CLAE Connections

JULY 18; VOLUME 6: ISSUE 2

Canadian League Against Epilepsy

MESSAGE FROM THE PRESIDENT

INSIDE THIS ISSUE:

Dear members,

It has been a busy first half of the year for the CLAE. Our annual meeting agenda has been finalized, and it looks amazing. The Education Committee under the leadership of Dr. Mark Keezer has worked hard in selecting your proposals for the different sessions as well as the abstracts submitted to the meeting. The meeting will have plenary and breakout sessions touching on very important aspects of pediatric and adult epileptology. Our main session on the first day of the meeting will focus on Autoimmune Epilepsies, a topic on vogue these days. We hope all of you register and attend the meeting in St. John's from September 21st to the 23rd. We are expecting to have record attendance! Also, let's get some exercise together early Saturday morning while in St John's by participating in our annual Fun Run/Walk. Consider forming a team from your institution or region of Canada to support the CLAE and CEA.

Given the success of our recent previous meetings, the CLAE Executive Committee has decided to have our scientific meeting every year. Suggestions for the location of future meetings are welcome. You are also encouraged to continue submitting proposals and abstracts to our meetings. There is also the possibility that every few years, during our meeting we will be hosting the North American Epilepsy Regional Congress. More news about it to come soon.

I would like to take the opportunity to congratulate the different awardees this year: CLAE clinical fellowship to Dr. Mansouri Alizera (University of Toronto), Mary Ann Lee Award to Dr. Jonathan Lau (Western University), and the Junior Investigator Award (a tie!) to Dr. Mark Keezer (University of Montreal) and Dr. Colin Josephson (University of Calgary). All these individuals will be recognized during our upcoming scientific meeting.

The Medical and Therapeutics Committee under the leadership of Dr. Juan Pablo Appendino has been also busy dealing with shortages of anti-seizure medications. Most importantly, they are currently about to finalize the CLAE statement on the use of Cannabis for epilepsy. We will be asking for feedback from all members before it is released to the public.

You have been contacted by the CLAE office seeking your input on two occasions over the last few months. The first one was to have you complete a survey on driving and epilepsy. The responses were not what we expected, therefore the survey was re-sent. If you have not had the chance to respond, please do so soon. The second occasion was to obtain information on activities done by our members abroad. Very few responded. I hope that if you did not respond or did not receive the email, please contact me or Laura Jurasek (University of Alberta). We know many of our members contribute to epilepsy care outside Canada and would like to know about it.

Finally, I would like to acknowledge the support of all of you in making CLAE better. I hope your dedication and engagement becomes stronger. Let's disseminate the word...join the CLAE!

See you in St John's.

Cheers,

Jorge

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RISING STAR

Dr. Robyn Whitney is a Pediatric Neurologist and Epileptologist who recently joined the Division of Neurology, Department of Paediatrics at the Hospital for Sick Children in Toronto, Ontario in October 2017. Dr. Whitney completed her undergraduate studies in Health Sciences at McMaster University in Hamilton, Ontario and then went on to also receive her medical degree from McMaster University. Following this she completed her residency in Pediatric Neurology at McMaster University, where she was the recipient of the Pediatric Neurology Teaching award on two occasions. During her residency, Dr. Whitney developed an interest in the care of children with epilepsy and their families and went onto successfully complete a two-year fellowship program in Pediatric Epilepsy and Neurophysiology at the Hospital for Sick Children, where she served as the chief epilepsy fellow.

During her fellowship, Dr. Whitney worked under the supervision and mentorship of Dr. Elizabeth Donner on the Canadian Pediatric SUDEP registry. She has presented this research both at national and international conferences and was the recipient of the CLAE trainee abstract award during her fellowship and Partners Against Mortality in Epilepsy (PAME) abstract travel award. In addition to her interest in SUDEP, Dr. Whitney also has a research interest in pediatric epileptic encephalopathies, including the use of novel therapies, as well as an interest in Tuberous Sclerosis Complex. Dr. Whitney's clinical interests are in the medical and surgical management of children with medically refractory epilepsy. She has a clinical interest in the use of dietary therapies to treat epilepsy and she works as a physician within the Ketogenic Diet Program. Dr. Whitney is a member of the Epilepsy Surgery Program and is involved in the evaluation of children undergoing epilepsy surgery. Furthermore, she recently joined as co-director of the Tuberous Sclerosis Clinic, within the Division of Neurology.

In addition to her clinical and research interests, Dr. Whitney has an interest in medical education. She was recently appointed Pediatric Epilepsy Fellowship Program Director at the Hospital for Sick Children in July 2018. She is actively involved in the education of both pediatric neurology residents and epilepsy fellows and is a member of the pediatric neurology residency education committee. She acts as the core supervisor for pediatric neurology residents during their epilepsy rotation and has helped in the design of this rotation. Dr. Whitney also facilitates and organizes the Pediatric Epilepsy Journal Club within the Division of Neurology. She is a member of the education committee for the Ontario Project Echo: Epilepsy Across the Lifespan and has helped in the design and delivery of the pediatric epilepsy curriculum. She was recently appointed a member of the CLAE fundraising committee.

Thank You note from the UCB Epilepsy Fellowship Award Winner

My name is Alireza Mansouri and I am a neurosurgeon aspiring toward an academic career in functional neuro-oncology, wherein my surgical practice is rooted in evidence-based medicine. Surgery for intrinsic brain tumors has seen a paradigmatic shift toward striving for maximal safe resections guided by functional brain boundaries. As such, a comprehensive understanding of the connectivity and plasticity of the brain is a prerequisite. Acquiring expertise as an epilepsy surgeon will add the unique skillsets that I will need for success in my chosen career.

As a mentor, Dr. Taufik Valiante has had a significant impact on my clinical and academic career. Under his supervision, we have been able to identify predictors of surgical candidacy for epilepsy patients admitted to our EMU. This was followed by our institutional report comparing and contrasting neurocognitive and seizure outcomes of patients undergoing selective amygdalohippocampectomy vs anterior temporal lobectomy ± amygdalohippocampectomy. In addition, based on a review of the health economics of surgery for medically-refractory epilepsy, we proposed guideline-based health policy changes to the healthcare system that can be implemented to promote timely referral of patients for a surgical opinion. Based on the high volume of adult and pediatric post-surgical outcomes available at the University of Toronto, and leveraging my post-graduate training in Clinical Epidemiology, we are now excited about the possibility of developing a unique seizure-freedom prediction score based on pre-operative parameters during my upcoming Fellowship. I am grateful and honored to be chosen for the UCB Fellowship Award. The support provided by the CLAE will be paramount in accomplishing my dreams and passions.

Congratulations Dr. Alireza Mansouri!

GLOBAL HEALTH AND CANADIAN EPILEPSY- PART 1: A VISIT TO THE TAY NGUYEN PLATEAU

In the next few newsletters this series of articles will focus on the various global health initiatives headed by Canadian epilepsy specialists across our planet.

Many epilepsy specialists in Canada are involved in projects aimed at improving the lives of patients living with epilepsy abroad. A group of epilepsy specialists recently joined forces to explore the current landscape of global health projects under Canadian leadership as well as learn from one another and share contacts and resources. The CLAE Global Health group formed last year under the leadership of Laura Jurasek, NP, MN (Edmonton, AB) and has since been hard at work collaborating on a number of topics, including how to spur interest nationally for more global epilepsy related projects.

In this issue we wanted to highlight the work realized by Dang Nguyen, MD, PhD from Université de Montreal. Here are some thoughts he shared with us during our interview:

Where is your project located?

In the Central provinces and Tay Nguyen highlands of Vietnam. We collaborate with the Hue University of Medicine and Pharmacy in partnership with my home institution, the University of Montreal Epilepsy Group (Canada). The former is one of the 3 biggest medical universities in Vietnam; its University Hospital is responsible for patients from central *provinces and the Tay Nguyen highland of Vietnam (~ which totals about 25 million habitants).*

Where did the interest come from to initiate such a project?

L'Association des Médecins de Langue Française organizes a continuing medical education course in a different country on a yearly basis. In 2007, they invited me to give a presentation on post-stroke epilepsy at a meeting they organized in Hue (Vietnam). Two years later, a local neurologist I met in 2007 contacted me to see if I would be interested in helping him and his team improve the care of epilepsy in their region. This was the beginning of a wonderful collaboration.

What does the project entail or consist of and what are its accomplishments to date?

Since 2010, the University of Montreal Epilepsy Group (here in Canada) and the Hue University of Medicine and Pharmacy have been working hard to improve the care of epileptic patients in the central provinces and Tay Nguyen Plateau (Vietnam). Our accomplishments until now have included:

- The training of a neurologist from Hue university for specialized care in epilepsy at the Montreal University Health Center (2012-2015).
- The training of a neurosurgeon from Hue University for epilepsy surgery at the Montreal University Health Center (2012-2015).
- The organization of epilepsy courses in Hue, Vietnam on the following dates: March 2013, March 2014, August 2015 and last year June 2017.
- The inauguration of an epilepsy clinic in Hue (Vietnam).
- The donation of one digital video-EEG machine and replacement of an old analog EEG machine with a new digital EEG machine.

What barriers did you encounter while trying to organize this?

There are many challenges including the lack of resources in the local hospitals (EEG machines, MRIs) as well as the lack of expertise (especially with EEG interpretation, evaluation of epilepsy surgery candidates etc.). Their healthcare system also does not afford a great deal of medical coverage for the poor. Much like some parts of North America, there is still ongoing scepticism regarding epilepsy surgery from physicians themselves and hospital administrators but fortunately, medical students, residents and young physicians are eager to learn.

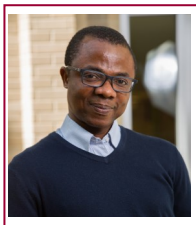
Where do you see this collaboration in the next 5- 10 years (i.e any long term plans for growth, sustainability?)

We will continue offering continuing medical education courses in epilepsy with the University of Hue. The next two-and-a-half day course will be June 26-28, 2019 (right after the IEC congress in Bangkok). We also hope to broaden our involvement by also training local physicians in the evaluation and care of not only epilepsy but also movement disorders. Finally our aim is to expand our collaboration to the Vietnam National University in Hanoi (visit planned for July 1st, 2019).

Dr. Dang Nguyen supervising the interview of a patient by local physicians (2017 Epilepsy Course).

By Tadeu A. Fantaneanu

PUBLICATION AWARD: FELLOW/POST DOC



Currently, more than 30-40% of children afflicted with epilepsy do not have seizure remission with the currently approved medications. This trend remains the same despite the advancement in anti-epileptic drug discovery. We started wondering about the reason for this and questioned the methods used to develop new anti-epileptic drugs. Dr. Deborah Kurrasch (my supervisor) and I, in conjuction, with our collaborator (Dr Jong Rho) decided to adopt a different approach to drug screening by developing a platform that focuses on metabolism rather than on channels and receptors. This new method mirrors the ketogenic diet and focuses on change in metabolism in the presence of disease. By screening repurposed FDA approved drugs in "epileptic" zebrafish, we discovered that vorinostat, an FDA approved drug currently used to treat cancer reduced the frequency of seizure in zebrafish and mouse epileptic models by about 60%. We recently published this findings in Brain, a journal of neurology with the title " A novel metabolism-based phenotypic drug discovery platform in zebrafish uncovers HDACs 1 and 3 as a potential combined anti-seizure drug target". Currently, I am a research associate in Dr. Deborah Kurrasch's laboratory at the University of Calgary, and I hope to start my own laboratory and continue to explore the mechanistic underpinning of epileptic seizures with hope to identify novel pathway targets and potential candidate drugs.

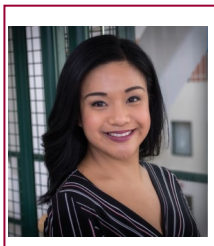
By the award winner, Kingsley Ibhazehiebo

PUBLICATION AWARD: MEDICAL STUDENT

Marna McKenzie is a third-year medical student at the University of Manitoba. The project leading to the publication of 'De Novo Mutations in YWHAG Cause Early-Onset Epilepsy' included 42 patients with epileptic encephalopathy (EE) and no previous genetic diagnosis. Rare coding variability was assessed in 20 candidate genes, prioritized by in silico modelling of brain co-expression with 51 established EE-associated genes. This identified a de novo mutation in YWHAG in one patient. Six additional patients with de novo mutations in YWHAG, and a concurrent early-onset epilepsy diagnosis, were subsequently identified through online tools. This study took place at the University of British Columbia (UBC), supervised by Dr. Matthew Farrer and Dr. Ilaria Guella. The project was the continuation of a research study, involving exome sequencing of 160 patients with early-onset, treatment-resistant epilepsy attending BC Children's Hospital, that began in 2014 while Marna was working with Dr. Farrer and Dr. Guella at UBC. Marna continues to have a strong interest in both neurology and research and plans on continuing research in the field throughout her residency and career.

By the award winner, Marna McKenzie

PUBLICATION AWARD: ALLIED HEALTH



I am the principal author of the recently published research paper entitled, "Academic outcomes in individuals with childhood-onset epilepsy: Mediating effects of working memory", which was published in the Journal of the International Neuropsychological Society in August 2017. For this project, I examined the interrelationships between seizure status (persistent seizures versus controlled seizures), a specific cognitive domain (working memory), and several academic outcomes (reading, spelling, arithmetic) in a sample of 91 children with epilepsy receiving treatment at the Hospital for Sick Children (SickKids) in Toronto. Through mediation analyses, I found that persistent seizures were associated with lower working memory ability, which in turn resulted in poorer academic performance. These findings offer further insight into the challenges that children with epilepsy face in acquiring skills that are foundational for academic and vocational success. I co-authored this paper with Dr. Mary Lou Smith, who was my supervisor during a research rotation that I completed as part of my pre-doctoral psychology residency at SickKids. I am currently a Post-Doctoral Fellow in Clinical Neuropsychology at SickKids. In addition to my research experience in epilepsy, I also have gained clinical experience with this population through previous practicum/fellowship rotations at both SickKids and Toronto Western Hospital.

By the award winner Ashley Danguecan

MARY ANNE LEE PUBLICATION AWARD

Dr. Jonathan C. Lau is a PGY-5 Neurosurgery Resident at the University of Western Ontario. He is a PhD Candidate at the Robarts Research Institute under the supervision of Dr. Ali R. Khan and Dr. Terry M. Peters where his research has focused on ultra-high field (>= 7 Tesla) MRI and its use in image-guided neurosurgery, and in particular, epilepsy surgery.

In this manuscript, we studied the effect that MRI distortion has on our ability to use these images for invasive investigations of epilepsy (i.e. stereo-electroencephalography) and other stereotactic procedures. By understanding the regional effects of distortion and their limits, we have identified a way to still exploit the enhanced signal at 7T, paving the way for more refined surgical targeting. This line of research has become particularly timely with the recent announcement by the U.S. Food and Drug Administration to clear 7T for clinical use. Portions of this work have been presented at several meetings including: the American Society for Stereotactic and Functional Neurosurgery Meeting as a platform presentation, the Multimodal Imaging for Navigation in Epilepsy Workshop as a course talk, and most recently, the Canadian League Against Epilepsy Scientific Meeting as a Top Trainee oral presentation.

By the award winner Jonathan C. Lau

CLAE JUNIOR INVESTIGATOR AWARD WINNERS

Note from **Mark Keezer MD CM, PhD, FRCPC**

I am honored to be a 2018 CLAE Junior Investigator award recipient.

In January 2016, I had the great fortune to join the epilepsy group at the Centre Hospitalier de l'Université de Montréal (CHUM), as well as become a clinician investigator at the CHUM Research Centre where I have developed my research program. This program aims to study the comorbidities of epilepsy, their relationship to epilepsy aetiology as well as their impact on seizure outcome, quality of life, and healthcare utilization. I am interested in the impact of frailty in the elderly with epilepsy, how this interacts with comorbidities, and influences antiepileptic drug efficacy and tolerability. This work is funded by peer-reviewed grants from the Canadian Frailty Network, the Savoy Foundation, and the CHUM Research Centre. I have received additional funding from UCB Canada and the Fondation le Jardin de l'arbre de vie. My research group includes 1 post-doctoral fellow and 2 MSc students, as well as a number of resident and summer-student projects.

I am very fortunate to have had generous mentors. Tina Wolfson taught me methodological rigour as well as humility in the face of the enormous challenge of carrying out the highest quality clinical research. Ley Sander taught me enthusiasm and ambition, the joy of exploring new fields and of challenging conventional wisdom. More recently Nathalie Jetté and Dang Nguyen have been of great help, providing me early career advice as well as opportunities that are allowing me to reach my career goals.

I look forward to working with the wider research community in Canada, to make a collective impact on the lives of individuals living with epilepsy.

Colin Josephson MD, MSc, FRCPC, CSCN (EEG) is an Assistant Professor of Neurology and clinician-scientist in the Department of Clinical Neurosciences and a member of the O'Brien Institute for Public Health at the University of Calgary. He completed his medical school and neurology residency at Dalhousie University and has completed fellowships in intracranial vascular malformations (University of Edinburgh) and epilepsy and EEG (University of Calgary). Throughout his studies, he has been extremely lucky to be exposed to inspiring mentors and supervisors such as Dr. Mark Sadler, Dr. Nathalie Jetté, and Dr. Samuel Wiebe who encouraged him pursue interests in clinical epilepsy, epidemiology, and biostatistics.

His major research theme has been the application of 'Big Data', electronic medical records (EMR), and machine learning as means of advancing the epidemiology of epilepsy and developing outcome-based prediction models. He has used large United Kingdom based EMRs to evaluate the intricate relationship between depression and epilepsy, the association between antiepileptic drugs and psychiatric symptoms, and has developed a clinical decision rule that guides the prescription of leveitracetam for his Masters thesis in epidemiology. In addition, he has particular interest in the elderly with epilepsy. Few evidence-based recommendations exist for managing this growing population and, therefore, in collaboration with Dr. Mark Keezer he has helped design Canadian and United Kingdom studies that directly address their unique needs.

His future aim is to establish a nationwide epilepsy registry. Currently, he is head of the Calgary Comprehensive Epilepsy Program registry that contains over 6,000 patients. Funding is in place both to link these data to provincial administrative health records, EEG, and MRI data as well as to create a Canadian consortium whereby standardised data are collected and stored to facilitate multicentre collaboration on observational studies and randomised controlled trials.

A PILOT PROJECT TO IMPROVE THE DETECTION OF NON-CONVULSIVE SEIZURES IN CRITICALLY ILL CHILDREN

We face a major challenge in caring for critically ill children with brain injuries, since one third to half of them will have non-convulsive seizures. A study showed that there is a higher risk of short-term brain injury, when seizures add up to more than twelve minutes per hour. If these seizures last longer than thirty minutes per hour, children have a higher risk of developing epilepsy, poor overall outcome, lower quality of life or even death.

It is very important to prevent further brain injury by recognizing and treating these seizures as quickly as possible. Continuous electroencephalography (CEEG) monitoring is the gold standard for seizure detection. In many centers including the pediatric intensive care unit (PICU) at McMaster Children's Hospital an experienced neurologist or neurophysiologist reviews the CEEG, intermittently every few hours. This process is time consuming and prolongs seizure detection. This means that seizures may persist for hours before they are treated.

Quantitative EEG (QEEG) panels can simplify and improve the efficiency of reading CEEG by summarizing large volumes of EEG data into simple graphs with easy-to-read patterns. Studies have shown that neurophysiologists can identify seizures on QEEG with reasonable sensitivity and low false positive rates. Critical care providers retrospectively analyzing QEEG post cardiac arrest have likewise been able to detect non-convulsive seizures.

A more efficient method would be critical care nurses and physicians regularly reading QEEG, detecting seizures, reviewing them with an expert and giving antiepileptic medication quickly. However there are no clinical studies to show us if this method of review is accurate and feasible. We need to know this before we can compare this method to other strategies in controlled clinical trials.

This pilot project involved establishing clinical guidelines for Continuous EEG monitoring, and developing written and computer-based teaching materials that allow quantitative EEG software to be used by nurses and physicians at the bedside to recognize subclinical seizures in the paediatric intensive care unit (PICU). Once caregivers were trained we displayed the QEEG trends and an automated seizure detection algorithm at the bedside and asked them to complete a bedside seizure log. The intensive care resident or fellow would call the neurologist if necessary to validate their findings with CEEG. This was done in addition to the standard of care i.e. intermittent review of the CEEG by the neurologist on call.

Since rolling out the project in September 2018 we have had a favorable response from the neurologists, critical care physicians and nurses at our hospital. This has led to establishing regular interdisciplinary neurocritical care rounds and improved collaboration. The project has enabled me to explore knowledge translation and develop research projects to assess the accuracy, short and long term outcomes and feasibility of this approach.

It also powerfully illustrates patient advocacy and partnerships between the community of Hamilton and the McMaster Children's Hospital Foundation. Hamilton Health Sciences and McMaster Children's Hospital were able to purchase the Persyst 12 quantitative EEG software – essential to the operationalization of the project– because of the advocacy of leaders of the pediatric neurology division with the community, and the generous support of Mellissa and Ian Thompson in support of the McMaster Children's Foundation Pediatric Neurology and Epilepsy fund.

Kevin Jones MB ChB, FRCPC

Comprehensive Epilepsy Program

McMaster Children's Hospital

CLAE 2018 SCIENTIC MEETING: PROGRAM HIGHLIGHTS

Friday, September 21, 2018

Keynote speaker: Autoimmune Epilepsies

Saturday, September 22, 2018

CLAE Fun Run/Walk

Diet therapy for Epilepsies

Brain on Fire: Inflammation and the Childhood Onset Epilepsies

Post-Traumatic Epileptogenesis: From Bench to Bed

Artificial Intelligence and Epilepsy

Quality of Life of Individuals with Epilepsy

Intracranial Recording for Focal Epilepsy in Children

Novel Models of Epilepsy

Sunday, September 23, 2018

Seizure Semiology Session

Adolescents with Epilepsy: The Issues of Transitioning them from Pediatric to Adult Care

Sleep and Epilepsy are Common Bedfellows

Non-Neuronal Cells in Seizures and Epilepsy

Canadian League Against Epilepsy

The Canadian League Against Epilepsy is an organization of medical and basic sciences professionals including physicians, basic scientists, nurses, neuropsychologists, neuroradiologists, students and other healthcare professionals.

NOTE FROM YOUR EDITOR

The next issue of the CLAE Newsletter (November ,2018) will include meaningful and relevant information to CLAE members, including but not limited to the following:

1. CLAE Stars: A member who has received local, national or international recognition for his/her research, teaching, innovation or advocacy.

2. Innovative new programs and services (clinical, research or advocacy). These include, but are not restricted to: new major regional/ institutional or provincial clinical programs, new research themes, platforms, consortium and networks, outreach programs in vulnerable/ marginalized communities, innovative educational programs and advocacy initiatives/projects.

3. Major publications by Canadians in the field of epilepsy during the last six months.

4. Information on epilepsy meetings, and epilepsy related social events.

5. Information on recruitment of patients for research studies and opportunities for research, educational and clinical collaboration.

6. Success and success stories in major grant competitions.

7. Colleagues we recently lost /an 'In Memorium' section.

If you are interested in contributing and providing content to the CLAE Newsletter, please contact Rajesh RamachandranNair (rnair@mcmaster.ca) before October 15, 2018.

Thank you.

Rajesh RamachandranNair, MD, FRCPC

Editor-in-Chief, CLAE Connections

EDITOR'S PICK

1. Incidence of sudden unexpected death in epilepsy in children is similar to adults. Keller AE, Whitney R, Li SA Pollanen M1, Donner EJ. Neurology. 2018 Jul 10;91(2):e107-e111.
2. Prescription trends and psychiatric symptoms following first receipt of one of seven common antiepileptic drugs in general practice. Josephson CB, Engbers JDT, Jette N, Patten SB, Sajobi TT, Marshall D, Lowerison M, Wiebe S. Epilepsy Behav. 2018 Jul;84:49-55.
3. Spike-related haemodynamic responses overlap with high frequency oscillations in patients with focal epilepsy. González Otárula KA, Khoo HM, von Ellenrieder N, Hall JA, Dubeau F, Gotman J.VBrain. 2018 Jan 18. doi: 10.1093/brain/awx383

Four Canadians attended the second international ILAE Training Course in Neuropsychology in Epilepsy from April 15-20, 2018 in Provence, France. From left to right: Drs. Veronique Latreille (Montreal), Amy Wilkinson (Toronto), Nicole Taylor (Winnipeg), Ashley Danguecan (Toronto), and Mary Lou Smith (Toronto, course faculty member). Dr. Wilkinson was supported by a bursary from the Canadian Epilepsy Alliance/Alliance Canadienne de L'Epilepsie. Participants engaged in lectures, case presentations and discussions designed to illustrate principles of differential diagnosis and case formulation in neuropsychological practice in epilepsy and epilepsy surgery. Course material was presented by an international faculty made up of the clinicians and researchers who are at the forefront of evidence-based practice in this field.