World Neurology Congresses: Accelerating the Cycle

As vice president, I initiated the process that resulted in moving the World Congresses from a four-year cycle to a two-year cycle. This has allowed for neurology to go where it is most needed. The main aim of congresses is to take neurology to parts of the world where it becomes accessible to neurologists and others interested in the nervous system who have no means of traveling internationally. The more frequent congresses also have allowed continuity in organization and the scientific program committee and have brought in more frequent income in an era of shrinking resources.

### Finance

Our finances are sound, thanks to our able Secretary-General Raad Shakir and proceeds from a combination of successful congresses and sound invest-

## DIGITAL

continued from page 8

visit the website only infrequently and rather search for specific content. Social media, in contrast, broadcasts news onto the social media of users, which for Gen-Y, are often smartphone based. This means that WFN has the chance to attract individuals to WFN content even when these individuals do not intend to visit the WFN's website (website content comes to the user).

The Website Committee has decided to offer three different social media services via Facebook, LinkedIn and Twitter, under responsibility of Walter Struhal (@walterstruhal).

### Facebook

Facebook is the largest social media site with 1,110 million active users worldwide (by March 2013). It allows users to present a personal profile, to follow friends and organizations, exchange and "like" messages. Facebook is used by many individuals for personal networking. WFN has



Facebook

started a Facebook page, which currently has 1,456 followers (Dec. 14).

In preparation for the 2013 World Congress, WCN initiated a Facebook photo contest. The contest winner Daehyun Kim proposed to his girlfriend while he was collecting his prize — WFN wishes the couple all the best for a wonderful future together!

### LinkedIn

LinkedIn has 259 million active users worldwide (by June 2013) and offers similar services as Facebook. However, LinkedIn is aimed at individuals in professional occupations and is mainly used for professional networking. Users do present their affiliations and skills and interconnect with other professionals. Interconnecting is more restricted in LinkedIn, which tries to prevent interconnections between people who don't know each other in real life. WFN has started a LinkedIn group, which currently has 864 members (December 14).

### Twitter

Twitter has 200 million active users worldwide (by February 2013) and has a different approach to social networking. In fact, it is rather a micro-blogging service, which allows users to write short messages with up to 140 characters. All

messages are online and open to the public to read, even for non-members of the service. WFN currently has 346 registered followers (December 14). Interesting content on WFN's social media services as well as lively discussions lead to a growing fan audience.

We invite you and your residents to follow our social media footage.

- Follow and interact with WFN on
- facebook ([www.facebook.com/wfneurology](http://www.facebook.com/wfneurology))
- twitter ([www.twitter.com/wfneurology](http://www.twitter.com/wfneurology))
- LinkedIn: World Federation of Neurology LinkedIn group ([linkedin.com](http://linkedin.com)) •

### References

1. Elkind MSV. Teaching the next generation of neurologists. *Neurology* 2009; 72(7):657-663.
2. Struhal W, Falup-Pecurariu C, Sztrihai LK, Grisold W, Sellner J. European Association of Young Neurologists and Trainees: position paper on teaching courses for Generation Y. *Eur Neurol* 2011; 65(6):352-354.



Twitter

ments. Our expanded activities also have required that we revamp the budgeting process, and we have implemented management accounting, whereby it is possible to monitor our income and expenditures on an ongoing basis that will allow for easier planning in the future.

**The Standards and Evaluation Committee**

As part of our expanded mission, we established standards, so that anything endorsed by the WFN stands for quality and value. This began as a working group headed by Aksel Siva, aided by Sarosh Katrak, and initially by Charles Warlow and later by Werner Hacke and has now been established as a new committee of the WFN. The higher standards have made the WFN's endorsements more valuable.

**Continental Initiatives**

**Africa:** My predecessor, President Johan Aarli made it his mission to do more with Africa, the continent in the greatest need of neurology.

It was at his behest that the first congress on the African continent took place in Marrakesh in 2011. Our Moroccan colleagues, led by Moustafa El Aloui, not only hosted an exemplary congress, but used the proceeds from the congress to establish a foundation to further neurological endeavors. Similarly, the WFN devoted part of its income to be used in Africa.

The WFN has been a participant of the annual neurology courses in Africa along with European Federation of Neurological Societies (EFNS), International Brain Research Organization and others. The training neurology center in Rabat has now been approved by the WFN, and discussions are under way with colleagues in Ghana and Tanzania for the possibility of setting up a training program in an English-speaking African country.

At the initiative and with funding from the Turkish Neurological Society, a program for visiting trainees has been established between Turkey and East Africa.

The high proportion of grassroots grants funded in Africa reflects both the great need and great opportunities to advance neurology in Africa.

**Asia:** We began the Asia Initiative led by Ryuji Kaji with modest help from the WFN, helping organize an infrastructure for the now thriving Asian Oceanian Association of Neurology.

**Latin America:** The formation of a Latin American initiative led by Gustavo Roman resulted in the Latin American Federation of Neurological Societies and in the democratic election of a regional director: Marco Medina.

Regarding the established continental regional neurological societies, namely the North American region (Canada and the United States) and the European Federation of Neurological Societies, our administration made a point of hav-

TABLE

| Project Title and Contact   | Requested Amount | Co-Funding Agency | Co-Funded Amount | Cost to WFN      |
|---|------------------|-------------------|------------------|------------------|
| Training and retraining child neurologists in Africa (Contact: Jo Wilmshurst)   | \$32,059         |                   |                  | \$32,059         |
| New edition of ATLAS (Contact: Donna Bergen)  | \$100,500        | WHO               | \$50,000         | \$50,500         |
| National postgraduate neurology in Tanzania (Contact: Marieke Dekker)   | \$41,600         |                   |                  | \$41,600         |
| Enhancing capacity for stroke recognition, documentation, care and prevention in Nigeria (Contact: Rufus Akinyemi)                                  | \$39,789         | WSO               | \$19,894         | \$19,894         |
| Proposal to establish neurology core curriculum for medical students and primary care doctors in Cambodia (Contact: Shri Mishra)                    | \$26,712         |                   |                  | \$26,712         |
| Africa-Canada international behavioral neurology videoconference rounds (Contact: Morris Freedman)  | \$8,400          | Global E-health   | \$4,200          | \$4,200          |
| Augmenting human resources for neurological care in East Africa (Contact: Ana-Claire Meyer)   | \$58,800         |                   |                  | \$58,800         |
| Addressing the education gap for epilepsy in Indian and SAARC countries (Contract: Manjari Tripathi)  | \$10,000         |                   |                  | \$10,000         |
| International maternal newborn stroke registry (Contact: Cheryl Bushnell)   | \$36,000         | WSO               | \$18,000         | \$18,000         |
| Development of an interactive Internet-based teaching platform for CME in clinical neurophysiology in Sub-Saharan Africa (Contact: Lawrence Tucker) | \$39,200         |                   |                  | \$39,200         |
| Neurological disease surveillance in Cameroon, a rural and urban based population (Contact: Esther Cubo)  | \$25,870         | MDS               | \$12,000         | \$13,870         |
|   | <b>\$418,930</b> |                   | <b>\$104,094</b> | <b>\$314,835</b> |

ing good and direct relationships with them. Specifically, we initiated an annual meeting of the leaders of the WFN and the AAN (Berch Griggs, Bruce Sigbee, Timothy Pedley and Cathy Rydell) that has fostered better understanding and greater cooperation between the two organizations. Similarly, it has been a pleasure to deal with the president of the EFNS, Richard Hughes, who was most cooperative in co-sponsoring the World Congress of Neurology in Vienna and in dealing with matters of mutual interest.

**Education Committee**

The single largest activity of the WFN is directed by the Education Committee. It has been led in an exemplary, complementary way by Stephen Sergay and Wolfgang Grisold who have organized, rationalized and focused the efforts of the Education Committee. Some of their achievements include the accreditation visits to training programs such as the one in Trujillo, Peru, and the activities reported under the Africa Initiative.

**The WFN: An Organization for All Ages and Career Stages**

As vice president, I facilitated the incorporation of a young neurologists

group led by Walter Struhal with the aim of making the WFN an organization for all ages and career stages. I am happy to report that there has been a considerable expansion in the participation of younger neurologists, particularly in regard to the website and using modern technology for communication and education. We also introduced a discount on the congress registration for senior neurologists in an attempt to make the World Congress of Neurology attractive and affordable throughout a full career span.

**Leadership Training**

Although the administration was elected for a four-year term, we divided it into two halves. For the initial two years, the committees and initiatives were kept small so that the member could get to know each other and learn to work together. For the second two years, the committees and initiatives were expanded and a number of vice chairs were appointed, typically younger individuals, more women and more individuals from different parts of the world. The two-year cycle gives opportunities for promotion to the most active individuals and the possibility of being involved in different committees and initiatives in sequence.

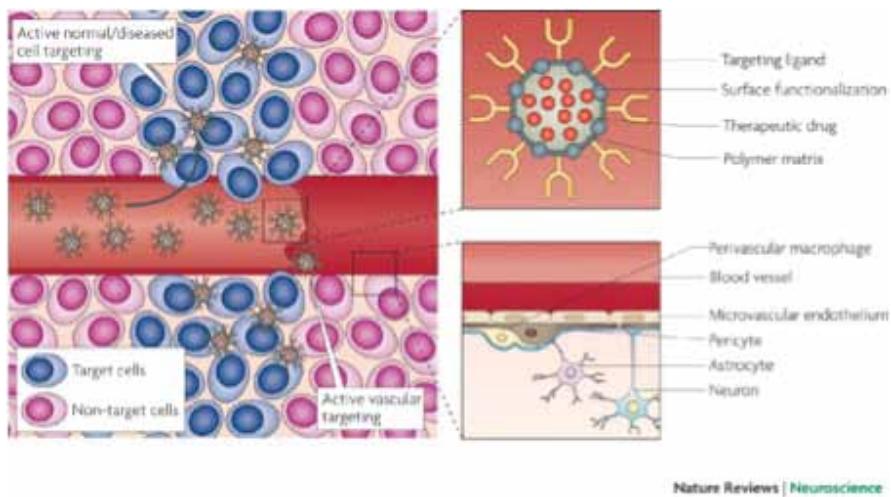
**Conclusion**

It is not for me to judge what we have achieved, except that it resulted from a collective effort.

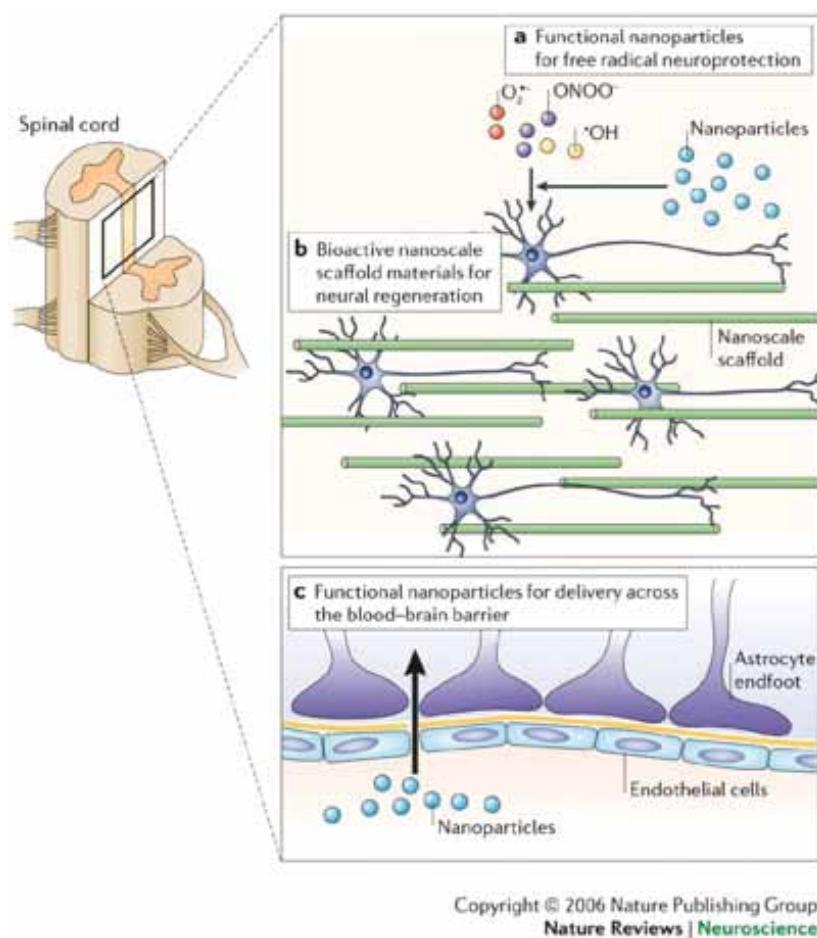
I would like to thank Vice President Hacke, Secretary-General Raad Shakir, and fellow Trustees, Donna Bergen, Wolfgang Grisold, Ryuji Kaji, Gustavo Roman and Stephen Sergay, in the central office, Keith Newton, Laura Druce and Helen Gallagher and in my office, Rebecca Clarke and the many around the world who know that they have made a difference.

I am particularly grateful to our Austrian colleagues under the leadership of the World Congress of Neurology, Eduard Auff who hosted a magnificent event. It would be hard to imagine a more splendid congress to culminate my presidency. I was especially privileged to have my Dream Waltz (orchestrated by Jason Stanford) premiered at the Musikverein as part of the Gala Concert. It is not too often that one can say that one's presidency ended literally on a high note.

I congratulate President-Elect Raad Shakir, Vice President-Elect William Carroll, Secretary-General-Elect Wolfgang Grisold, elected Trustee Gallo Diop and continuing elected Trustee Gustavo Roman and wish them every success in fulfilling the mission of the WFN to "foster quality neurology and brain health worldwide." •



**Figure 2.** The neurovascular unit (bottom right panel) regulates the dynamic and continuous crosstalk between circulating blood elements and brain cellular components, including perivascular macrophages, astrocytes and neurons. At the interface between blood and brain (the blood-brain barrier), endothelial cells and associated astrocytes are stitched together by structures called tight junctions. The blood-brain barrier hinders the delivery of many potentially important diagnostic and therapeutic drugs to the CNS. The barrier results from the selectivity of the tight junctions between endothelial cells in the blood vessels that restricts the passage of solutes. Astrocyte cell projections called astrocytic feet surround the endothelial cells of the blood-brain barrier, providing biochemical support to those cells. The pericytes shown in this figure are undifferentiated mesenchymal-like cells that also line and support these vessels contributing to the complex layering of cells forming the blood-brain barrier. Nanocarriers (top right panel) are materials that can be configured into several different shapes (tubes, spheres, particles, rods, etc.) and can be loaded with drugs for sustained delivery to specific sites that are targeted by coating the surface of the material with peptides. In this figure, the nanocarrier contains a therapeutic drug, a targeting peptide to increase the penetration of the drug into the brain tissue and a functionalized surface consisting of, for example, an antibody to target a specific antigen or a steric coating made of polyethylene glycol or dextrans. Active targeting (left panel) enhances the biodistribution of drug-loaded nanocarriers in the brain tissue, improving the therapeutic efficacy of drugs. Once particles have extravasated in the target tissue, the presence of ligands on the particle surface facilitates their interaction with receptors that are present on target cells resulting in enhanced accumulation and cellular uptake through receptor-mediated processes (Ref. 4; reproduced with permission from Nature Publishing Group © 2009)



**Figure 3.** Applications of nanotechnology in clinical neuroscience. Nanotechnology can be used to limit and/or reverse neuropathological disease processes at a molecular level or facilitate and support other approaches with this goal. (a) Nanoparticles that promote neuroprotection by limiting the effects of free radicals produced following trauma (for example, those produced by CNS secondary injury mechanisms). (b) The development and use of nanoengineered scaffold materials that mimic the extracellular matrix and provide a physical and/or bioactive environment for neural regeneration. (c) Nanoparticles designed to allow the transport of drugs and small molecules across the blood-brain barrier (Ref. 7; reproduced with permission from Nature Publishing Group © 2006.)

## NANO

continued from page 13

vention, management and treatment of neurological disorders.

In terms of delivery across the BBB, two basic approaches, namely the molecular approach and the polymeric carrier approach can be applied. In the molecular approach, nanonization or ligand attachment of the drugs can be employed to target brain cells, and the drugs can further be enzymatically activated afterward inside the target cell<sup>4</sup>. However, the availability of such modifiable drugs is low, and only certain drugs with specific functionality can be targeted molecularly. Additionally, a metabolic pathway is always required to activate these drugs inside CNS — further narrowing the options. The second approach of employing polymeric carriers such as drug-loaded nanoparticles can be termed as a universal approach with flexibility of choosing the matrix or polymer system and additionally can be administered by the route of choice: intravenously, intrathecally or as an implantable cerebral device. (See Figure 2.)

In this way, the BBB can be circumvented via systemic administration or CNS implantation with an ability to control as well as target the release of various bioactive agents used in the treatment of neurodegenerative disorders (NDs). The majority of nanotechnological drug delivery systems for the treatment of NDs are in the form of polymeric nanoparticles. Polymeric nanoparticles are promising for the treatment of NDs as they can pass through tight cell junctions, cross the BBB, achieve a high drug-loading capacity, and be targeted toward the mutagenic proteins.

Specific nanosystems explored for advanced experimental treatment of Alzheimer's disease (AD), Parkinson's disease and other CNS disorders are listed in Table 1.

Nano-enabled systems in the form of biodegradable and non-biodegradable templates for regeneration of damaged neurons and peptide-based self-assembling molecules have been employed as scaffolds for tissue engineering, neuroregeneration, neuroprotection and photolithography etching<sup>5</sup>. Nanoparticulate strategies in the form of bioactive nanoparticles are being employed to provide resealing, repair, regeneration, restoration and reorganization of neural tissue after traumatic spinal cord injury. Nanoparticles are capable of achieving this via the control of secondary injury cascade, reassembly of the tethered membranous structures, creating a neuropermissive microenvironment, rebooting the neuropathophysiological connections, and recovery of the sensorimotor responses<sup>6,7</sup> (See Figure 3.) Silva and co-workers, 2004, reported the potential of self-assembling peptide nanofibers (SAPN)

in neural tissue engineering wherein the nanofibers provided the “neurite-promoting laminin epitope IKVAV,” thereby inducing a rapid differentiation of cells into neurons via the amplification of bioactive epitope presentation and further restricting the development of astrocytes<sup>8</sup>.

The current therapeutic paradigms (using conventional drug delivery systems) employed to provide functional recovery in NDs lack adequate cytoarchitecture restoration and connection patterns required to overcome the restrictive blood-brain barrier. In addition to the restrictive blood brain barrier; the neuroactive drug therapies present various other challenges such as:

- higher doses are required to provide significant therapeutic benefit
- low bioavailability further aggravating the first condition
- poor absorption even after systemic delivery
- the unwanted severe side-effects due to preferential uptake of drugs by peripheral cells.

The introduction and application of nanotechnological strategies may help in overcoming and even completely removing these neurotherapeutic challenges<sup>9</sup>.

Although various studies have claimed and demonstrated the potential of nanoparticles for CNS targeting, drug release and even gene delivery, rapidly biodegradable poly(butylcyanoacrylate) (PBCA) nanoparticulate system is the only successful nano-based drug delivery system that is being employed for the *in vivo* administration of drugs targeted to the brain. However, the mechanism of performance of this successful system has not been confirmed yet with three different reports stating entirely different mechanisms:

1. polysorbate 80 coated PBCA nanoparticles reportedly cross the BBB via a carrier based approach by plasma adsorption of apolipoproteins resulting in receptor-mediated endocytosis by brain capillary endothelial cells<sup>9</sup>
2. Kreuter and co-workers, 2002, suggested phagocytosis or endocytosis by endothelial cells as the possible transport mechanism through the BBB<sup>10</sup>
3. Vauthier and co-workers, 2003, suggested that nanoparticle adhere to the cell membrane with subsequent escape by the P-glycoprotein efflux system to reach the CNS<sup>11</sup>.

These contrasting reports may lead to delay in regulatory approval of these promising nanosystems, and hence, further research into the exact elucidation of the mechanism of nanoparticle transport across the BBB is required.

Nanoscale classes of neuroactives will widen the scope of therapeutic action beyond merely modifying transmitter function to include stem cell and gene therapies that could offer a more selective mode of targeting. Nanoresearch focused on the regeneration

| Type of Nanostructure                       | Bioactive Delivered                | Mechanism of Action  |
|---|------------------------------------|--|
| <b>Alzheimer's disease</b>                  |                                    |  |
| N-butylcyanoacrylate nanoparticles          | Clioquinol                         | Cu <sup>2+</sup> /Zn <sup>2+</sup> chelator to solubilize $\beta$ -amyloid plaques |
| Poly(butylcyanoacrylate) nanocapsules       | Thioflavin-T                       | Detection of $\beta$ -amyloid in senile plaques                                    |
| MPB-PE or PDP-PE nanoparticles              | D-penicillamine                    | Iron-chelating limiting toxicity   |
| Citrate-coated peptide nanoparticles        | Gold (Au)                          | Destruction of $\beta$ -amyloid fibrils and plaques                                |
| <b>Parkinson's disease</b>                  |                                    |  |
| Polyethylenimine (PEI)/DNA nanocomplexes    | DNA plasmids                       | Halt or prevent neurodegeneration  |
| Nanorobots                                  | Stem cells                         | Dopaminergic neuron differentiation  |
| PEGylated nano-liposomes                    | Antibodies                         | Gene replacement therapy   |
| ORMOSIL nanoparticles                       | Oligonucleotides, genes            | Non-viral vector for gene transfection and delivery                                |
| <b>Other CNS applications</b>               |                                    |  |
| Poly(lactic-co-glycolic acid) nanoparticles | Paclitaxel                         | Targeted cytotoxicity  |
| Solidified Oil nanodroplets                 | Iron oxides, contrast agents       | Imaging the CNS by MRI   |
| Silicone nanotubes                          | Cultured nerve cells               | Regeneration of damaged neurons  |
| Peptide nanofibres                          | Neural progenitor or retinal cells | Promotes the growth of neurites  |
| Carbon-60 fullerenes                        | Fullerenols                        | Antioxidant and free radical scavenger   |

**Table 1. Overview of various nano-enabled neurotherapies and interventions for CNS disorders (Ref. 5; reproduced with permission from Elsevier B.V. Ltd. © 2009.)**

and neuroprotection of the CNS will significantly benefit from the parallel advances in neurophysiology and neuropathology research. Therefore, for nanotechnology applications in neurology and neurosurgery to come to fruition, the following need to be considered:

- advancements in pharmaceutical chemistry and materials science that produce sophisticated synthetic and characterized approaches
- advancements in molecular biology, neurophysiology and neuropathology of the nervous system
- the design and integration of specific nano-enabled applications to the CNS which take advantage of the first two points.

If these areas are developed in an integrated and parallel manner, nanotechnology based applications for NDs may begin to reach the clinic. As with all therapeutic approaches, for the treatment of CNS disorders, the challenge of targeting the material, device or drug

to the site where it is needed always remains. Therefore, in order for nanotechnology applications directed toward NDs to be fully exploited, it would be important for neurosurgeons, neurologists and neuroscientists to contribute to the scientific process along with pharmaceutical scientists and engineers. True to the highly interdisciplinary nature of this area of research, it is important that technological advancements occur in conjunction with basic and clinical neuroscience advancements<sup>5</sup>.

Modi is professor and head of Neurology, and the academic head of clinical neurosciences, Faculty of Health Sciences, University of the Witwatersrand. Pillay is professor of Pharmaceutics, Faculty of Health Sciences, University of the Witwatersrand.

#### References

1. Modi G, Pillay V, Choonara YE. Advances in the treatment of neurodegenerative disorders employing nanotechnology. *Ann NY Acad Sci*. 2010;1184:154–172.

2. Nanomaterials. [http://ec.europa.eu/environment/chemicals/nanotech/faq/definition\\_en.htm](http://ec.europa.eu/environment/chemicals/nanotech/faq/definition_en.htm) (accessed on 20 November, 2013)
3. Re F, Gregori M, Masserini M. Nanotechnology for neurodegenerative disorders. *Nanomedicine: NBMedicine* 2012;8:S51–S58.
4. Orive G, Anitua E, Pedraz JL, Emerich DF. Biomaterials for promoting brain protection, repair and regeneration. *Nat Rev Neurosci*. 2009;10:682–692.
5. Modi G, Pillay V, Choonara YE, Ndesendo VMK, du Toit LC, Naidoo D. Nanotechnological applications for the treatment of neurodegenerative disorders. *Prog Neurobiol*. 2009;88:272–285.
6. Kumar P, Choonara YE, Modi G, Naidoo D, Pillay V. Nanoparticulate strategies for the 5 R's of traumatic spinal cord injury intervention: restriction, repair, regeneration, restoration and reorganization. *Nanomedicine*, Manuscript accepted, In press, To be published in Feb 2014.
7. Silva GA. Neuroscience nanotechnology: progress, opportunities and challenges. *Nat*

8. Silva GA, Czeisler C, Niece KL, Beniash E, Harrington DA, Kessler JA, Stupp SI. Selective differentiation of neural progenitor cells by high-epitope density nanofibers. *Science*. 2004;303:1352–1355
9. Kreuter J, Ränge P, Petrov V, Hamm S, Gelperina SE, Engelhardt B, Alyautdin R, von Briesen H, Begley DJ. Direct evidence that polysorbate-80-coated poly(butylcyanoacrylate) nanoparticles deliver drugs to the CNS via specific mechanisms requiring prior binding of drug to the nanoparticles. *Pharm Res*. 2003;20:409–416.
10. Kreuter J, Shamenkov D, Petrov V, Ränge P, Koch-Brandt C. Apolipoprotein-mediated transport of nanoparticle-bound drugs across the blood–brain barrier. *J Drug Target*. 2002;10:317–325.
11. Vauthier C, Dubernet C, Chauvierre C, Brigger I, Couvreur P. Drug delivery to resistant tumors: the potential of poly(alkyl cyanoacrylate) nanoparticles. *J Control Release* 2003;93:151–160.