

# WORLD NEUROLOGY

THE OFFICIAL NEWSLETTER OF THE WORLD FEDERATION OF NEUROLOGY

EXPERIMENTS INTO READINESS FOR ACTION

## 50th Anniversary of the Bereitschaftspotential

BY LÜDER DEECKE

A special session inaugurated and chaired by Mark Hallett, Bethesda, Maryland, at the International Congress of Clinical Neurophysiology (ICCN2014) in March 2014 in Berlin celebrated the 50th anniversary of the Bereitschaftspotential. The session included lectures by Lüder Deecke, Vienna: “Experiments Into Readiness for Action — Bereitschaftspotential;” Hiroshi Shibasaki, Akio Ikeda, Kyoto, Japan: “Generator Mechanisms of BP and Its Clinical Application;” Gert Pfurtscheller, Graz, Austria: “Movement-Related Desynchronization and Resting State Sensorimotor Networks;” and Ross Cunnington, Brisbane, Australia: “Concurrent fMRI-EEG and the Bereitschafts-BOLD-Effect.” The session was well accepted.

In this paper, I would like to give an outline of the history of the Bereitschafts-

potential and a selection of the main research results of our experiments into readiness for action.

### The History of the Bereitschaftspotential

In 1964, my mentor Hans Helmut Kornhuber (1928-2009) and I discovered the readiness potential (Kornhuber and Deecke, 1964). We submitted the full paper in the same year. It was published in the first 1965 issue of “Pflügers Archiv” (Kornhuber and Deecke, 1965).

We described a novel method, reverse averaging, for recording brain electrical activity prior to voluntary movement in humans by noninvasive means and presented the first fundamental results obtained with this method. We found that a negative electrical cortical potential consistently preceded human



voluntary movement and named it the Bereitschaftspotential (BP) or readiness potential. (See Figure 1B.)

The BP is the electrophysiological sign of planning, preparation and initiation of volitional acts. How did the idea come up to record brain potentials preceding human voluntary movements in the EEG? It began on a Saturday in May 1964 when Kornhuber invited his doctoral student L.D. for lunch into the ‘Gasthof zum

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## The World of Neurology Comes Together at the AAN Annual Meeting

The 2014 Annual Meeting of the American Academy of Neurology (AAN) attracted more than 13,000 neurology professionals to Philadelphia, a city rich in its own neurology-related history. More than 2,500 presentations of cutting-edge research were available to attendees from across the world. The number of non-U.S. attendees was nearly 4,000.

Science and continuing medical education are the main draws to the Annual Meeting, and this year was no exception. One of the highlights was the Presidential Plenary Session, the AAN's premier lecture awards for clinically relevant research. James L. Bernat, MD, FAAN, gave

the Presidential Lecture on “Challenges to Ethics and Professionalism Facing the Contemporary Neurologist.” The George C. Cotzias Lecture featured Stefan M. Pulst, MD, FAAN, speaking on “Degenerative Ataxias: From Genes to Therapies.” The Sidney Carter Award in Child Neurology went to Darryl C. De Vivo, MD, FAAN, who expounded on “Rare Diseases and Neurological Phenotypes.” Finally, David M. Holtzman, MD, FAAN, shared “Alzheimer's Disease in 2014: Mapping a Road Forward,” as the Robert Wartenberg lecturer.

The Hot Topics Plenary Session presented recent research findings and clinical implications regarding identifica-

tion of a unique molecular and functional microglia signature in health and disease; emerging concepts in chronic traumatic encephalopathy; functional connectivity and functional imaging in movement disorders; and the global epidemic in stroke.

Abstracts related to new therapeutic developments, clinical applications of



basic and translational research, and innovative technical developments were shared and discussed at the Contemporary Clinical Issues Plenary Session. This year's topics were acute ischemic stroke, Friedrich's ataxia, insomnia, epilepsy, functional (psychogenic) disorders and the Parkinson's disease Progression Marker Initiative.

At the Frontiers in Translational Neuroscience Plenary Session, attendees heard about the clinical aspects of tissue environments for brain repair;

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**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.

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*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.

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## FROM THE EDITOR-IN-CHIEF

## AAN Meeting in Review

BY DONALD SILBERBERG

As an addendum to the report from the American Academy of Neurology in this issue, I wish to add that in 2012 the AAN established a Global Health Section. At the section meeting during the 2014 AAN meeting in Philadelphia, Jerome Chin, the outgoing president of the section, announced that the section now has more than 300 members, including many from outside the U.S.

The section elected Farrah Mateen from in the Department of Neurology at Massachusetts General Hospital as its new president. If you are interested in seeing the activities of the Global Health Section, contact Franziska Schwarz at [Franziska.Schwarz@aan.com](mailto:Franziska.Schwarz@aan.com).

International activities during the Philadelphia meeting included:

a conference titled “Controversies in Global Health: Corticosteroids for Meningitis,” a seminar on “Global Health Challenges: Neurology in Developing Countries,” an



DONALD H. SILBERBERG

International Colloquium that included topics such as “Dealing With Common Disorders With Limited Resources,” “Successful Examples of International Collaboration,” and Information on

fellowships in the U.S. An Integrated Neuroscience Session featured oral presentations on the “Global Impact of Non-Communicable Neurological Diseases,” with poster sessions before and after. Finally, an Ethics Colloquium included a presentation on “Clinical Trials Involving International Subjects.”

In these ways, the AAN is now playing an important role in global neurology together with the World Federation of Neurology. •

## IAPRD AND PSN JOIN HANDS:

## First Movement Disorder Course and Botox Workshop

BY ABDUL MALIK, MBBS, DCN, MD

The specialty of neurology shows remarkable growth in last decade in Pakistan. The 21st meeting of the Pakistan Society of Neurology (PSN) was organized in collaboration with the International Association of Parkinson's and Related Disorders (IAPRD) March 28-30 in Karachi, Pakistan.

There were eight scientific sessions and a half-day Botox Hands-On Workshop in this conference. The speakers from Netherlands, the United States, Saudi Arabia and Pakistan shared their experiences pertaining to neurology. The core of the discussion was the advances in movement disorders and the newer therapies now emerging. The guest faculty from the IAPRD had given a detailed overview on the topic.

An ample demonstration on patients was given with the title of “Botulinum Toxin Hands-On Use in Dystonia” by Prof. Daniel Truong from The Parkinson and Movement Disorder Institute (U.S.). He also delivered a lecture on Clinical Approach and Management of Dystonias. Prof. Ronald Pfeiffer, vice chair of the Department of Neurology at the University of Tennessee Health Science Center (U.S.) gave us an updated overview on Autonomic Dysfunction in Parkinson's Disease and Drug-Induced Movement Disorders. The keynote speaker was Prof. Erik Wolters, IAPRD president, who is working in the Universities of Maastricht and Zurich. He delivered his lectures on the topics of Behavioral Dysfunction in Parkinson's Disease and Parkinson's Disease — Revisited.

More than 200 exceedingly participative audiences from all parts of the country attended all of the scientific sessions. In the inaugural session of the three-day

conference, the Sardar Alam, outgoing Pakistan Society of Neurology (PSN) president, welcomed the delegates and presented the report of the last two years of the society's works. Prof. M. Wasay, chairman of the organizing committee, stated the statistics of neurology care and neurologist in Pakistan. He said that for every one million people only one neurologist is available.



PSN conference organizers and faculty with Erik Wolters, Daniel Truong and R. Pfeiffer.

In the scientific sessions, Asif Moin, from Saudi Arabia, delivered the talk on utilization of SPECT and PET in epilepsy; Qasim Bashir discussed initial experience in establishing an interventional neurology/neuroendovascular surgery program in Lahore: procedural types and outcomes; Qurat Khan from AKU deliberated on introduction to behavioral neurology; Bushra Afroze talked on biotinidase deficiency — clinical presentation, diagnosis

and treatment while neurodegeneration in children: diagnostic issues in developing countries was presented by Tipu Sultan from Children Hospital Lahore. A unique and thought-provoking session of this was in the Neurology Training and Advocacy session. This session highlighted the glimpses on post-graduate neurology in Pakistan by Sarwar Siddiqi, psychiatric care and interface with neurology by Prof. Iqbal Afridi, neurosurgery care and interface with neurology by Prof. Junaid Ashraf and advocacy for neurological care in Pakistan Prof. Rasheed Jooma.

There were 15 original oral presentations and 20 poster presentations from all major institutes of the country. This

year, PSN officially had given best oral presentation and poster presentation awards. There was also an inaugural dinner in which the primary guest was Prof. Asghar Butt, vice president of CPSP. Prof. Masood Hameed Khan, vice chair of DUHS was honored during the social portion of the evening.

The conference was a great success in terms of participation, and the quality of training and education was superb. •



## PRESIDENT'S COLUMN

# Neurology Cooperation Around the World

Since I wrote my last column, many events have occurred. The neurological world is moving so fast. The WFN remains at the forefront of developments of international activities and is leading in cooperation and promotion of neurology.

In January, the Sudanese Neurological Society held its ninth annual meeting in Khartoum. I had the privilege to be invited as well as the president of the Pan African Association of Neurological Sciences, Prof. Riadh Gouider, and the president of the Pan Arab Union of Neurological Societies Prof. Mohammad Tamawy. The attendance and interest was large and intense. There was an impressive eagerness to learn among young neurology trainees in all topics, and the hands-on workshops with bedside patients were fully subscribed. It is heartening to see that relatively small societies in Africa can provide so much high-quality teaching and care. Congratulations to Prof. Ammar El Tahir and Prof. Osheik Seidi for their efforts.

The 15th Cairo Neurology Congress was held in February and again the topics and attendance were impressive. Prof. Wolfgang Grisold, WFN Secretary-Treasurer General attended the meeting. Tamawy and Prof. Osama Abdul Ghani are to be congratulated for an excellent effort. I am sure that across the world many national societies have had their annual congresses and this only enriches the field. The WFN will be delighted to be involved in any way and to help promote and advertise these congresses.

**From national to regional congresses.** The Asian Oceanian Congress of Neurology (AOCN) 2014 was organized by the Hong Kong Neurological Society and held in Macau. The congress was attended by members from all over Asia. The Hong Kong Society in collaboration with the Chinese Neurological Society was instrumental in producing an excellent program. Prof. William Carroll, WFN first vice president, attended the congress, and Man Mohan Mehendiratta, AOAN president, was also present; the organization was excellent. Profs. Wing-Ping Ng and Laurence Wong are again to be congratulated. (See Figure 1.)

It seems that wherever in the world neurologists meet, there is always a sense of camaraderie and togetherness. It is also clear that topics vary in their scientific slant and their emphasis on training; but the eagerness to learn among neurologists in training is the same across the world.

Teaching courses with live and videotaped cases attract a huge interest and create lively discussions.

The WFN grants round is now open, and we hope to receive as many applications as possible. The Grants Committee will start work after the closing date, and decisions will be conveyed to the applicants immediately. The plan is that the WFN will partner with other organizations to increase the amounts of the grants.

The Vienna World Congress was not only a scientific success but also a great financial success for the WFN. I, on behalf of the WFN, am most indebted to the Austrian Society for its hard work; and to the EFNS which suspended its annual congress for 2013 to allow just one major neurology congress to take place in Europe. The financial returns to all indeed exceeded expectations, which bodes well for the financial survival and strength of the WFN.

As this issue is being published, the amalgamation of the EFNS/ENS in the joint meeting in Istanbul will have taken place. This will create a most solid association. The WFN looks forward to the birth of the European Academy of Neurology (EAN) and the elections of its officers so that our relations and close collaboration will continue as before with its two predecessors. The WFN's strength and ability to reach its goals can only be achieved with the help of strong regional associations willing to collaborate to further the cause of advancing neurology globally. If one reads the EAN's Purpose and Values, these goals are well laid out in Article 4 of its bylaws.

The WFN was born on the July 22, 1957, and during the Vienna World Congress, the Council of Delegates voted to commemorate that day every year as the World Brain Day. The task was given to Prof. Mohammad Wasay, chair of the Public Awareness and Advocacy Committee. The details are in the April issue of *World Neurology*. By the time this is published, all delegates should have received further correspondence.

The WFN history is rich and diverse. Prof. Johan Aarli, WFN past president, is the author of *The WFN History: The First 50 years*, published by Oxford University Press. By the time this issue of *World Neurology* is distributed, the book will be



**Figure 1.** (From left to right) Jonas Yeung, president of the Hong Kong Neurological Society; Man Mohan Mehendiratta, president of AOAN; Wai-Sin Chan, deputy director, Health Bureau, Macau Special Administrative Region; Chin Ion Lei, director, Health Bureau, Macau Special Administrative Region; Patrick Li, president of the Hong Kong College of Physicians; Ping Wing NG, co-chair of AOCN 2014; Leonard Li, co-chair of AOCN 2014; Lawrence Wong, secretary of AOAN and chair, Scientific Committee, AOCN 2014.

launched during the joint EFNS/ENS meeting in Istanbul. The book is essential reading for all.

The WFN and other peer organizations have created the World Brain Alliance. See <http://www.wfneurology.org>. This was started during the previous presidency, and I had the honor of being present during its inception in 2010. The presidents of peer societies last met in Vienna and will meet again to formulate a structure and proceed as the force speaking for all those involved in brain health.

Other activities to report are the collaboration with the WHO. This has matured and is progressing well. The Department of Mental Health and Substance Abuse is where neurology lies in the WHO structure. Shekhar Saxena and Tarun Dua are major contributors to the success of the collaboration. Moreover, Oleg Chestnov, WHO's assistant director general, has agreed to talk to the attendees of the World Congress of Neurology in 2015 in Santiago, Chile. The WFN is a major funder to our WHO activities and will continue to be so. The ICD11 process is being finalized, and the process is on target. The WFN and the WHO are again collaborating in the production of the successful *Neurology Atlas*, second edition, as the first edition is now 10 years old. This process involves gathering information from Ministries of Health and all WFN member societies so that the data are verified and are useful tools for all.

The involvement of the WFN with the Non Communicable Diseases (NCDs) declaration is vital for the future of neurology. There is now a clear perception that the WHO is moving from the preventative

mode, which has fully dominated its activities, to the area of disease management and appreciation of the huge burden of neurological diseases in the world. This, when it evolves further, is a seismic shift in thinking, and the WFN should be ready when it happens. The close collaboration and financing of many projects through the WHO is crucial for neurology, and the WFN should be at the top table in the decision-making process.

Many tasks lie ahead for the WFN trustees. For examples, finding and hiring a PCO when the contract with the current PCO Kenes expires with the last contracted congress in WCN 2015 in Santiago; and finding a publisher for *JNS* when the contract with Elsevier expires at the end of 2014. These are important decisions, and the trustees will have to look at all of the options and come up with the most suitable ones for the WFN.

As delegates were informed, the Nominating Committee is soliciting nominations for the post of elected trustee. Prof. Gustavo Roman will finish his second term and is not eligible for re-election. His contributions to the WFN as a trustee and as chair of the Latin America Initiative are immense. I, on behalf of all trustees, committees and member societies, would like to thank him for a wonderful job, which was done with grace, elegance and professionalism.

The next Council of Delegates meeting will be held in September in Boston, Massachusetts. This will be during the joint meeting of the American and European MS societies, and we look forward to seeing as many society representatives there as possible. •



RAAD  
SHAKIR

# Stroke in Literary Works Around the World

BY AXEL KAREMBERG

There are few other neurological disorders with such a constant presence in literary works as apoplexy. As early as 1600, the notions “apoplexy” and “apoplejia” appear in dramas written by Shakespeare and Lope de Vega. More detailed descriptions of the disease enrich popular novels of the 19th century. Authors such as Balzac, Dumas, Flaubert and Zola must be mentioned here as well as the epical sagas of Dostojewski and Tolstoi<sup>1,2</sup>. The American author John Steinbeck used a “stroke” in his work *East of Eden* as did Philip Roth in his morbid narratives. In the German-speaking world, stroke is dealt with in more than 100 fictional works.



Axel Karenberg

Naturally, literary productions treating this subject resort to contemporary medical knowledge<sup>3</sup>. Until the middle of the 20th century, literature focused mainly on two aspects of apoplexy: its typical symptoms and explanations of its origin. The presentation of symptoms abide by a strict code: sudden onset, motor deficiency and unfavorable outcome. The majority of authors was deeply impressed by the loss of the ability to produce speech — above all after Goethe’s early depiction of motor aphasia in *Wilhelm Meister’s*

Apprenticeship (VII,6; 1795/96): “Altogether unexpectedly my father had a shock of palsy; it lamed his right side, and deprived him of the proper use of speech. We had to guess at everything that he required; for he never could pronounce the word that he intended ... His impatience mounted to the highest pitch: his situation touched me to the inmost heart.”

The diverse causes of the disease taken up in the “belles lettres” reflect its multifactorial origin conceived in premodern medicine. Melancholic “gloominess” or “thick blood” was grounded on the ancient idea of an abnormal blending of the bodily humors. In this

ters and supplemented by technical diagnosis and therapeutic options. To exemplify this shift, there are George Simenon with his Non-Maigret book *The Bells of Bicetre* (1962) and Kathrin Schmidt’s novel *You Won’t Die* (2009).

In literary works, apoplexy serves different goals. The sudden outbreak of the disease can set the plot going, let take it the defining turn or end a story line. Above all, in recent prose texts, the symptoms bring the fictional patients to get to the bottom of their former life. But the illness also can assume a metaphoric function. The recurrent cerebral insults of the protagonist Oblomow in Iwan

A. Gontscharow’s homonymous epic (1859) were meant to illustrate the agonizing czaristic feudal system. In a similar way, the American author John Griesemer in his New York novel *Heart Attack* (2009) fixed the acute symptoms of his protagonist on 9-11 in order to link individual and collective fate, facts and fiction to a meaningful picture.

Fictional texts are never bare clinical case histories, they never render exclusively neurological textbook knowledge. It is the components that lie beyond the medical horizon that arouse the interest of physicians and a broader public. The anthropological dimension, the look at human despair and hope can further



*Effi Briest* by Theodor Fontane. Original cover of the first edition (1896).

perspective, the disease could be provoked by the “cold and moist evening air” or by “taking a bath at 9° C.” (e.g. in E.T.A. Hoffmann, 1825 and in Theodor Fontane’s *Effi Briest*, 1894/95). Only approaching present times, the thematic focus and the narrative perspective shifted slowly but constantly. Along with a more detailed description of the symptoms, the story is now set in hospitals and rehab cen-



Johann Wolfgang von Goethe (1749-1832), author of “*Wilhelm Meister’s Apprenticeship*.”

the understanding of a patient’s fate and help to support present-day stroke medicine. •

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Karenberg is from the Institute for the History of Medicine and Medical Ethics, at the University of Cologne, Germany.

## Mark Your Calendars 2014

### 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, United States

<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>

## BOOK REVIEW

# Neuroanatomy of Language Regions of the Human Brain

Academic Press, 2014; 186 pages

The human brain contains billions of neurons, and these neurons interact in a variety of ways that are only beginning to be understood. One of the great challenges that humans confront is determining the way in which the human brain can support complex behaviors such as reading and understanding this text. We can begin to confront this challenge by improving our understanding of human neuroanatomy.

Michael Petrides is an internationally renowned neuroanatomist. His new, large format book is titled, “*Neuroanatomy of Language Regions of the Human Brain*.” The book is generously illustrated in color, including unique illustrations from his own work. The illustrations are clearly labeled. The accompanying text is authoritative and describes the relevant anatomical features in clear language.

The book is divided into three major sections. The first section of the book focuses on gross anatomy of the human brain. There is a comprehensive discussion of the gross morphological features of the brain. This is accompanied by images that can be obtained with MRI. Petrides illustrates gross anatomy in axial, sagittal and coronal orientations with a T1 sequence obtained at 3 tesla with 1 mm isotropic voxels, but few additional details of the imaging sequence are provided. These illustrations are useful since most volumetric imaging is obtained at 3 tesla with 1 mm3 voxels, although a 7 tesla scanner may have illustrated the anatomy with additional detail. Slices are provided at approximately every 4 mm. Each slice is associated with an orienting location in the space of the Montreal Neurological Institute ICBM152 generation VI average brain, and most sulci are labeled on

each slice of each image.

The second section of the book focuses on cytoarchitecture. Large format images are provided that illustrate the layers of the cortex from each of the critical areas of the brain. Brodmann labeling is used for most illustrations, although Economo and Koskinas labels are used for some critical areas. The location of most samples is illustrated with images of gross location on a brain illustrating Brodmann’s areas, and some corresponding anatomic loci in the macaque monkey brain are also provided.

The third section of the book describes the named, long white matter projections of the human brain. Corresponding projections in the macaque monkey brain are illustrated as well. White matter connectivity is illustrated primarily within the left hemisphere, and hemispheric differences are not detailed. In addition to the averaged results of white matter projections, in situ tractography in individual subjects is provided to demonstrate each of the major white matter fasciculi. The text provides an important discussion of the distinction between the superior longitudinal fasciculus and the arcuate fasciculus, and considers



## ANNUAL MEETING

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opportunities and challenges of robot-assisted and facilitated neurorecovery; network-based neurodegeneration; using fixed circuits to generate flexible behaviors; advances in the Human Connectome Project; and the nightlife of astrocytes.

The Controversies in Neuroscience Plenary Session featured pairs of experts debating three of the most current and controversial issues in neurology: “Does preventing relapses protect against progressive MS?” “Is intervention for asymptomatic AVM useful?” and “Should neurologists prescribe marijuana for neurological disorders?”

The Clinical Trials Plenary Session addressed important topics that affect patient care identified from submitted abstracts that had recently been presented at other society meetings, including stroke, MS, migraine, intracranial hypertension and glioblastoma. The week concluded with the Neurology Year in Review Plenary Session, which examined advances in MS, headache/pain, neuromuscular diseases, movement disorders, neurocritical care and Alzheimer’s disease.

More science was available at numerous platform sessions, seven poster sessions and a new, fast-paced series of Poster Blitz presentations.

Another new feature at this year’s meeting was an International Lounge, which provided an opportunity for foreign guests to mingle, network with leading neurologists from the U.S. and other coun-

tries, and relax before the next session.

A significant portion of the meeting was devoted to helping U.S. neurologists understand the many changes initiated by Congress and federal regulatory agencies as part of health care reform. Neurologists, like other physicians, are under tremendous pressure to reduce treatment costs without compromising the quality of care.

The AAN works hard to guide members through these issues using a variety of resources and tools, while advocating on their behalf with members of Congress and administration officials in Washington, DC. U.S. Senator Bob Casey (D-PA) spoke with neurologists concerned about cuts to federal health programs for the elderly and the economically disadvantaged.

Another Pennsylvania legislator, Congressman Chaka Fattah of the U.S. House of Representatives, spoke at the Brain Health Fair about his initiative to support brain research. This fair is a free public event presented by the American Brain Foundation. The fair typically draws 1,000 to 2,000 people from the region who are living with brain disease or caring for a family member or friend. They hear about new research and treatments from neurologists, health organizations and the medical industry.

Media from across the globe gathered to provide powerful coverage of neurology’s largest meeting. Reporters and photographers shared the latest news in brain research with their readers and listeners back home. The AAN pressroom was lively with representatives from

major national and international news outlets and neurology trade publications.

AAN President Timothy A. Pedley, MD, FAAN, remarked on the strong media interest in the meeting.

“The frequently tragic and debilitating nature of so many brain diseases provides a focus for our attention when we come together at the Annual Meeting to share our experiences and chart our progress,” said Pedley. “The scale of media coverage and public interest reminds us of the tremendous responsibility we have to work even harder to discover more effective treatments and, eventually, cures or

preventive strategies for the neurologic diseases that can be so devastating to our patients.”

Plans are already under way for the 2015 Annual Meeting, to be held April 18-25 in Washington, DC. Until then, the AAN will continue to connect neurologists with the best in science and education through several gatherings, including The Sports Concussion Conference in July; the AAN Fall Conference in October; and Breakthroughs in Neurology 2014: Translating Today’s Discoveries into Tomorrow’s Clinic, to be held in December.

As always, the world is invited. •

## What Have You Learned at the AAN Annual Meeting That You Will Take Back to Your Practice?

“I attended the Global Health Challenges: Neurology in Developing Countries. It was eye-opening to learn about the global burden of disease and specifically the difficulties in treating epilepsy in developing countries.

It won’t affect my current practice but reminds me of the need to think outside of the small world in which I practice. It also reignited an interest in participating in short-term medical mission work like I was able to do in medical school.”

David B. Watson, MD  
Morgantown, West Virginia

“I live in Zambia and there are only two neurologists in Zambia for 13 million people. It’s a very small community! Coming here, I get to meet the people face-to-face that I’ve emailed, spoken to and trained with over the years. We are talking about collaboration and building our global health programs. This AAN meeting — it’s neurology on steroids!”

Omar Siddiqi, MD  
Lusaka, Zambia

“I like that the issue of ethics was addressed in the Presidential Plenary Session and its impact to medicine. We are all living with ethics in our daily lives.”

Barbara A. Dworetzky, MD  
Boston

“I attended a very educational series of debates on the controversies pertaining to ICU EEG monitoring of critically ill patients. It was great to hear from experts in the field arguing their viewpoints on an important unanswered question in neurocritical care. This has inspired me to review the literature myself and come to my own conclusion. Clearly, there is more research that needs to be done.”

Krishnan Vaishnav  
Boston, MA

“The clinical sessions, especially those on the new agents for multiple sclerosis, are very good. MS treatment has been closed, very routine and patients are getting tired of the same injections.

It’s good to see that clinical research is progressing in this area. Hopefully in a few years — not 10 years — there will be new drugs available for MS patients. Patients are being included earlier in studies and being treated better and earlier.”

Douglas Sato, MD  
Sendai-Miyagi, Japan

“I really appreciate the speakers who gave a high level interpretation of the clinical trials. We all know the data. It’s the interpretation that really helps us start a discussion and collaborate nationally.”

Ishida Koto, MD  
New York

“The ICU monitoring session was very helpful. I work at the V.A. We are short-staffed, and we are short on staff qualified to perform multiple tasks such as ICU monitoring. The ideas I learned about ICU monitoring is directly applicable to my facility.”

Gabriel Bucurescu, MD  
Philadelphia

“For me, it’s learning the research ideas for the future. I’m a junior resident so I’m enjoying all the sessions, especially the genetic talks.”

Janice Wong, MD  
Boston, MA

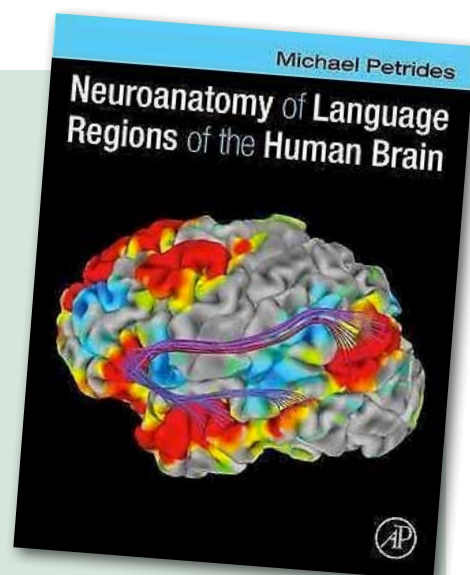
“What I’m hearing is confirmatory: In stroke, there often is no clear decision. So, it’s confirmation to what’s been discussed here.”

Markus Naumann, MD  
Augsburg, Germany

in detail the dual-route hypothesis the postulates dorsal and ventral projections between anterior language regions in the frontal lobe and posterior temporal language regions.

Petrides provides an interesting historical discussion of the development of our understanding of the neuroanatomy of language, beginning with Pierre Paul Broca’s revolutionary presentation of Leborgne and Lelong. He also provides interesting illustrations of MRIs of the brains of these two patients. Major figures such as Wernicke, Marie and Dejerine are mentioned as well, although other seminal early investigators such as Lichtheim are not acknowledged. Petrides also reviews the seminal electrical stimulation studies of Penfield. Indeed, interesting historical perspectives are provided throughout the book.

It is appropriate that a volume about neuroanatomy focuses on language since this topic is the historical origin of our study of human cerebral anatomy. Petrides notes at the beginning of the book that most areas of the brain are arguably related to language. The focus of the book is tilted toward the language regions of the brain, but Petrides generously describes



essentially all cerebral regions and provides key illustrations from macaque monkey.

A truly positive feature of this book is the multiple perspectives that are adopted in a single, comprehensive volume. An additional perspective might have been provided by the anatomically based neurotransmitter work from Zilles and Amunts. •

This book was reviewed by Murray Grossman, professor of neurology, director of the Fronto-Temporal Dementia Center at the University of Pennsylvania School of Medicine.

## BEREITSCHAFTSPOTENTIAL

continued from page 1

Schwanen' at the foot of the Schlossberg hill in Freiburg, Germany (near the Black Forest).

We sat in the beautiful garden and discussed our frustration with the fact that the brain was investigated — at that time — only as a responsive apparatus, i.e. as a mere reacting system. Neurophysiologists were engaged worldwide only in what was called “the responsive brain” (later culminating in a book with this title by McCallum & Knott, 1976). We felt that it would be far more exciting to investigate what is going on in our brain before we make a voluntary movement. No sooner said than done.

We went back to the lab and started immediately planning the experiment. However, we soon ran into an important problem: Brain potentials in the EEG are the result of averaging. For us to get the results we needed, the averaging process must be triggered by the movement or action itself. But how can you trigger on an event that comes as unpredictably and spontaneously as a human voluntary movement?

It was Hans Kornhuber, who found the solution: We would store the EEG on magnetic tape along with the electromyogram (EMG) of the movements and then play the tape backward in the time-reversed direction from the present back to the past, i.e. using reverse averaging with the start of the movement as the trigger. At that time, magnetic tape recorders only had a high-speed rewind, and programmable computers were not yet available, so we were literally removing the tape reels from the recorder, turning them around, and placing them back on the recorder. By these means, we found a brain potential, which was electrically negative and started already 1½ to 1¼ seconds prior to the movement or action. Negativity in the brain means activity.

This method of recording of the readiness potential — Bereitschaftspotential by reverse averaging was the basis of my doctoral thesis, which I completed in 1965 at the University of Freiburg with Kornhuber as my doctoral supervisor. The experiments that led to the discovery of the Bereitschaftspotential were inspired by a positive concept of will, i.e. individual humans have, indeed, their own will and own decision-making power, so that we are capable of designing our lives largely by ourselves and use goal-oriented action to create our own future.

Kornhuber lectured on human freedom in a seminar for students of all faculties. He conducted a survey among his listeners as to who is freer: humans or chimpanzees, chimpanzees or rhesus monkeys, rhesus monkeys or cats, cats or salamanders, salamanders or spiders, and so on until down to the earthworm. The seminar participants answered the question of freedom unambiguously, namely according to the position of the animal in the evolution.

Obviously, we interpret evolution as a process making organisms freer and freer; one also can say making them more and more autonomous. Similarly, we consider an adept, e.g. Shaolin monk, who works hard on his own personality, to become more and more free. Kornhuber was of the opinion and demonstrated that one can make freedom a topic of scientific investigation. Not to deal with freedom only philosophically but also to explore it using scientific means (Kornhuber, 1978; 1984; 1987; 1988; 1992; 1993).

Immanuel Kant, the great German philosopher of the enlightenment (who coincidentally was born in the same town, Königsberg, as Kornhuber) was the first to distinguish between two fundamental aspects of freedom, namely freedom *from* and freedom *to*. Freedom *to* is the much more important aspect here, and this distinction was taken up and further developed by Kornhuber. The scientific breeding ground for the experiments toward the Bereitschaftspotential was thus already prepared well in advance. Rather than being a serendipitous discovery, the Bereitschaftspotential was therefore the result of a new branch of research planned by Kornhuber and myself.

### The Laboratory: Original Experimental Setup in Freiburg/Germany

During the experiments, the subject sat in a Faraday cage for electrical shielding. The EEG was recorded using a Schwarzer-EEG Type E 502 with tube amplifiers and the EMG by a Tönnies-EMG and Stimulation Unit. Data were stored using a Telefunken four-channel magnetic tape recorder M 24-4, frequency-modulated. The tape reels were turned around for reversed averaging. The center-piece of the experimental setup is shown in Figure 1A: Mnemotron CAT Computer 400 B with Mosely Autograf. (See Figure 1: How Kornhuber and I came to the opportunity to use this then-ultra-modern device for our experiments.)

Figure 1B gives one of our first results, a slowly increasing ramp-up of negativity was recorded, which was stronger over the contralateral hemisphere. Negativity culminated at movement onset (and after the action returning to positivity), which we called the Bereitschaftspotential. In the lower set of graphs in Figure 1B, this negativity was demonstrated by a bipolar recording to show phase reversal around the precentral electrode. We called the pre-movement negativity the “Bereitschaftspotential” and in our English summary of Kornhuber and Deecke (1965) offered the English translation “readiness potential.” Somehow the tongue-twister Bereitschaftspotential was preferred and is now a German word in the English language.

We instructed our subjects to make their movements:

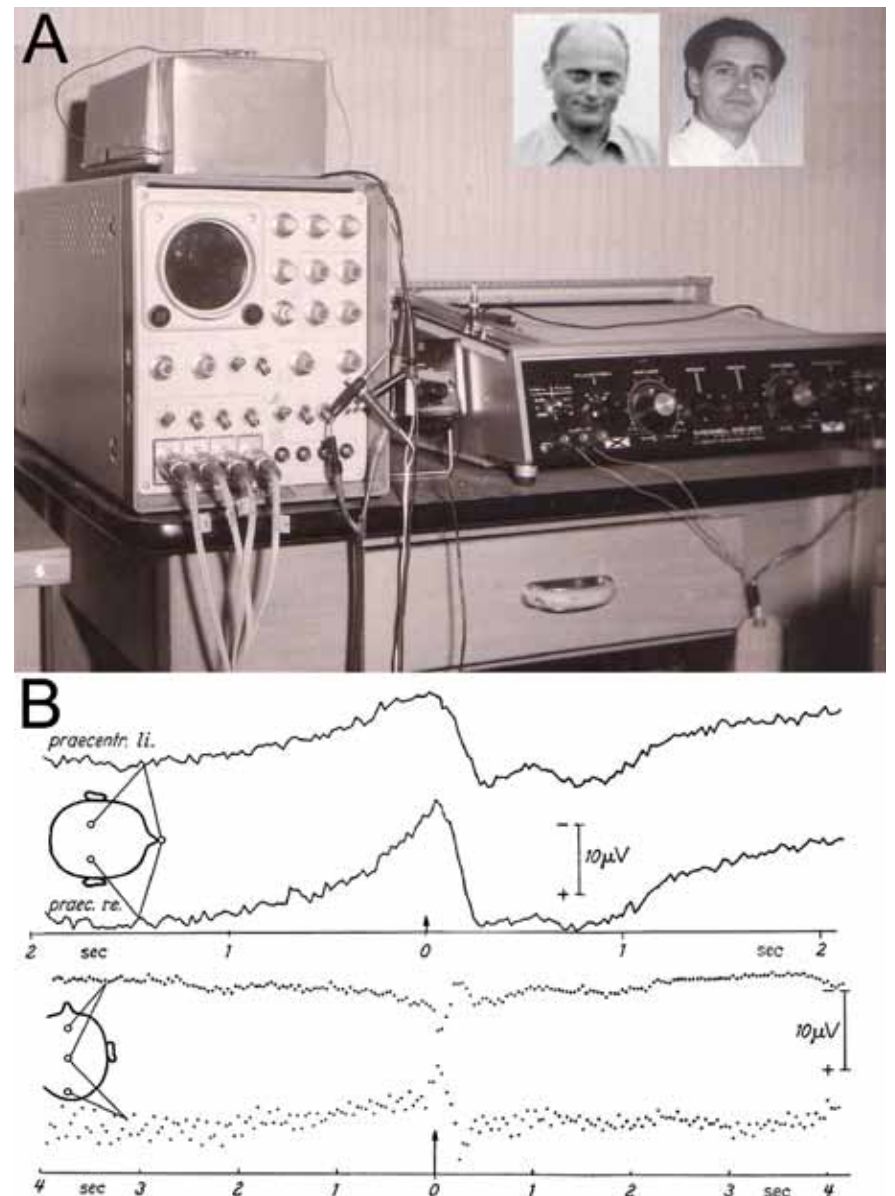
- at irregular intervals
- out of *free* will
- of their own accord

The movements we analyzed were therefore entirely *self-initiated* without

external stimuli. We dislike the term “self-paced,” suggesting regular pace, while it is so important to make the movements at irregular intervals, which make them more volitional, and regular pace makes them more automatic. At that time (1964), this was a remarkable instruction for subjects, to which I think we owe our success. And, thus, a brain potential evolved completely different from W. Grey Walter's (1924-1971) expectance wave or CNV (both having been first published in 1964). By the way, Walter came from Bristol in 1964 to make summer vacation in the Black Forest, which was fashionable for British

at the time. He visited Richard Jung, and Kornhuber and I showed Walter our first results. It was Walter who in a later publication coined the term “opisthochronic averaging” for our methodology. Our first movements under study were simple movements (rapid flexions of the forefinger).

Another methodological prerequisite is to investigate *monophasic* movements, i.e. that the flexed finger remains in the flexed position until the end of the analysis epoch. Using wrist extension and flexion in one flick of the hand is not good, since this employs two movements instead of one.



**Figure 1:** Original experimental setup (A) and first results (B) in Freiburg, Germany, at the University Hospital of Neurology with Clinical Neurophysiology, Hansastr. 9a, Freiburg, known popularly as “Neurophys.”

**A:** The centerpiece of the laboratory — the Mnemotron CAT Computer (Computer of Average Transients) 400 B and Mosely Autograf (XY-Plotter). Prof Richard Jung, head of the hospital, had been offered a post at the Max Planck Institute in Munich. For rejecting this, his home University of Freiburg gave him the CAT Averager as a present for staying. The two inserted photos show Hans Helmut Kornhuber on the left (age 36 in 1964) and Lüder Deecke on the right (age 26 in 1964).

**B:** Above: Changes in brain potentials with voluntary movements of the left hand based on unipolar recordings of the precentral region versus the nose (Subject G.F., average of 512 movements). Onset of movement at the arrow (0 sec) — left of the arrow brain activity prior to movement onset — right of the arrow brain activity after the onset of movement. Note the negative potential at readiness and the positive potential after the action. The graph shows higher amplitudes over the contralateral (right) hemisphere. Negative polarity is up.

Below: The bipolar serial recording with sagittal electrodes with voluntary movements of the right hand (average from 400 movements. Subject B.C.). The graph shows phase reversal around the precentral electrode: The premotor negativity and the postmotor positivity are strongest over the central region. In the fronto-precentral recording negativity of the precentral electrode is down, in the pre-centro-occipital recording negativity of the precentral electrode is up.



By comparing active movements with analogous passive ones, we aimed to show that the BP occurs prior to active movements only. To initiate passive movements, the experimenter pulled a string that was fixed to the subject's finger and ran over a pulley, so that pulling would cause the subject's finger to flex. Indeed, we did not detect any BP prior to such passive movements, but recorded evoked potentials after movement onset elicited by the passive movement. Post-movement onset potentials also occurred in the active state. We referred to these as "reafferent potentials" because the term "evoked potentials" should, by definition, be reserved for potentials that are elicited by external stimuli.

### Citation Classics

Our first full paper (Kornhuber and Deecke, 1965) became a Citation Classic on Jan. 22, 1990. Eugene Garfield of the journal database *Current Contents (CC)* "awarded" this label to papers that were frequently cited. For a paper written in German, this does not occur too often. Garfield gave a translation of the German title: "Changes in Brain Potentials With Willful and Passive Movements in Humans: the Readiness Potential and Reafferent Potentials." As part of receiving Citation Classic status, we were asked to write up how we arrived at our discovery (Citation Classic Commentary), and we gave our commentary the title: "Readiness for Movement – The Bereitschaftspotential Story" (Kornhuber HH & Deecke L (1990).

The Citation Classic Commentary was published both in *CC Life Sciences* and in *CC Clinical Medicine*. Three more of our papers became Citation Classics: No. 2 was Deecke, Scheid, Kornhuber (1969). Here we continued our investigation into the cerebral activity preceding willful movement, and also compared finger movements with arm movements. The 1963 Nobel Laureate for medicine, Sir John Eccles was interested in our work. In his 1977 book, "The Self and Its Brain," which he co-authored with Karl R. Popper, he wrote about our research: "There is a delightful parallel between these impressively simple experiments and the experiments of Galileo Galilei who investigated the laws of motion of the universe with metal balls on an inclined plane."

In his previous book, "The Understanding of the Brain" (Eccles JC 1973), he wrote (page 108): "In an initial investigation by Grey Walter, the subject was trained to perform a movement after a double stimulus sequence: a conditioning, then a later indicative stimulus. An expectancy wave was observed as a negativity over the cerebral cortex before the indicative stimulus. Essentially, this wave is produced by the conditioned expectancy of the indicative stimulus and not by a voluntary movement. The problem is to have a movement executed by the subject entirely on his own volition, and yet to have accurate timing in order to average the very small potentials recorded from

the surface of the skull. This has been solved by Kornhuber and his associate who used the onset of the movement to trigger a reverse computation of the potentials up to 2 seconds before the onset of the movement. The subject initiates these movements "at will" at irregular intervals of many seconds.

In this way, it was possible to average 250 records of the potentials evoked at various sites over the surface of the skull, as shown by the numbers in Figure 4-3 and the corresponding traces. (Figure 4-3 is taken from Deecke, Scheid, Kornhuber [1969] and shows the comparison between

finger and arm movements.) These experiments at least provide a partial answer to the question: What is happening in my brain at the time I am deciding on some motor act?"

Citation Classic No. 3, Deecke, Grözinger, Kornhuber (1976), resulted from my habilitation thesis, a requirement to become a professor at a German university. This paper in *Biological Cybernetics*, "Voluntary Finger Movement in Man: Cerebral Potentials and Theory," comprises a lot of experiments performed in Ulm with many figures and a comprehensive analysis of the BP and its components. Three different brain potentials preceding voluntary rapid finger flexion were distinguished:

1. Early negative activity of the Bereitschaftspotential — widespread
2. Pre-motion positivity, PMP — widespread
3. Motor potential (MP) — unilateral, restricted to the contralateral motor cortex.

Two years later, Citation Classic No. 4 (Deecke & Kornhuber, 1978) was published. This paper in *Brain Research*, "An electrical sign of participation of the mesial 'supplementary' motor cortex in human voluntary movements" first suggests that the early component of the BP, BP1 or BPeary is generated by the SMA and — as we found later — also by the cingulate motor area (CMA). Both being clinicians, Kornhuber and I also investigated patients and were early on able to link Parkinson's disease (PD) with the Bereitschaftspotential. Working with patients means investigating lesion experiments made by nature, and if carefully studied, their pathological state can tell us a lot about the normal function.

Kornhuber had worked on the basal ganglia and cerebellum and found that the

basal ganglia are an important component of the cortico-basal ganglia-thalamocortical loop. This loop was known by neurosurgeons long ago and created the prerequisites for the thalamotomies in classical stereotaxic surgery. The cortico-basal ganglia-thalamocortical loop was lat-

er confirmed and called motor loop by Alexander et al (1986), and by Mahlon DeLong (1990). Nowadays, we have to "think in loops," and the motor loop is the key to the understanding of Parkinson's disease. In our Citation Classic No. 4 (Deecke & Kornhuber 1978), we found differences in the BP between Parkinson's disease patients and normals. One of the best examples of how the BP

in Parkinsonian patients looks like came from an elderly woman among our subjects — she was a duchess — suffering from Parkinson's disease who was trying hard in our BP experiment to meet our performance criteria. The main feature was that we found a high amplitude BP over the vertex but not very much of a BP in the contralateral and ipsilateral precentral leads due to her PD. Experiments were carried out in patients with bilateral Parkinsonism selected for pronounced akinesia but minimal tremor, and in age-matched healthy control subjects. The vertex maximum of the Bereitschaftspotential had previously been explained by volume conduction.

It was argued that a vertex electrode collects activity from both motor cortices. In bilateral Parkinsonism, however, we see a bilateral reduction of the Bereitschaftspotential in the precentral area, whereas over other cortical areas (in particular vertex and mid-parietal), it was not significantly reduced. This publication therefore established the SMA participation in the generation of the BP, and our findings were confirmed by CD Marsden (1938-1998) (Marsden et al 1996). Barrett, Shibasaki & Neshige (1986) reported that the BP is normal in PD. But Dick et al (1989) found that the BP is abnormal in PD. Our group repeated the experiments and confirmed the findings of Dick et al 1989. Harasko, van der Meer et al 1996 cited in Lang and Deecke 1998 *ibidem* Figure 5 on page 235. Results: In the PD patients (N=8), the BP starts later and is initially lower in amplitude as compared to the normal controls (N=8). After the onset of movement, the amplitudes are equal and even sometimes larger in the PD patients as compared to the controls. Thus, Parkinsonian patients start later with their BP, but then keep up with the normal controls.

In May 1979, Kornhuber and I organized the MOSS V congress (one of the series of the EPIC congresses) in Reissensburg Castle, near Ulm, Germany. Afterward, we edited a book of the conference proceedings: *Progress in Brain Research Vol 54* (Kornhuber & Deecke [Eds] 1980). The next conference on the Bereitschaftspotential was an international symposium in April 1988 in Vienna, which I organized in honor of Kornhuber's 60th birthday. The proceedings also were published as a book (Deecke, Eccles, Mountcastle [Eds] 1990).

### The Dispute With Libet

In October 1988, Sir John Eccles invited scientists working on the motor system to contribute to a study week in the Vatican, titled "The Principles of Design and Operation of the Brain" and a resulting book (Eccles & Creutzfeldt [Eds] 1990). I met Benjamin Libet at earlier conferences, and he also attended the Vatican Study Week. We liked each other and became friends, although not being of the same opinion regarding the freedom of human will. He worked with Wundt's event clock and asked his subjects to remember the position of a red dot on the clock at the instant when the "conscious urge to move" occurred to him or her. Libet made a big claim in his Vatican lecture (Libet 1990) by saying that freedom is firmly linked with consciousness, the state of full awareness. He brings it to the point in his own words: "The unconscious initiation of a freely voluntary act." Libet is correct in this statement, but his interpretation is not correct. He takes it for granted that in our unconscious or preconscious inner world there is no freedom, and thus concluded that we have free will in the control of the movement but not in its initiation. This is because the "W" in his paradigm (conscious wish) comes later than the start of the readiness potential.

Kornhuber and I, joined by the philosopher Daniel C. Dennett, are of the opinion that there are conscious and unconscious agendas in the brain, and both are important. The conscious and unconscious agendas of the brain were the subject of a workshop at the European Neurological Society (ENS) Congress 2010 in Berlin, where Dennett and Adrian Owen were the speakers. I also expressed our view in a paper in *Brain Sciences* (Deecke L, 2012). Libet's paradigm is a mixture of cerebral and subjective events, and the problem lies in the subjective event (W).

It is hard to trace back split seconds, and 200 msec is very, very short. I tried the Libet paradigm myself with students, and we were not able to accurately perform in his paradigm with Wundt's event clock position that has to be recalled retrospectively. Wundt's event clock has been designed for sensory psychophysical experiments.

In a voluntary movement paradigm (BP-paradigm), it is like a "foreign body," because it is an external stimulus and thus disturbs the "volitionality," so to say,

the willfullness of the movement or action. In conclusion, Kornhuber and I feel that the importance of consciousness has been underestimated by the behaviorists. It is not an epiphenomenon. If after brain injury, consciousness is regained, the lesion can (partially) be compensated, however never without consciousness. Conscious awareness is a shining light of freedom, although it should not be overestimated either.

For most of the vital functions, consciousness is not necessary, and it is not the only sign of freedom. The experiment of Libet et al (1983), which showed that the BP is not, right from the beginning, accompanied by a consciousness about the intention of movement is taken at present as the main argument for advocating a total determinism, a complete unfreedom of humans. This position is not tenable. What would be essential to study is the original planning and decision. This, however, has been completed already before the beginning of the experiment, when subjects gave their informed consent to the experimenter's instructions. Repetitions of stereotyped simple movements are not suitable for such an investigation.

Thoughts of planning and motivation are as we all know performed in the light of consciousness. The conscious awareness to want to make a movement does occur, in investigations of the BP, about 200 ms prior to the muscle contraction — Libet's W. This is roughly the same time span needed for a motor reaction upon an expected auditory stimulus. Although the decision to act already has been made earlier, consciousness is switched on in order to be able to make changes to the movement if necessary — changes that can go as far as not executing the action at all (Libet's veto), and to be able to learn from the success of the movement. In both cases, the following brain areas are activated: the SMA, the pre-SMA, the anterior portion

of the cingulate cortex (CMA) and a part of the motor cortex (Cunnington et al 2000), for which the basal ganglia do the groundwork (Kornhuber and Deecke 2012). However, with the self-initiated movement — but not with externally triggered movements — additionally the basal ganglia are activated before the movement (Cunnington et al, 2002). This preparatory process for the spontaneous movement, through which the readiness for movement in the SMA builds up, remains unconscious for the first 400 ms, as Libet has demonstrated.

It is not unusual for something to happen unconsciously in the brain as well as

in sensory systems. In the motor system, processes that are initially conscious can become unconscious through automatization (also cf. Wu et al 2004). The switching on of consciousness shortly before the movement is a great expenditure for the brain and shows that even such "unimportant" repeated movements needed for the averaging procedure are controlled, if they are voluntary.

Consciousness is known to be restricted and its time is valuable, only important events get access to it. As measurements of the "channel capacities" of the senses in psychophysical experiments have shown, there is a selection/filtering of the important matters between the information flow in our senses and that in our consciousness. This sophisticated selection also is unconsciously organized and represents an enormous compression of information of at least  $10^4$ ; information flow through the receptors and afferent nerves is at least  $10^3$  bit/sec (by order of magnitude), whereas only 10 bit/sec show up in consciousness. The will, however, always takes part, albeit sometimes merely to the degree that it delegates as much as possible to unconscious routines and expert systems of the brain. The unconscious processes therefore do not lessen freedom; on the contrary, they form its primary basis.

#### Magnetoencephalography (MEG)

In 1981, Hal Weinberg invited me as a distinguished visiting professor to the Simon Fraser University in Greater Vancouver, Canada, and we were the first to record the MEG equivalent of the BP, the "Bereitschaftsfeld, BF" (Deecke,

— their activities cancel each other. We were using two strategies to overcome the problem of cancellation. The first, published by Lang et al (1991), involved investigating a patient with a stroke in one of his SMAs (the right in this case). The patient had only one SMA left, and we were able to record early starting magnetic fields of his left SMA — he performed right-sided movements. The paper's abstract summarizes this: "Previous studies by magnetoencephalography (MEG) failed to consistently localize the activity of the supplementary motor area (SMA) prior to voluntary movements in healthy human subjects. Based on the assumption that the SMA of either hemisphere is active prior to voluntary movements, the negative findings of previous studies could be explained by the hypothesis that magnetic fields of current dipole sources in the two SMAs may cancel each other. The present MEG study was performed in a patient with a complete vascular lesion of the right SMA. In this case, it was possible to consistently localize a current dipole source in the intact left SMA starting about 1,200 msec prior to the initiation of voluntary movements of the right thumb."

Our second strategy was to use a multichannel whole scalp MEG instrument on healthy subjects. In Vienna, we had a CTF system with 143 channels and used a sophisticated analysis (two-dipole and three-dipole model in the same subject) to study the Bereitschaftsfeld (BF) prior to tapping movements (Erdler et al 2000). The paper's abstract states: "Despite the fact that the knowledge about the structure and

the function of the supplementary motor area (SMA) is steadily increasing, the role of the SMA in the human brain, e.g., the contribution of the SMA to the Bereitschaftspotential, still remains unclear and controversial. The goal of this study was to contribute further to this discussion by taking advantage

of the increased spatial information of a whole-scalp MEG system enabling us to record the magnetic equivalent of the Bereitschaftspotential 1, the Bereitschaftsfeld 1 (BF 1) or readiness field 1. Five subjects performed a complex, and one subject a simple, finger-tapping task. It was possible to record the BF 1 for all subjects. The first appearance of the BF 1 was in the range of -1.9 to -1.7 s prior to movement onset, except for the subject performing the simple task (-1 s). Analysis of the development of the magnetic field distribution and the channel waveforms showed the beginning of the Bereitschaftsfeld 2 (BF 2) or readiness field 2 at about -0.5 s prior

to movement onset. In the time range of BF 1, dipole source analysis localized the source in the SMA only, whereas dipole source analysis containing also the time range of BF 2 resulted in dipole models, including dipoles in the primary motor area. In summary, with a whole-head MEG system, it was possible for the first time to detect SMA activity in healthy subjects with MEG."

#### fMRI – functional Magnetic Resonance Imaging

In 2003, Marjan Jahanshahi and our chairman of the session, Mark Hallett, edited a book titled, "The Bereitschaftspotential — Movement-Related Cortical Potentials" (Jahanshahi M & Hallett M 2003). The closing chapter is written by Deecke and Kornhuber (Deecke & Kornhuber, 2003). The book and chapter for the first time compile all of the evidence that the BP or better "BP-like movement-related activity" can be recorded from the basal ganglia. This cannot be done by EEG or MEG, but requires the fMRI. And not just the routine fMRI but an fMRI improved in such a way that the temporal resolution is high enough to justify the term "event-related fMRI" and in our special case "movement-related fMRI." This was achieved by Cunnington et al (1999) who showed that it was feasible to record a BP equivalent in the haemodynamic response of the fMRI. Using single-event fMRI in combination with fuzzy clustering analysis, it is possible to analyze the "Bereitschafts BOLD effect" in the form of the haemodynamic response time course. This haemodynamic response resembles the BP or BF but is delayed in time (Cunnington et al 2002).

The movement-related fMRI experiments of Cunnington et al (2002) had great localizatory power and were particularly valuable for mapping the mesial surfaces of the hemispheres, where SMA and CMA are located. In this paper, self-initiated movements were compared with externally triggered movements. In both conditions, the following structures were active: pre-SMA, SMA proper and CMA (cingulate motor area, i.e. part of the anterior cingulate gyrus. The border between pre-SMA and SMA proper is the VAC line (vertical anterior commissure line). Although both pre-SMA and SMA proper are active in self-initiated movements and also in externally triggered ones, there are slight differences: The activity with self-initiated movements is slightly more anterior. It is true that the pre-SMA has somewhat greater involvement in self-initiated movements, but it is clear that it is not the pre-SMA alone that is active (Shibasaki & Hallett 2006) but that both pre-SMA and SMA proper are always activated in voluntary movement.

Using the fMRI, it also was possible to show that the SMA/CMA is active, when a movement is not executed but only imagined. Kasess et al (2008) compared movements that are actually executed with those that are only imagined. They

## The movement-related fMRI experiments of Cunnington et al (2002) had great localizatory power and were particularly valuable for mapping the mesial surfaces of the hemispheres, where SMA and CMA are located.

Weinberg Brickett 1982). We investigated the Bereitschaftsfeld accompanying foot movements as did Riita Hari and her group (Hari et al 1983). We also investigated slow magnetic fields of the brain preceding speech in Vancouver (Weinberg et al 1983).

Using our own MEG in Vienna, we later investigated the problem of why the SMA (and CMA) activity was not so visible in the MEG (the onset time of the BF was not earlier than 600 msec). The answer is that the two SMAs on the mesial surface of the brain are opposing each other, and if they are both active — which is the case most of the time





**Figure 2:** Chairman and speakers in the session “Bereitschaftspotential – 50 Years After Its Discovery” at the International Congress of Clinical Neurophysiology 2014 (ICCN2014) on March 20, 2014, in Berlin. From left to right: Gert Pfurtscheller, Graz, Austria; Ross Cunnington, Brisbane, Australia; Lüder Deecke, Vienna; Hiroshi Shibasaki, Kyoto, Japan; and Mark Hallett, Bethesda, Maryland (Chairman).

obtained the interesting result that SMA/CMA were active in both imagination and execution, however the motor cortex, M1, was active in executed movements only. In this context, we may report on earlier work using DC-EEG (Uhl et al 1990) and Single Photon Emission Computed Tomography (SPECT) (Goldenberg et al (1989) in mental imagery. We were able to show that the frontal cortex (of which the SMA/CMA form a part) is necessary to bring about the mental imagery (Lang et al 1988; Uhl et al 1990).

Mental imagery is the term in the psychological literature meaning our ability to see something in our mind's eye. In Uhl et al 1990, we investigated the slow cerebral potentials (DC potentials) accompanying mental imagery. The interesting result was that — with the willful attempt to see something in your mind's eye (mental imagery) — the frontal cortex was activated first and only thereafter the posterior (sensory) areas of the brain were activated. The strong initial DC negativity of the frontal cortex demonstrated that these frontal areas fulfill an important role in mental imagery: They show that mental imagery is an act of volition, and these frontal areas are needed for the act of bringing about the imagery. In the SPECT study (using the same subjects), analogous results were obtained. These experiments have shown that our “motivational brain” is not only involved when it “exerts itself” in the form of movement or action, but also when it comes to “endogenous acts” (pure mental acts) such as mental imagery, learning with mental rehearsal and thinking. We all know from introspection

that the generation of an image in our “mind's eye” may need considerable effort, and when we increase the effort we achieve a sharper image.

Another important finding of the fMRI studies was that movement-related activity also was recorded from the basal ganglia (Cunnington et al 2002). This finding is important and makes perfect sense in view of the cortico-basal ganglia-thalamocortical loop (cf. Kornhuber, 1974a; Alexander et al (1986); DeLong, 1990). The activity traveling through this loop comes from the SMA/CMA and goes to the M1. On this way, it not only informs the basal ganglia that a movement is about to be initiated but also draws upon the expertise of the basal ganglia as large stores of (over) learned movements and skills. The basal ganglia do the groundwork for the motor cortex M1. In this context, the “chunking hypothesis” of the Hallett group is attractive (Gerloff et al, 1997). These findings are exactly in line with our SMA hypothesis, where we envisage the SMA as a job distributor and supervisor. The SMA organizes sequential tasks in such a way that it breaks down the sequences into handy pieces and reserves the appropriate time slots for their launch. This is what we understand by spatial and temporal coordination. The interesting finding of Cunnington et al (2002, Figure 21) was, however, that activity in the lentiform nucleus (at the junction between the putamen and the external pallidum) was found for *self-initiated* movements only. For externally triggered movements, there was no evidence of increased activation within the basal ganglia.

A last word about the CMA, the cingulate motor area: Kornhuber and I

have reported on this area since the 1990s, but the researcher who worked most intensively on its function is Jun Tanji (Tanji 1994). The cingulate motor areas, located in the banks of the cingulate sulcus, constitute a portion of the cingulate cortex of primates. The rostral cingulate motor area (CMAr) is crucial for reward-based planning of motor selection, whereas the caudal (CMAc) is not (Shima et al 1991). Cunnington recently expanded on this, and investigated concurrent fMRI-EEG and the Bereitschafts-BOLD-effect (cf. his abstract at the end).

To conclude, let me shortly report on the visual hand-tracking experiments of brothers Wilfried and Michael Lang (Lang et al 1983; Deecke et al 1984). In these tracking experiments, designed by them, the temporal course of the moving stimulus was known to the subject while the *direction* of the moving stimulus (which changes suddenly at a certain time) was unpredictable: The SMA showed anticipatory behavior in that the BP declined  $\frac{1}{2}$  sec before the expected change, whereas the directed attention potential (which had its maximum over the parietal area) continued to remain high until 200 msec after the direction change of the stimulus, when the sensory processing was completed. Thus, the frontal lobe, after deciding what to do, *delegated* further action to posterior cortical areas, which are competent to use visual stimuli and to decide in detail how to perform the tracking task.

From these and similar experiments and from previous results on lesions (Kleist, 1934; Shallice, 1991), Kornhuber developed a theory on the components of volition and their functional localization in the frontal lobes (Kornhuber, 1984; Lang et al, 1983, 84; Deecke et al, 1985). One of the stages of volition is planning, and for planning, a working memory is required. The brain is a cooperative system, but one with strategic organization. There is little doubt that in humans the prefrontal-orbital cortex controls the highest level of planning and decision-making. The frontal lobe is the most humane part of humans. It is due to our frontal lobe that we have the personality we have, equipped with what we call reasoned free will.

This is all laid out in a book that was recently published in English in the U.S.,

which may be recommended as further reading (Kornhuber & Deecke 2012).

I am ending with the photo taken at the session with Mark Hallett's camera, and with the abstracts of the other speakers. They are published in *Clin. Neurophysiol.* and can be found at [www.ICCN2014](http://www.ICCN2014).

#### S4 Generator Mechanism of BP and Its Clinical Application

HIROSHI SHIBASAKI, AKIO IKEDA (KYOTO/JP)

Since discovery of the slow negative electroencephalographic (EEG) activity preceding self-initiated movement by Kornhuber and Deecke in 1964, various source localization techniques in normal subjects and epicortical recording in epilepsy patients have disclosed the generator mechanisms of each identifiable component of the movement-related cortical potentials (MRCPs). Regarding simple movements, the initial slow segment of BP (early BP) begins about 2 sec before the movement onset in the pre-supplementary motor area (pre-SMA) with no movement site-specificity and in the SMA proper with some somatotopic organization, and shortly thereafter in the lateral premotor cortex bilaterally with relatively clear somatotopy. About 400 ms before the movement onset, the steeper negative slope (late BP) occurs in the contralateral primary motor cortex (M1) and lateral premotor cortex with precise somatotopy. Both early and late BPs are influenced by complexity of the movements while late BP is influenced by discreteness of finger movements. Volitional motor inhibition or muscle relaxation is preceded by BP, which is quite similar to that preceding voluntary muscle contraction. Regarding movements used for daily living such as grasping and reaching, BP starts from the parietal cortex, more predominantly of the dominant hemisphere. BP has been applied for investigating pathophysiology of various movement disorders.

Early BP is smaller in patients with Parkinson disease, probably reflecting the deficient thalamic input to SMA. BP is smaller or even absent in patients with lesions in the dentato-thalamic pathway. Because BP does not occur before involuntary movements, BP is used for detecting the participation of the “voluntary motor system” in the generation of apparently involuntary movements in patients with psychogenic movement disorders.

#### S5 Movement-Related Desynchronization and Resting State Sensorimotor Networks

GERT PFURTSCHELLER (GRAZ/AT)

Preparation for a voluntary movement is not only accompanied by the “Bereitschaftspotential” (BP) and the pre-movement desynchronization (ERD) of central alpha and beta band rhythms but also by a concomitant heart rate (HR) deceleration. The intimate connection between brain and heart was enunciated by Claude

Bernard more than 150 years ago (Darwin 1999, pp. 71-72, originally published 1872) and is based on central commands projecting to cardiovascular neurons in the brain stem and modulating the HR.

One interesting question is, why do BP, ERD and HR changes start already some seconds prior to movement onset? It has been documented that the resting state sensorimotor network can oscillate at ~ 0.1 Hz observed in EEG, NIRS-HbO<sub>2</sub>/Hb and fMRI-BOLD signals (Vanhatalo et al PNAS 2004, Sasai et al Neuroimage 2011). This suggests that the ongoing brain activity can display slow/ultraslow excitability fluctuations in the range of ~10 sec, and voluntary movements are most likely initiated if the excitability in resting state sensorimotor networks reaches a specific threshold. Remarkable is that a close coupling can exist between cerebral and cardiovascular ~0.1 Hz oscillations.

### S97 Concurrent fMRI-EEG and the Bereitschafts-BOLD-Effect

\*ROSS CUNNINGTON

1University of Queensland, School of Psychology & Queensland Brain Institute, Brisbane, Australia

The cortical correlates of voluntary actions precede movement by up to 1-2 sec, as evident in the Bereitschaftspotential. This sustained activity prior to movement is strongly influenced by attention and by arousal levels, showing less activity when actions are relatively unattended and when arousal level is low. While fMRI has revealed key regions that contribute to pre-movement activity, the relationship between activity in these regions and the Bereitschaftspotential is not well understood. By using concurrent EEG and fMRI measurement and single-trial correlation analysis, we find that the cingulate motor area in the mid cingulate cortex plays a key role in driving sustained activity in the higher motor areas prior to voluntary action. Specifically, we find that trials in which early Bereitschaftspotential activity is large are associated with greater activity in the mid cingulate cortex, and a greater influence of the mid cingulate cortex on sustained activity in the supplementary motor area. This key role of the cingulate motor area in driving sustained activity of the supplementary motor prior to movement can explain how factors such as attention and arousal level also have such a strong influence on early neural activity of the Bereitschaftspotential.

Thanks go to Dr. Volker Deecke, senior lecturer, Centre for Wildlife Conservation, University of Cumbria, UK, for his comments and help with the English.

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# Editor's Update and Selected Articles From JNS

BY JOHN D. ENGLAND, MD

On behalf of the Editorial Board, I would like to thank all of the individuals who review articles for the *Journal of the Neurological Sciences (JNS)*. The integrity of a scientific journal such as *JNS* depends heavily upon the quality of independent peer-review.

I continue to be impressed with the high quality and thoroughness of the reviewers' critiques of manuscripts.

I am especially impressed and thankful that such busy and committed individuals still take the time to review articles.

One of my goals for this year is to seek advice from the Editorial Board and Elsevier about how we might



John D. England, MD

be able to recognize the efforts and importance of our reviewers in a more tangible manner.

Most readers are becoming aware of the fact that Elsevier, the publisher of *JNS*, now provides free access to selected articles from *JNS* for members of the World Federation of Neurology. In consultation with members of the Editorial Board, I select two "free-access" articles, which are profiled in each issue of *World Neurology*.

In this issue, we feature two paired articles:

1) Hellmann, et al. reviewed the response to maintenance intravenous immunoglobulin (IVIg) in a cohort of 52 patients with myasthenia gravis (MG) who had not responded adequately to pyridostigmine, prednisone, azathioprine, or combinations of these medications. Fifteen of the patients did not respond to an initial trial of IVIg, and were not treated with additional doses of IVIg. Thirty-seven patients respond-

ed to the initial trial and were treated with maintenance IVIg (0.4 g/kg every three to six weeks) for an average of 5.9 years (range 1 to 17 years). Twenty-three patients achieved mild improvement, and 14 patients achieved moderate improvement as measured by the Myasthenia Gravis Foundation of America (MGFA) clinical classification scheme. A beneficial response was associated with bulbar onset, seropositivity and high titer of acetylcholine receptor antibody, and older age of disease onset. Probably the most important observation in this study was that none of the patients achieved full remission with maintenance IVIg. Although IVIg improved symptoms of MG and allowed reduction of other medications, it did not provide a sustained effect or true remission of the disease. (Hellmann MA, Mosberg-Galili R, Lotan I, Steiner I. Maintenance IVIg therapy in myasthenia gravis does not affect disease activity. *J Neurol Sci* 2014;338:39-42)

2) Marinou Dalakas provides a thoughtful editorial on the above-noted article and places its results into the perspective of current treatment options for myasthenia gravis (MG). He emphasizes the point that IVIg appears to exert only a short-term and transient immunomodulation in MG and does not provide immunosuppression of the disease. At this time, the evidence supports restricting the use of IVIg in MG to short-term treatment of unstable patients until immunosuppressive treatments become effective. However, only a prospective trial of IVIg therapy for MG will provide definitive conclusions regarding its long-term effectiveness in managing this disease. (Dalakas M. IVIg in the chronic management of myasthenia gravis: Is it enough for your money? *J Neurol Sci* 2014;338:1-2) •

England is editor-in-chief of the *Journal of the Neurological Sciences*.

## IN MEMORIAM

THEODORE L. MUNSAT, MD

## A Tribute from the Sociedad Neurologica Argentina

**N**ever too late for a tribute, especially for a man like Theodore Leon Munsat (1930-2013). He was an extraordinary man and a natural educator who gave the opportunity to improve neurology worldwide.

Among other educational activities, Munsat helped launch the American Academy of Neurology's (AAN's) continuing education publication, *Continuum*, was chairman of the World Federation of Neurology (WFN) Amyotrophic Lateral Sclerosis (ALS), chairman of WFN Research and Education Committees, served as president of the AAN (1989-91), and was emeritus professor of neurology at Tufts University Scholl of Medicine, between other relevant activities. Indeed, exceptional merits for only one man.

He was honored with the A.B. Baker Award for Education from the AAN, the Sheila Essey Award for ALS Research and the Lifetime Achievement Award from the WFN Research Group on Neuromuscular Diseases.

He developed a number of successful educational programs. More than 42 countries all over the world were benefited with a continuing medical education (CME), using the journal *Continuum*, generously donated by the AAN with an extraordinary local impact.

He worked within the WFN to improve neurology and education in many developing countries, including educational programs in Honduras and Argentina. He directed his energies to teaching neurology internationally.

I met Munsat at the WFN World Congress of Neurology 1997 in Argentina with his wife Carla. We invited him to an International Symposium as part of the scientific activities after the congress, in Tucumán, Calchaquies Valleys, in the North of Argentina, where several conferences of ALS took place, with Alan Mac

Comas, Roberto Sica and other international leaders in neuromuscular diseases.

In that opportunity began the idea to develop an educational program for Argentina.

The educational program began in 2003 and benefitted over a decade of continuity to hundreds of neurologists in our country with a significant educational imprint.

I want to highlight his passion for educa-

tion, intelligence, humor, kindness with a great ability to make easier the hardest things, a natural leader, a gentleman, an honorable man. He had a warm and sincere



**Ted Munsat worked with the WFN to improve education in developing countries like Argentina in 1999.**

personality. he loved helping others every chance he could.

I admired and respected him as a man, as a professional and as a teacher. He has left a profound mark on the world of neurology. The Sociedad Neurológica Argentina wishes to give this tribute and extend our gratitude. Dear Ted, thank you very much for all you have done; we shall remember your legacy always. •

## Maynard M. Cohen (1920-2014)

**G**reat scientist, one of the pioneers of the American modern neurology, lover of philosophy and culture, philanthropist. Maynard M. Cohen, MD, PhD, professor and chairman emeritus in the Department of Neurological Sciences at the Rush-Presbyterian-St. Luke's Medical Center in Chicago, and past AAN president, died on Feb. 18, 2014, in Miami in his 94th year.

As the world-renowned neurologist, he was the U.S. delegate to the World Federation of Neurology (1985-1989). At the delegates' preparatory meeting (1987) in New Delhi for the XIVth WCN, he strongly supported the organization of the symposium, proposed by Yugoslav and Indian neurologists: "Neurology in Developing Countries" during the New Delhi WCN in 1989. After the successful symposium, in which our respected friend gave a beautiful contribution, the then-WFN

President Richard Masland and the then-Chairman of the WFN Research Council John Walton proposed to form a new

Research Group on Organization and Delivery of Neurological Services (WFN RG ODNs) in order to search for best solutions in delivery of neurological services around the world (both in industrial and developing countries), respecting local and regional, social and economic conditions.

Cohen accepted to serve as secretary



**Maynard M. Cohen, MD, PhD**

treasurer of the new research group, participating in the new activities in the Federation. As co-editor of the book, he cared that contributions from less developed countries find a place in it. He concluded his own chapter with visionary words: "This symposium, the support of the World Federation of Neurology, and the formation of the Research Group on Organization and Delivery of Neurological Services are but the initial steps. The larger task still lies ahead." (Neurology in Developing Countries, B.I. Churchill Livingstone, 1991, p.75).

Despite his years, he showed remarkable enthusiasm and energy as co-organizer of our meetings (New Delhi, Vienna, Marrakesh, Vancouver and others), as well as initiatives in many parts of the world. He organized an important symposium, "Ethical Problems in Neurology," concerning problems in managing neurological ailments due to

various cultural and religious traditions (XVth WCN Vancouver 1993), engaging the leading experts in the field from the U.S. and other countries of the globe.

During his service (until 1995), he supported activities of the group. When we needed new, experienced colleagues for the organization, he proposed new active members for the RG Committee: Donna Bergen and Don Silberberg, who have stayed active in the WFN. His wife, Doris Vidaver, participated kindly with her experience in humanities and in medicine, especially in neurology.

The World Federation of Neurology will memorialize his activities, for which he received in 1993 the WFN Certificate of Appreciation. They are now being continued also as an integrative part of the WFN mission and programs. Many neurologists active in those years still remember our early initiatives and the humane care of Maynard M. Cohen for people around the world. •

Bosko Barac, MD, DMS, is the founding chairman of the WFN RG ODNs (ret.).





WORLD FEDERATION OF NEUROLOGY



World Brain Day  
Our Brain Our Future



# World Brain Day

## Our Brain Our Future

**WORLD Brain Day** 22nd July

### Brain is the most amazing and complex organ in the human body.

The human brain consists of millions and millions of electrical wires which are known as axons

This distance is the equivalent of travelling around the earth four times in a row! It is thought that there are about eighty billion neurons within the human brain. There are about ten trillion connections between these neurons which help us to read, write, watch, learn, plan, think, feel, move and solve problems on a daily basis.



### Diseases affecting brain such as Stroke,

Diseases affecting the brain include Stroke, Epilepsy, Depression, Tumors, Traumatic Injury, Alzheimer's Disease, Infections, Headache, Sleep Disorder and Genetic Disorders.



Diseases affecting the brain are the single most important cause of disability in the world



It's time to act. Let's get together to promote better brain health globally.

Exercise, healthy eating, avoidance of tobacco, drugs and alcohol, reading and problem solving promotes brain health.



### Our brains are at a crossroads now!



One in three of us will get dementia or stroke during our life time. This can occur at any age-any time-anywhere! Both these disorders are preventable-treatable for the most part.



WORLD FEDERATION OF NEUROLOGY

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