## Hong Kong

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SUPPLEMENT 5

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## List of Speakers

## Name

## Affiliation

Dr Jill Abrigo	The Chinese University of Hong Kong, Hong Kong SAR
Prof Andrew Bleasel	Westmead Hospital, Australia
Prof Natan Bornstein	Tel-Aviv Sourasky Medical Center, Israel
Dr Andrew LT Chan	Queen Elizabeth Hospital, Hong Kong SAR
Dr Rou-Shayn Chen	Chang-Gung Memorial Hospital, Taiwan
Dr Andy CO Cheng	Hong Kong Sanatorium & Hospital, Hong Kong SAR
Dr Frankie Choi	Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR
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Dr Howan Leung	The Chinese University of Hong Kong, Hong Kong SAR
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Prof Einar Wilder-Smith	National University of Singapore, Singapore
Prof Dean M Wingerchuk	Mayo Clinic, United States
Prof Patrick CM Wong	The Chinese University of Hong Kong, Hong Kong SAR
Dr Raymond SM Wong	The Chinese University of Hong Kong, Hong Kong SAR

## SCIENTIFIC PROGRAMME

## Venue: Grand Ballroom, Level 3, JW Marriott Hotel, Admiralty, Hong Kong SAR

## 14 November 2015, Saturday

08:15 - 08:45	Registration	Poster Room
08:45 - 09:45	<b>FREE PAPER PRESENTATIONS</b> Chairpersons: Mona Tse, Betty Ng Judges: CM Chang, KK Lau	POSTER PRESENTATION
09:45 - 10:00	Coffee Break	-
10:00 - 11:25	<b>DISSERTATION HIGHLIGHTS</b> Chairpersons: <i>Mona Tse, Betty Ng</i> Judges: <i>CM Chang, KK Lau</i>	-
11:25 – 12:15	MERCK SERONO MULTIPLE SCLEROSIS SYMPOSIUM Chairperson: WK Cheng	
	<b>Treating Multiple Sclerosis in the 21st Century</b> <i>Gavin Giovannoni</i>	
12:15 – 13:15	GENZYME LUNCH SYMPOSIUM Chairperson: KH Chan	_
	<b>Emerging Insights in Multiple Sclerosis: Re-evaluation</b> <b>of Treatment Algorithm</b> <i>Mark Freedman</i>	
13:25 – 13:50	<b>OPENING CEREMONY</b> Guest of Honour: Prof Francis Chan, Dean, Faculty of Medicine, The Chinese University of Hong Kong	-
13:50 – 15:00	<b>MULTIPLE SCLEROSIS SYMPOSIUM</b> (CO-ORGANISED WITH HKMSS) <b>THEME: Multiple Sclerosis in 2015</b> Chairpersons: <i>KL Shiu (President of HKMMS), TH Tsoi</i>	
	<b>Neuromyelitis Optica Spectrum Disorders (NMOSD):</b> <b>Treatment Update</b> <i>Dean M Wingerchuk</i>	
	<b>Magnetic Resonance Imaging in Multiple Sclerosis</b> <i>Jill Abrigo</i>	
15:00 - 15:30	Coffee Break	_
15:30 – 17:00	<b>EPILEPSY SYMPOSIUM</b> (CO-ORGANISED WITH HKES) Chairpersons: <i>Colin Lui, Jason Fong</i>	
	THEME: Neuroimaging in Epilepsy	
	<b>Can Seizure Semiology Direct Our Neuroimaging</b> <b>Investigations in Refractory Epilepsy?</b> <i>Andrew Bleasel</i>	
	<b>SPECT and PET in Epilepsy</b> <i>Frankie Choi</i>	
	<b>Epilepsy Imaging</b> — the Things You May Not Know Deyond Siu	
18:00	Faculty Dinner (by invitation only)	

	15 November 2015, Sunday	
08:30 - 09:00	Registration	Poster Room
09:00 – 10:30	SYMPOSIUM ON COGNITIVE NEUROLOGY THEME: Frontotemporal Dementia Chairpersons: SH Ng, Eric Chan	POSTER PRESENTATION
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	Frontotemporal Dementia—Insights into a Complex Disorder Jonathan Rohrer	
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	<b>Stroke in Neuro-Ophthalmology</b> Andy CO Cheng	
	Update on Treatment of Ischaemic Stroke Christopher Levi	
	Filling the Gaps in Bleeding Management in Stroke Patients Taking NOACs: from Laboratory Tests to Reversal Agent Development Raymond SM Wong	

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12:15 – 13:15	<b>PFIZER LUNCH SYMPOSIUM</b> Chairperson: <i>YL Yu</i>	Poster Room <b>POSTER</b>
	Secondary Stroke Prevention in Patients with Atrial Fibrillation: Balancing the efficacy and Safety Natan Bornstein	PRESENTATION
13:30 – 15:00	UCB MOVEMENT DISORDERS SYMPOSIUM Chairpersons: Nelson Cheung, Mandy Au-yeung	
	THEME: Parkinson's Disease: Facts and New Perspectives	
	The Natural History of Parkinson's Disease SY Lim	
	The Perspective of Gait Issue in Parkinson's Disease: from Clinical Phenomena to Basic Mechanism RS Chen	
15:00 - 15:15	Coffee Break	
15:15 – 16:45	NEUROPHYSIOLOGY SYMPOSIUM THEME: Recent Advances in Neurophysiology Chairpersons: Winnie Wong, CN Lee	
	<b>Peripheral Nerve Disorders</b> — from Nerve Conduction <b>Studies to Ultrasound</b> <i>Einar Wilder-Smith</i>	
	High-frequency Oscillations in the Neurophysiology of Epilepsy Howan Leung	
16:45 – 17:00	Closing Remarks & Award Presentation	

## **Montreal Cognitive Assessment: One Cutoff Never Fits All**

Adrian Wong, Lorraine SN Law, WY Liu, ZL Wang, Eugene SK Lo, Alexander Lau, Lawrence KS Wong, Vincent CT Mok Department of Medicine and Therapeutics, Lui Che Woo Institute of Innovative Medicine, The Chinese University of Hong Kong, Hong Kong SAR

**Background:** To examine the discrepancy between single versus age- and education-corrected cutoff scores in classifying performance on the Montreal Cognitive Assessment (MoCA) in patients with stroke or transient ischaemic attack (TIA). The norms for the Hong Kong version of the MoCA total and domain scores and the total score of the MoCA 5-minute protocol were described.

*Methods:* A total of 1713 subjects participated in this study. MoCA norms were collected from 794 functionally independent and stroke- and dementia-free persons aged  $\geq$ 65 years. Magnetic resonance imaging was used to exclude subjects with significant brain pathology and medial temporal lobe atrophy. Cutoff scores at 16th, 7th, and 2nd percentiles by age and education were derived for the MoCA and MoCA 5-minute protocol. MoCA performance in 919 patients with stroke or TIA was classified using the single and norm-based cutoff scores.

**Results:** Only 65.1% and 25.7% healthy controls and 45.2% and 19.0% patients scored above the conventional cutoff scores of 21/22 and 25/26 on the MoCA, respectively. Discrepancy between locally derived cutoff score of 21/22 was up to 42.4%. Discrepancy increased with higher age and lower education level, with the majority being false positives by single cutoff scores. With the 25/26 cutoff of the original MoCA, discrepancy further increased up to 67.3% with the highest false-positive rates of 74.3%.

**Conclusions:** Conventional single cutoff scores are associated with substantially high rates of misclassification especially in older and less-educated stroke patients. These results caution against the use of 'one-size-fit-all' cutoffs on the MoCA.

## The Montreal Cognitive Assessment 5-Minute Protocol is a Brief, Valid, Reliable, and Feasible Cognitive Screen for Telephone Administration

Adrian Wong<sup>1</sup>, David Nyenhuis<sup>2</sup>, Sandra E Black<sup>3</sup>, Lorraine SN Law<sup>1</sup>, Eugene SK Lo<sup>1</sup>, Pauline WL Kwan<sup>1</sup>, Lisa Au<sup>1</sup>, Anne YY Chan<sup>1</sup>, Lawrence KS Wong<sup>1</sup>, Ziad Nasreddine<sup>4</sup>, Vincent Mok<sup>1</sup>

<sup>1</sup> Department of Medicine and Therapeutics, Lui Che Woo Institute of Innovative Medicine, The Chinese University of Hong Kong, Hong Kong SAR

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<sup>3</sup> Sunnybrook Health Sciences Centre, Department of Medicine, University of Toronto, Toronto, Canada

<sup>4</sup> Centre Diagnostique et Recherche sur la Maladie d'Alzheimer, Québec, Canada

**Background:** The NINDS-CSN vascular cognitive impairment (VCI) Harmonization working group proposed a brief cognitive protocol for screening of VCI. We investigated the validity, reliability, and feasibility of the Montreal Cognitive Assessment 5-minute protocol (MoCA 5-min protocol) administered over the telephone.

*Methods:* Four items examining attention, verbal learning and memory, executive functions/language, and orientation were extracted from the MoCA to form the MoCA 5-min protocol. Overall, 104 patients with stroke or transient ischaemic attack (TIA), including 53 with normal cognition (Clinical Dementia Rating [CDR]=0) and 51 with cognitive impairment (CDR=0.5 or 1), were administered the MoCA in clinic and a month later, the MoCA 5-min protocol over the telephone.

**Results:** Administration of the MoCA 5-min protocol took 5 minutes over the telephone. Total score of the MoCA 5-min protocol correlated negatively with age (r= –0.36, P<0.001) and positively with years of education (r=0.41, P<0.001) but not with gender (rho=0.03, P=0.773). Total scores of the MoCA and MoCA 5-min protocol were highly correlated (r=0.87, P<0.001). The MoCA 5-min protocol performed equally well as the MoCA in differentiating patients with cognitive impairment from those without (area under the curve [AUC] for MoCA 5-min protocol=0.78; MoCA=0.74, P>0.05 for difference; Cohen's *d* for group difference, 0.80-1.13). It differentiated cognitively impaired patients with executive domain impairment from those without (AUC=0.89, P<0.001; Cohen's *d*=1.7 for group difference). 30-Day test-retest reliability was excellent (intraclass correlation coefficient=0.89).

*Conclusions:* The MoCA 5-min protocol is a free, valid, and reliable cognitive screen for stroke and TIA. It is brief and highly feasible for telephone administration.

# Relations Between Recent Past Leisure Activities with Risks of Dementia and Cognitive Functions After Stroke

Adrian Wong<sup>1</sup>, Eugene Lo<sup>1</sup>, Michael Tang<sup>1</sup>, ZL Wang<sup>1</sup>, WY Liu<sup>1</sup>, Nicole Tanner<sup>1</sup>, Natalie Chau<sup>1</sup>, Lorraine Law<sup>1</sup>, L Shi<sup>1</sup>, Winnie CW Chu<sup>2</sup>, Jie Yang<sup>4</sup>, YY Xiong<sup>5</sup>, Bonnie YK Lam<sup>1</sup>, Lisa Au<sup>1</sup>, Alexander YL Lau<sup>1</sup>, Anne YY Chan<sup>1</sup>, Yannie Soo<sup>1</sup>, Thomas WH Leung<sup>1</sup>, Lawrence KS Wong<sup>1</sup>, Linda CW Lam<sup>3</sup>, Vincent CT Mok<sup>1</sup>

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<sup>5</sup> Department of Neurology, Jinling Hospital, Nanjing University School of Medicine, Nanjing, China

**Background:** Effects of leisure activities participation upon cognitive functions and risk of dementia after stroke are unclear. The objective of this study was to examine the effects of recent past leisure activities participation upon cognitive functions and risk of dementia after stroke.

*Methods:* This was a hospital-based, retrospective cohort study. Of 1013 patients with stroke or transient ischaemic attack but no prestroke dementia, 88 were diagnosed to have incident poststroke dementia (PSD) 3 to 6 months after stroke. Regular participation ( $\geq$ 3 times per week) in intellectual, recreational, social, and physical activities over the year before the index stroke was retrospectively recorded at 3 to 6 months after stroke.

**Results:** Logistic regression analyses showed that regular participation in intellectual (relative risk=0.36; 95% confidence interval, 0.20-0.63) and stretching and toning physical exercise (0.37; 0.21-0.64) was significantly associated with a reduced risk of PSD after controlling for age, education, prestroke cognitive decline, stroke subtype, prior strokes, and chronic brain changes including white matter changes, old infarcts, and global atrophy. Results were similar in patients with recurrent strokes in univariate models. Controlling for the effects of prestroke cognitive decline, recent participation in greater number of intellectual and recreational activities and strenuous aerobic and mind-body exercises was significantly associated with better poststroke Mini-Mental State Examination performance.

*Conclusions:* Regular participation in intellectual activities as well as stretching and toning exercise was associated with a significantly reduced short-term risk of PSD in patients with and without recurrent strokes. Participation in greater number of recent past leisure activities was associated with better poststroke cognitive performance.

## Prevalence of Vitamin D Insufficiency in Patients Suffering from First Acute Ischaemic Stroke

FP 4

WT Wong, KK Lau, B Sheng, MK Fong, YP Chu, HH Kwan, WK Ng Princess Margaret Hospital, Hong Kong SAR

**Background:** Vitamin D deficiency or insufficiency is a common condition in the Chinese population. The prevalence was reported to be ranging from 40% to 90% in previous publications. Apart from the classical effects of vitamin D on calcium metabolism and on bone health, emerging evidences also show that vitamin D status can play pivotal role in extra-skeletal diseases such as cerebrovascular disease. Low vitamin D level is an independent risk factor for stroke as suggested in an epidemiological study. This study aimed to evaluate the prevalence of vitamin D deficiency or insufficiency in the subset of patients suffering from first-ever acute ischaemic stroke.

*Methods:* This was a cross-sectional study conducted in the Acute Stroke Unit of Princess Margaret Hospital from March to June 2015. Overall, 100 consecutive patients suffering from first-ever acute ischaemic stroke with good premorbid functional status (defined as modified Rankin Scale of  $\leq$ 3) were recruited. Serum levels of 25-hydroxycholecalciferol (25(OH)D), which is well accepted as the best indicator of whole-body vitamin D status, were checked within 48 hours after their admissions. Vitamin D deficiency, vitamin D insufficiency, and vitamin D sufficiency were defined as 25(OH)D level of  $\leq$ 25 nmol/L, 26-50 nmol/L, and  $\geq$ 51 nmol/L, respectively.

**Results:** The mean age of the 100 patients was  $69.1 \pm 12.8$  years; 63% were male. The mean 25(OH)D level was  $43.4 \pm 14.0$  nmol/L. Of the patients, 74% had either vitamin D deficiency (4%) or insufficiency (70%). The prevalence of vitamin D deficiency or insufficiency was even higher in the subgroup of female patients (78.4%) and patients aged over 80 years (81.0%).

*Conclusion:* Patients suffering from first-acute ischaemic stroke have a high prevalence of vitamin D insufficiency.

# Effectiveness of a Multidisciplinary Parkinson's Disease Clinic in Improving Quality of Life

<u>HF Chan</u>, YF Cheung, A Leung, V Kwok, CS Fong, D Chau, P Lau, M Poon, I Chan, C Li, T Fung, A Wang, WC Fong Queen Elizabeth Hospital, Hong Kong SAR

*Background:* Parkinson's disease (PD) has been recognised as a multi-dimensional disease with motor and non-motor problems. Besides, it is more than a neurodegenerative disease of dopaminergic deficiency. Unfortunately, people still practise monodisciplinary doctor-centred approach which heavily relies on medical treatment acting on the dopaminergic pathway. Therefore, multidisciplinary management approach may be useful in improving daily functioning and quality of life of PD patients. We conducted a prospective observational study to evaluate the effectiveness of a multidisciplinary PD clinic in a tertiary hospital in Hong Kong.

*Methods:* All Chinese PD patients referred to the multidisciplinary PD clinic of Queen Elizabeth Hospital were recruited. Those who failed to give a valid consent were excluded from the study. All subjects received a comprehensive baseline assessment by different disciplines during their first visit. Their demographic information was documented. Their motor and non-motor function, daily functioning, and quality of life were assessed. The patients then received a tailor-made management plan with referral to the appropriate disciplines. The primary outcome was the quality-of-life score (Parkinson's disease questionnaire [PDQ39]) measured at 1 year while the secondary outcomes were the Unified Parkinson's disease Rating Scale (UPDRS) motor score, Non-Motor Symptom Scale (NMSS), and Hospital Anxiety and Depression Scale (HADS) measured at 1 year.

**Results:** We recruited 131 patients between November 2013 and June 2015. The mean PDQ39 score improved from 74.18 at baseline to 63.55 at 1 year (P=0.05). As for the secondary outcome, there was no significant difference in the motor and non-motor function between baseline and at 1-year follow-up. However, there was a trend towards better mood, which might account for the improvement of quality of life. **Conclusion:** This study suggested that a multidisciplinary programme might be useful in improving the quality of life of PD patients.

# Detection of Paroxysmal Atrial Fibrillation by 7-Day Event Loop Recorder in Patients after Acute Ischaemic Stroke or Transient Ischaemic Attack

Patricia Che Ruttonjee Hospital, Hong Kong SAR

*Background:* Atrial fibrillation is a frequent cause of ischaemic stroke. The risk of stroke in atrial fibrillation is 5-fold which further increases with previous stroke, age, and many other factors. Atrial fibrillation–related stroke carries particularly high morbidity and mortality. Stroke recurrence and consequences can be effectively reduced by anticoagulant therapy. Thus, detection of atrial fibrillation is of utmost importance after ischaemic stroke or transient ischaemic attack (TIA). Since atrial fibrillation is frequently paroxysmal and occult, it is easily missed by routine 12-lead electrocardiography (ECG). Strategies with high sensitivity such as prolonged cardiac monitoring is necessary. In this study, we aimed to evaluate the effectiveness of 7-day event loop recording (ELR) in detection of paroxysmal atrial fibrillation in patients after acute ischaemic stroke or TIA in a local setting. Also we aimed to identify the predictors of atrial fibrillation to guide future targeted effective use of ELR.

*Methods:* We prospectively enrolled consecutive patients admitted to our acute stroke unit with an acute ischaemic stroke or TIA. Those with a known history of atrial fibrillation were excluded. A total of 194 patients were eligible and systematically screened for atrial fibrillation in a stepwise ECG algorithm. All patients had admission ECG and for those with no atrial fibrillation detected, additional ECG was performed based on clinical grounds. Patients with no atrial fibrillation despite any standard ECG subsequently underwent 7-day ELR.

**Results:** A total of 27 (13.9%) cases of new atrial fibrillation were detected. Admission ECG detected new atrial fibrillation in 5.7% (11/194). Additional ECG detected new atrial fibrillation in 2% (3/154) of those with normal admission ECG. 7-Day ELR identified 8.0% (13/162) of new paroxysmal atrial fibrillation in those with normal admission plus/minus additional ECG with a number needed to screen (NNS) of 12.5. A total of 7-day ELR is significantly more effective in detection of paroxysmal atrial fibrillation after stroke than 24-hour recording (8.0% vs 1.9%; NNS 12.5 vs 54). Age, history of stroke and cryptogenic stroke were associated with atrial fibrillation detection by ELR. Among all, cryptogenic stroke was the strongest predictor.

**Conclusion:** 7-Day event loop cardiac recording is an effective means of prolonged cardiac monitoring in detection of new paroxysmal atrial fibrillation after acute ischaemic stroke or TIA in those with normal standard ECG. We recommend a minimum of 7 days prolonged cardiac monitoring by means of event loop recorder for detection of paroxysmal atrial fibrillation after acute ischaemic stroke or TIA in future.

DH 1

## Discriminative Radiological Features of Multiple Sclerosis and Neuromyelitis Optica in Hong Kong

Stephen Cheng Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR

**Background:** Multiple sclerosis (MS) and neuromyelitis optica (NMO) are both recurrent demyelinating diseases of the central nervous system (CNS). However, recent evidence showed that they are clinically distinct entities with different management and treatment. Differentiation can be challenging, especially with a negative serum anti-aquaporin-4 antibody. Barkhof has described the typical brain locations affected by MS in the McDonald criteria. In recent years, the presence of brain lesions was also increasingly recognised in NMO. International studies have shown that certain radiological features on the magnetic resonance imaging (MRI) may be helpful in discriminating NMO from MS. Asian studies that compare the relative discriminative values of these features were scarce. This study aimed to identify discriminating radiological features of MS and NMO in Hong Kong.

*Methods:* Between October 1993 and December 2014, all patients with recurrent demyelinating diseases of the CNS seen by the Department of Medicine at Pamela Youde Nethersole Eastern Hospital were identified. The diagnosis of MS was by the 2010 McDonald criteria and that of NMO or NMO spectrum disorders (NMOSD) was by the 2006 Wingerchuk criteria. Subjects who did not fulfil either diagnosis were excluded. Specific radiological features in the MRI spine and brain were collected, including longitudinally extensive transverse myelitis (LETM), multiple short segments TMs, location of the myelitis, cervical and medullary involvement, presence of cord swelling, T1 hypointensity, asymptomatic cord lesions, involvement of the brainstem in particular the area postrema, presence of lesions at the corpus callosum, periventricular, juxtacortical and subcortical areas, as well as the Dawson's fingers and tumefactive appearance of brain lesions. Univariate and multivariate analyses were performed on these features to identify those that had specific correlations with MS and NMO. Subgroup analysis between the seropositive and seronegative NMO patients was then conducted to examine any intra-group difference among NMO patients.

**Results:** Overall, 159 subjects with demyelinating disease of the CNS were identified. Of the patients, 70 fulfilled the diagnosis of MS and 31 fulfilled that of NMO or NMOSD; 63 patients did not fulfil either diagnosis, and 3 who fulfilled MS were excluded due to absence of any retrievable MRI data. Features that were significantly correlated with NMO included LETM (P<0.01), T1 hypointense cord lesions (P<0.01), cord swelling (P<0.01), peripherally located cord lesions (P<0.01), involvement of the area postrema (P<0.01), and a tumefactive appearance of brain lesions (P<0.01). Features that favoured the diagnosis of MS included multiple short TMs (P<0.01), asymptomatic cord lesions (P<0.01), centrally located cord lesions (P<0.01), presence of brain lesions in the periventricular, juxtacortical and subcortical areas (P<0.01), and the Dawson's fingers appearance (P<0.01). There was no intra-group difference in terms of radiological features between seropositive and negative NMO patients.

*Conclusion:* Certain MRI features in the brain and spinal cord were helpful in differentiating MS from NMO. They were also applicable in seronegative NMO patients. Features of severe myelitis were correlated with worse outcome. NMO appeared to fare worse than MS in terms of outcome and prognosis.

## Intravenous Thrombolysis Therapy in Acute Ischaemic Stroke Patients Not Fulfilling Conventional Criteria

MS Chi

Department of Medicine, Tuen Mun Hospital, Hong Kong SAR

**Background:** Intravenous recombinant tissue plasminogen activator is the only approved thrombolysis treatment in acute ischaemic stroke. However there were many exclusion criteria that enable many patients being excluded from the treatment. This study was to compare the safety and short-term treatment outcome between those fulfilling these criteria and those not fulfilling the criteria.

*Methods:* All acute ischaemic stroke patients treated with intravenous thrombolysis in the period of 2004 to 2014 in our hospital were recruited. They were retrospectively divided into on-label group if they did not have any of the contra-indication and off-label group if any of the contra-indication present. Primary outcome of symptomatic haemorrhage and secondary outcome of early neurological change, 3-month mortality, and functional outcome were measured. Multivariate analysis with logistic regression with adjustment of baseline characteristics which was found to have relationship in the univariate analysis was done.

**Results:** Overall, 294 patients received intravenous thrombolysis and 145 (49.3%) had at least one contraindication. All the contra-indications were not associated with symptomatic intracranial haemorrhage. Secondary outcomes analysis revealed minor stroke patients had better functional outcome (odds ratio [OR]=202.71, P<0.001). High blood pressure at presentation was associated with fewer early neurological improvement (OR=0.25, P=0.016) and a trend of unfavourable functional outcome (OR=0.18, P=0.054). Severe stroke was related to increased mortality (OR=4.83, P=0.014) and none have good functional outcome. Malignancy was associated with higher mortality (OR=39.07, P=0.005).

*Conclusions:* This study showed the safety of giving intravenous thrombolytic therapy for acute ischaemic stroke in off-label group with comparable symptomatic intracranial haemorrhage risk. However some subgroups have less favourable outcome, including high blood pressure, severe stoke, old age, and malignancy. This may be due to the underlying comorbid condition and less rehabilitation potential rather than thrombolysis itself.

## What Are the Risk Factors of Intracranial Artery Calcifications (IAC) and Whether IAC Serve as an Independent Predictor of Future Cerebrovascular and Cardiovascular Morbidities and Mortalities: a Retrospective Cohort of a Local Regional Hospital

MF Ip North District Hospital, Hong Kong SAR

**Background:** The relationship between calcification of coronary arteries and ischaemic heart disease is well established. However, controversies still exist for the implications of intracranial artery calcifications (IAC). The current study aimed to investigate the risk factors associated with IAC and to investigate whether heavy IAC correlates with subsequent cerebrovascular and cardiovascular morbidities and mortalities.

*Methods:* This was a retrospective cohort study conducted at the North District Hospital. Patients with a principal diagnosis of acute ischaemic stroke or transient ischaemic attack (TIA) between 1 October 2008 and 31 March 2009 were recruited into the cerebrovascular accident (CVA) group. A control group, consisting of patients with plain computed tomography (CT) brain done from 1 October 2008 to 31 December 2008 for indications other than CVA, was set up for comparison. The degree of calcification of seven intracranial vessels (left and right vertebral arteries, basilar artery, left and right intracranial carotid arteries, left and right middle cerebral arteries) was assessed on plain CT brains of the two groups. Patients were categorised into low or high IAC category according to the total IAC score of the seven vessels. The IAC score of the CVA and control groups was compared and vascular risk factors associated with high IAC category were identified. The risk of ischaemic stroke or TIA, acute coronary syndrome, and mortality in the following 5 years was assessed.

**Results:** Patients of the CVA group had significantly higher IAC score compared with the control group ( $5.2 \pm 4.05$  vs  $3.82 \pm 3.81$ ; P<0.001). Age (odds ratio [OR]=1.090; 95% confidence interval [CI], 1.056-1.125; P<0.001), previous history of stroke (OR=2.072; 95%CI, 1.109-3.872; P=0.022), and history of chronic kidney disease (OR=2.677; 95% CI, 1.349-5.313; P=0.005) were independent factors associated with higher IAC category. High IAC category (OR=2.223; 95% CI, 1.102-4.483; P=0.026) was independently associated with higher 5-year ischaemic stroke risk after adjusting for other cardiovascular risk factors.

*Conclusions:* Heavier burden of IAC is associated with various vascular risk factors, including hypertension, diabetes mellitus, atrial fibrillation, history of ischaemic heart disease, older age, history of ischaemic stroke, and chronic kidney disease. Among these, the latter three factors were independently associated with IAC. Heavy burden of IAC is independently associated with higher risk of future ischaemic stroke or TIA. Presence of heavy IAC on CT brain should urge clinicians to aggressively manage vascular risk factors.

## Cerebral Venous Thrombosis: Retrospective Analysis of Cases from Tertiary Hospitals in Hong Kong

<u>Jessica Li</u>

Queen Elizabeth Hospital, Hong Kong SAR

*Background:* Cerebral venous thrombosis (CVT) is an important cause of stroke. Patients frequently present with headache, seizure, and focal neurological signs, and this disease is associated with various prothrombotic conditions. The majority of case series are from Caucasian countries, while data from Asia are comparatively scarce. It is essential to obtain distinctive local data on CVT reflecting the clinical presentation, treatment strategies, and functional outcome in Hong Kong, with the aim to identify prognostic indicators for the functional outcome.

*Methods:* Subjects were recruited from Queen Elizabeth Hospital, United Christian Hospital, and Tseung Kwan O Hospital in the period from 2003 to 2014. In the study, CVT was diagnosed and confirmed mainly via computed tomography or magnetic resonance imaging. Clinical manifestations, investigation results, and functional outcomes at 1, 6, and 12 months were recorded. Unfavourable outcome was defined as modified Rankin Scale score (mRS) of >2. Primary outcome was defined as functional dependence or death (mRS >2) at 1 month. A literature review of various aspects of CVT was conducted based on the local data obtained in this study cohort. Kaplan-Meier survival analyses were performed.

**Results:** In this study cohort, 98 patients were included; 57 (58.2%) were female. Their common presentations were headache (64.3%), seizure (38.8%), nausea and vomiting (35.7%), and hemiparesis (27.6%). Common predisposing conditions included the use of oral contraceptive pills (14.3%), malignancy (14.3%), infections (10.2%), and congenital thrombophilia (9.2%). Of the cohort, 50 (51%) patients displayed no known causes. At 1 month, 35 (35.7%) patients had unfavourable outcomes, while 21 (21.4%) and 16 (16.3%) patients had unfavourable outcomes, while 21 (21.4%) and 16 (16.3%) patients had unfavourable outcomes at 6 and 12 months, respectively. Using a logistic regression model, predictors of death and dependence at 1 month were found to be age >65 years (odds ratio [OR]=8.27), hemiparesis (OR=4.06), non–central nervous system (non-CNS) tumour (OR=44.52), intracerebral haemorrhage (OR=11.48), and mass effect on imaging (OR=19.68). Over a median follow-up duration of 51 months, 16 patients died, while another 11 patients had a recurrence of CVT and venous thromboembolism from other sites. Five (5%) patients had seizure recurrence in our study cohort.

**Conclusion:** Prognosis of CVT patients in Hong Kong was comparable to the reported literature covering other geographical areas. Older patients, having hemiparesis on presentation, intracerebral haemorrhage or mass on imaging, or those with an underlying non-CNS tumour were at risk of unfavourable outcomes. Future research is necessary to clarify whether more intensive treatment and rehabilitation may benefit these patients.

## Clinical Characteristics and Predictors of Death and Poor Outcome of Status Epilepticus: an 11-Year Retrospective Study in Two Local Hospitals in Hong Kong

Kate Lui

Tseung Kwan O Hospital, Hong Kong SAR

**Background:** Status epilepticus (SE) is a common medical emergency that is associated with high mortality and morbidity. Older age, duration of SE, and SE due to cerebrovascular accident were reported as predictors of poor outcomes in previous studies. This study aimed to review the clinical characteristics and to evaluate the predictors of mortality and poor outcome in patients with SE treated in the intensive care units.

*Methods:* A retrospective review was done in patients with SE managed in the intensive care units of two acute hospitals in Hong Kong from June 2003 to June 2013.

**Results:** A total of 87 SE episodes in 82 patients were analysed. The mean age was 49.3 (standard deviation, 14.9) years. Breakthrough seizure (21%) and encephalitis/meningitis (18%) were the main aetiologies. Convulsive SE was the commonest seizure type (87.4%), followed by non-convulsive status epilepticus (NCSE) [10.3%). Focal spike/slow + spatial evolution were the commonest electroencephalogram finding (33.7%). Phenytoin was the commonest anti-convulsant used (86.2%). General anaesthetic treatment was given in 55.2% of cases. The 30-day mortality rate was 18.4%. Of the patients, 46% had worsened functional outcome upon discharge. Older age was the statistically significant independent predictor associated with poor outcome upon discharge (P=0.001; odds ratio=1.083; 1.031-1.131). There were significantly more patients without a history of epilepsy developing NCSE (15.5% vs 0%; P=0.026). In addition, those without a history of epilepsy were more likely to have poor outcome upon discharge (56.9% vs 24.1%; P=0.004).

*Conclusion:* This study suggested that older age was the statistically significant independent predictor associated with poor outcome upon discharge and there were significantly more patients without a history of epilepsy developing NCSE, and those without a history of epilepsy were more likely to have poor outcome upon discharge. High index of suspicion is necessary to make a correct diagnosis of NCSE especially in those without a history of epilepsy.

## **Treating Multiple Sclerosis in the 21st Century**

#### <u>Gavin Giovannoni</u>

Centre for Neuroscience & Trauma, Blizard Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, United Kingdom

Multiple sclerosis (MS) is the most common non-traumatic disabling condition to afflict young adults. Although the prognosis of MS is highly variable, given sufficient time the majority of people with MS will become disabled. In the case of established MS disease–modifying therapies the long-term impact of these therapies on MS prognosis is becoming better defined, but appears promising. In the case of the newer therapies the short-term data are very promising. Despite this there is an emerging consensus that early treatment, at least in the relapsing phase of the disease, will prevent or at least delay the progressive stage of the disease. The problem associated with using highly effective therapies, be they induction or escalation therapies, is that they come with greater known and undefined unknown risks. How do we balance the risks of these therapies with their potential long-term benefits? In this talk Professor Giovannoni will review the prognosis of MS and the rationale for treating early and to target of no evident disease activity (NEDA). In addition, the talk will focus on education and the role of the expert patient in helping make the right decision regarding individualised treatment plans.

### Emerging Insights in Multiple Sclerosis: Re-evaluation of Treatment Algorithm

## S 2

#### Mark Freedman

Department of Medicine, Neurology, University of Ottawa; Multiple Sclerosis Research Unit, Neurology, Ottawa Hospital-General Campus, Canada

With an expanding array of agents proven to reduce relapses and magnetic resonance imaging activity in the hope of slowing disease progression, neurologists must have a "plan of action" before embarking on a therapy. Though the exact mechanism of action is unknown or unproven for many of the agents, they all probably operate differently. This means if one agent fails to produce an optimal response, it is wise to choose another agent with a different mechanism of action. Efficacy for most of the approved agents is similar, so choosing among the drugs often means evaluating the potential for adverse events; that is, evaluating benefit versus risk. The paucity of head-to-head trials means that few drugs are proven to be more effective than others, but there are some and more emerging. Typically one would choose an agent with the least chance of adverse event to begin therapy unless there is a suggestion that the disease in a given individual is more aggressive than usual, warranting the choice of a riskier drug in the hope of achieving an early and greater response to treatment. The key to further management is the monitoring for emergence of disease activity early in the course of treatment (ie first year), evaluating the activity and determining whether to change therapy for another one with the same risk profile or escalating to a potentially more harmful drug that is perceived to have greater efficacy. The overall goal is to minimise the build up of potentially damaging inflammatory activity which accumulates, leading to an earlier disability.

## Neuromyelitis Optica Spectrum Disorders (NMOSD): Treatment Update

Dean M Wingerchuk

Division of Multiple Sclerosis and Autoimmune Neurology, Mayo Clinic, United States

Early and accurate diagnosis of neuromyelitis optica spectrum disorders (NMOSD) is important because the therapeutic approach differs from that of the other main diagnostic consideration, multiple sclerosis (MS). Although acute relapses of NMOSD and MS may each be treated with corticosteroids and plasma exchange, attack-prevention strategies are quite different; in fact, some MS disease-modifying therapies may aggravate NMOSD. Although there are no completed randomised controlled trials of NMOSD, retrospective and limited prospective cohort data suggest that immunosuppressive therapies reduce attack frequency and preserve neurological function. Current treatment approaches using oral immunosuppressive drugs (corticosteroids, azathioprine, mycophenolate mofetil) and parenteral drugs (rituximab, mitoxantrone, methotrexate) will be discussed. Emerging agents such as tocilizumab and eculizumab and current randomised controlled trials of anti-CD19, anti-C5 (eculizumab), and anti-IL6R drugs will be described. Finally, novel therapeutic approaches that take advantage of our knowledge of anti-AQP4 mechanisms will be introduced.

### **Magnetic Resonance Imaging in Multiple Sclerosis**

### **S**4

#### Jill Abrigo

Department of Imaging and Interventional Radiology, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong SAR

Magnetic resonance imaging (MRI) is the most sensitive paraclinical tool for the diagnosis and longitudinal assessment of multiple sclerosis. Familiarity with the technique and imaging findings are essential given the increasing incidence of the disease in Hong Kong. In this talk, we revisit the MRI features of the McDonald criteria (2010) which allow for increased detection and earlier diagnosis of multiple sclerosis, and discuss the role of MRI in the monitoring of patients during treatment. We also review the limitations and pitfalls of the technique which should be considered when designing the scanning protocol for these patients. We describe our imaging strategies for the Hong Kong Multiple Sclerosis Registry, where limited sequences and fine-cut sections are performed to allow acquisition of clinical and research data within a reasonable time frame. Finally a few advanced MRI techniques will be presented to provide an overview of ongoing research efforts to further understanding of the injury and repair mechanisms in multiple sclerosis.

**S** 3

# Can Seizure Semiology Direct Our Neuroimaging Investigations in Refractory Epilepsy?

Andrew Bleasel

Neurology and Neurophysiology, Westmead Hospital, Westmead, NSW, Australia

The assessment for epilepsy surgery in refractory focal epilepsy depends upon the localisation of a single epileptogenic region. Localisation of the ictal onset and the often larger epileptogenic zone is determined by evidence from clinical, neurophysiological, and neuroimaging data.

Careful evaluation of the patient's seizure semiology should be the starting point. This is often the most informative guide to localisation. The patient's own history, witness accounts, and video recording can be examined for localising and lateralising clues.

Many semiological features have been proposed as localising. The initial symptoms, the aura, are perhaps the most helpful in terms of localisation. Several features of a patient's seizures allow characterisation of a focus as temporal or extratemporal. However, localisation between extratemporal regions and within the frontal lobe remains great challenges. Systematic examination of seizure semiology will often show localisation of seizure onset to be correct in approximately 70% to 80% of cases. Rapid seizure propagation between subcortical and cortical regions explains the exceptions and illustrates the potential for false localisation. Increasing experience with intracranial electroencephalography evaluations has shown the importance of cerebral networks on the production of the symptoms and signs of epileptic seizures. The symptomatogenic zone, the ictal onset, and the epileptogenic zone must be considered in defining the role of seizure semiology in surgical evaluation.

The lecture will examine some of the basics of semiological evaluation and illustrate how seizure semiology can direct additional investigations.

## **SPECT and PET in Epilepsy**

#### Frankie Choi

PET Centre, Department of Nuclear Medicine, Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR

Single-photon emission computed tomography (SPECT) and positron emission tomography (PET) are in the realm of nuclear medicine, requiring administration of radiopharmaceuticals to serve as radiotracers for specific in-vivo biological processes. The array of radiotracers for clinical or research uses is able to target the brain perfusion, different metabolic pathways, or neuro-receptors binding. Current clinical role of SPECT and PET on evidence bases is predominantly for non-invasive presurgical evaluation of refractory partial epilepsy and prediction of postsurgical outcomes. Epileptogenic zones can often be localised or lateralised by SPECT findings of ictal hyperperfusion and interictal hypoperfusion, and also by PET findings of interictal glucosehypometabolism. These functional data are particularly essential when magnetic resonance imaging (MRI) detected no structural lesion or found multifocal abnormalities, or when surface electroencephalography (EEG) is discordant with other findings. The high-resolution PET data can also help evaluate the metabolic integrity of eloquent cortex, and may help hypothesise pathogenesis for observed neurocognitive or behavioural abnormalities. Further data post-processing, notably cross-modality image co-registration with mathematical and statistical analyses, can often facilitate interpretation and enhance objectivity. Functional data misinterpretation may nevertheless arise from a plethora of pitfalls, such as subclinical seizure activity, postictal switch phenomenon, concomitant neuropsychiatric disorder, psychotropic medication, prior intracranial procedure, and gross cortical malformation. With technological developments, there is hybrid PET-MRI integrated system on the horizon to enable simultaneous functional-structural data acquisition, hence a potential superiority regarding image co-registration and interpretation. The complexity of epilepsy syndromes and diversity of seizure semiology often demand a judicious combination of imaging modalities to complement clinical and EEG findings towards a comprehensive presurgical evaluation and treatment planning.

S 6

## Epilepsy Imaging — the Things You May Not Know

Deyond Siu

Department of Diagnostic and Interventional Radiology, Kwong Wah Hospital, Hong Kong SAR

Epilepsy is not an uncommon condition which may affect patients with normal function. For those patients refractory to medical treatment, a significant proportion of them are candidates of surgical treatment which may be curative and seizure-free afterwards. Accurate imaging technique is very important to identify the lesional cases and surgical candidates.

In this talk the recommended imaging protocol, typical imaging findings of common epileptogenic pathologies, and management of non-lesional cases will be discussed.

## Frontotemporal Dementia: Local Perspective

S 8

#### Andrew LT Chan

Divisions of Geriatrics and Neurology, Department of Medicine, Queen Elizabeth Hospital, Hong Kong SAR

Frontotemporal dementia (FTD) is often overlooked as a cause of dementia. Epidemiological studies have reported that FTD is one of the important causes of neurodegenerative dementia in patients younger than the age of 65 years. However, FTD has rarely been reported in Chinese populations.

Unlike Alzheimer's disease in which memory decline is a common presenting feature, FTD is a group of disorders characterised by early behavioural changes or language deficits. There are three subtypes of FTD: behavioural variant of frontotemporal dementia (bvFTD), progressive non-fluent aphasia (PNFA), and semantic dementia (SD).

During the talk, an overview of FTD among local Chinese will be discussed through illustrative cases.

## Frontotemporal Dementia—Insights into a Complex Disorder

Jonathan Rohrer

The Dementia Research Centre, Institute of Neurology, Box 16, Queen Square, London WC1N 3BG, United Kingdom

Frontotemporal dementia (FTD) is a clinically, genetically, and pathologically heterogeneous neurodegenerative disorder. The major clinical syndromes of FTD are known as behavioural variant FTD (bvFTD), which presents with a change in personality, and primary progressive aphasia (PPA), which presents with language impairment. PPA has three well-defined subtypes known as the semantic, nonfluent, and logopenic variants. As all of these conditions progress they can overlap with each other and also with motor neuron disease (FTD-MND) and the atypical parkinsonian disorders. Around a third of FTD is familial with mutations in the progranulin (GRN), microtubule-associated protein tau (MAPT) and C9orf72 genes being the most common genetic causes. Rarer genetic causes include mutations in the VCP, TARDP, FUS, SQSTM1, and DCTN1 genes. Pathologically, neuronal inclusions are found containing abnormal forms of one of three different proteins: tau, TDP-43, or fused-in-sarcoma (FUS). Each of these proteinopathies has a number of further subtypes. This heterogeneity makes diagnosis difficult during life, with poor correlation between the clinical syndrome and the underlying genetic or pathological cause. Recent biomarker studies have aimed to improve these correlations through investigation of neuroimaging as well as blood and cerebrospinal fluid markers. Such studies also indicate that biomarker changes occur prior to symptom onset with multicentre consortia such as the Genetic FTD Initiative (GENFI) aiming to develop measures of disease onset and progression that can be used in forthcoming interventional trials for FTD.

## **Neural Bases of Language Learning: Implications for Cognitive Therapy**

## S 10

#### Patrick CM Wong

Brain and Mind Institute and Dept of Linguistics & Modern Languages, The Chinese University of Hong Kong, Hong Kong SAR

Research on second-language learning provides evidence for changes in an extensive cortical and subcortical network as a result of learning in adulthood. Interestingly, such an extensive network overlaps with the network of cognitive decline due to ageing. In this presentation, I will provide an overview of research from my laboratory concerning the neural bases of language learning. Time permitting, I will discuss our preliminary effort in using language learning as preventive therapy for cognitive impairment in older adults.

## Stroke in Neuro-Ophthalmology

## S 11

#### Andy CO Cheng

Department of Ophthalmology, Hong Kong Sanatorium & Hospital, Hong Kong SAR

Normal visual perception depends on the integrity of both the afferent visual pathway and efferent ocular motor mechanism. The afferent visual pathway starts from the optical mechanism of the eye, retina, the optic nerve, and the optic tract anteriorly, through the lateral geniculate body, optic radiation to the primary visual cortex posteriorly. The main ocular motor effector mechanism is located in the brainstem, straddling the midbrain to the lower pons. It receives input from the frontal cortex and deep parieto-occipital-temporal junction superiorly and the cerebellum and vestibular nuclei inferiorly. It can be seen that stroke affecting different parts of the brain may result in different neuro-ophthalmological presentations, and both the afferent or efferent pathway can be involved. This presentation aimed to illustrate some of the more common neuro-ophthalmological presentations from stroke affecting different parts of the brain, with emphasis on a thorough neuro-ophthalmological examination, which may aid in the diagnosis and localisation of lesion. Recent trends in the management of anterior visual pathway stroke syndrome will also be discussed.

### **Update on Treatment of Ischaemic Stroke**

## S 12

#### Christopher Levi

School of Medicine and Public Health, Faculty of Health and Medicine, The University of Newcastle, Australia

There has been major advances in both the implementation of thrombolytic therapy in acute ischaemic stroke and the definition of the role of endovascular clot retrieval in selected cases. Although thrombolysis implementation remains a challenge, there are now recognised strategies capable of boosting implementation rates and improving the work flow to enable speedier treatment. These strategies will be reviewed. Endovascular clot retrieval for selected patients with major vessel occlusion is now demonstrated to be superior to intravenous thrombolysis, however optimal selection criteria and implementation strategies remain challenges. The use of advanced imaging–based selection for endovascular therapies will be reviewed and strategies to enhance implementation discussed.

# Filling the Gaps in Bleeding Management in Stroke Patients Taking NOACs: from Laboratory Tests to Reversal Agent Development

#### Raymond SM Wong

Division of Haematology, Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Hong Kong SAR

Several direct oral anticoagulants (DOACs), including direct thrombin inhibitor and factor Xa inhibitors, have entered the clinical arena for stroke prevention in patients with atrial fibrillation. They are administered orally at a fixed dose, regular monitoring is not necessary, interaction with other drugs or nutrition occurs less than with vitamin K antagonists (VKAs), and they are at least as effective as VKAs for most indications tested. They are associated with about 50% less intracranial bleeding than VKAs. Nevertheless, they are still associated with bleeding complications. In such situations rapid assessment of the effects on coagulation and reversal of the anticoagulant effect is highly desirable.

DOACs can prolong various routine laboratory coagulation parameters, including the activated partial thromboplastin time (aPTT), the prothrombin time (PT), and the thrombin time (TT). aPTT appears to provide a reasonable qualitative assessment of the anticoagulation effect of dabigatran while TT is far more sensitive, and the PT is less sensitive to dabigatran therapy. The PT provides a relatively more sensitive assessment of rivaroxaban and apixaban than the aPTT. However, PT prolongation by direct factor Xa inhibitor is sensitive to the thromboplastin reagent and conversion to the international normalised ratio increases measurement variability. Quantitative assessments are available but their values on the clinical management of bleeding patients on DOACs.

Current management of bleeding associated with DOAC includes the removal of all antithrombotic medications and supportive care. Non-specific procoagulant agents (prothrombin complex concentrates and activated factor VIIa) have been used in case of serious bleeding. Currently, some specific antidotes for the DOAC are under development. Idarucizumab is a fragment of an antibody (Fab), which is a specific antidote to the oral direct thrombin inhibitor dabigatran. Interim analysis of the prospective cohort study (REVERSE-AD) demonstrated that idarucizumab could completely reverse the anticoagulant effect of dabigatran within minutes in patients who had serious bleeding or required an urgent procedure. Andexanet alfa is a truncated form of enzymatically inactive factor Xa, which binds and reverses the anticoagulant action of the factor Xa inhibitors (eg rivaroxaban, apixaban, and edoxaban). Aripazine (PER-977, ciraparantag; Perosphere Inc) is a synthetic small molecule (~500 Da) that reverses oral dabigatran, apixaban, rivaroxaban, as well as subcutaneous fondaparinux and low-molecular-weight heparin in vivo. These antidotes could provide an alternative for management of life-threatening bleeding events in patients taking DOACs.

# Secondary Stroke Prevention in Patients with Atrial Fibrillation: Balancing the Efficacy and Safety

Natan Bornstein

Stroke Unit, Department of Neurology, Tel-Aviv Sourasky Medical Center, Israel

Patients living with atrial fibrillation are at 5-fold increased risk of stroke and systemic embolism, and these risks are particularly higher in patients who have already had a previous episode of ischaemic stroke or a transient ischaemic attack.<sup>1</sup> In the subgroup analysis of the ARISTOTLE study, patients with previous stroke or transient ischaemic attack had a 2 to 3 times higher risk of stroke or systemic embolism, major bleeding, intracranial haemorrhages, and mortality than those without stroke or transient ischaemic attack.<sup>2</sup> Vitamin K antagonists/warfarin are effective agents in reducing risk of stroke by approximately 60%.<sup>3</sup> However, the efficacy and safety profile of warfarin are heavily influenced by the narrow therapeutic range that can be interfered by dietary and drug interactions.<sup>4</sup>

As suggested by the American College of Cardiology/American Heart Association Task Force on practice guidelines and Heart Rhythm Society suggested that heparins are not recommended for patients with atrial fibrillation immediately after acute stroke, Aspirin followed by initiation of warfarin for long-term secondary stroke prevention in usual care.<sup>5</sup> In recent years, a new class of medication known as novel oral anticoagulants (NOACs) has emerged as a new option for stroke prevention in patients with atrial fibrillation. With fixed dosing, predictable pharmacokinetics/pharmacodynamics, does not need for routine monitoring, less intracranial bleeding, NOACs can potentially replace warfarin in the long-term secondary stroke prevention. But perhaps the controversial topic remains is identifying when anticoagulant can be started safely in atrial fibrillation patients who have had an ischaemic stroke or a transient ischaemic attack.

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## The Natural History of Parkinson's Disease

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Parkinson's disease (PD) is a progressive neurodegenerative disorder. However, there is substantial heterogeneity in clinical manifestations and the rate of disease progression. The introduction of effective treatments including levodopa, and other pharmacological and surgical therapies, has had a significant impact on morbidity and mortality, but features that are not (or only partially) dopa-responsive which develop especially after a long duration of disease, such as axial motor disability (dysfunction of posture, gait and balance; dysarthria and dysphagia) and dementia, are currently major areas of unmet need. Relevant aspects for discussion include studies from the pre-levodopa era, PD motor (and non-motor) subtypes, milestones of advanced disease, non-motor symptoms and disease versus medication effects, the impact of age, progression of neuropathology (including Braak hypothesis), biomarkers and new methods/technologies for assessing disease severity, incidental Lewy body disease, concomitant pathologies, and a possible role for the gut in disease pathogenesis/progression.

# The Perspective of Gait Issue in Parkinson's Disease: from Clinical Phenomena to Basic Mechanism

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The gait and postural control are essential for an independent as well as productive life. Therefore, perturbation of gait and balance predicts quality of life in many neurodegenerative diseases as Parkinson's disease (PD). Recently a new clinical classification scheme has been proposed in *Movement Disorders* journal. This scheme is based on clinical observation and analysis to take into account the presentation while taking initial steps and dynamic walking, and might provide useful spotlights on the puzzle of diverse pathophysiology of abnormal gait.

Recent works on pathophysiology of gait abnormalities in PD have proposed that locomotion and postural control networks should depend on intensive cooperation of the central and peripheral nervous systems. The gait and balance are no longer perceived as purely motor tasks or reflexes, but are viewed as complex sensorimotor behaviours, affected by cognitive and affective aspects. The hypothesis for pathogenesis in these issues organised from the most peripheral (central pattern generators in the spinal cord) to the most central in the frontal.

The most important value of pathophysiological consideration is to explain clinical phenomenon. Gait disturbance in PD could be characterised by 'continuous gait disturbance' and 'episodic gait disturbance'. The episodic gait disturbance received intensive works in recent research with specific focus on the freezing of gait (FOG), which makes patients with PD exhibit transient inability to create effective initial stepping.

Although the underlying mechanism of FOG remains insufficiently understood, several recent studies suggested that anticipatory postural adjustment (APA) may play an important role. Using single-photon or positron emission tomography, activation of the supplementary motor area (SMA) is evident during actual and imagined gait or step initiation. In these perspectives, we conducted a study to elucidate the role of SMA on gait performance with the APA parameter by manipulating the cortical plasticity through theta burst stimulation in PD patients.

In this talk we will try to summarise the clinical aspects of gait perturbation in PD, to explain the possible pathogenesis of gait abnormality with focus on FOG, and to discuss the possibility of therapeutic intervention by the modulation of cortical plasticity.

## Peripheral Nerve Disorders — from Nerve Conduction Studies to Ultrasound

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Advances in the understanding of peripheral nerve disorders occur when new techniques allow a better insight into the underlying pathophysiology. Functional tests have led the way in furthering our understanding of peripheral nerve disorders. An electromyogram (EMG) was rapidly followed by nerve conduction studies and further technical refinements enabled the use of evoked potentials and intraneural microneurography. Similar to what happened in the exploration of the central nervous system, there was a gap until useful imaging of the peripheral nerves has rapidly become part of clinical routine. In this review, we will be looking at how functional and imaging techniques complement each other to provide a comprehensive evaluation of the peripheral nervous system.

## High-frequency Oscillations in the Neurophysiology of Epilepsy

S 18

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Electroencephalography (EEG) is the cornerstone of diagnosis and localisation in epilepsy. In focal epilepsy, presurgical evaluation is important in providing lateralisation and localisation information. The majority of patients may be operated on based on concordance of surface EEG results and other mutlimodal investigations. Among patients who may have discordant information or non-lesional magnetic resonance imaging, intracranial EEG may be deployed using either grid, strip, or stereotactic (depth) electrodes. The interpretation of intracranial EEG is not without difficulty: (1) Rapid spread of electrical discharges along large surfaces of grid electrodes may render it difficult for one to determine the ictal onset using conventional frequency ictal patterns. (2) In some cases the first registered discharge pattern may take a range of different morphology (eg other than low-amplitude fast activities). (3) Some epileptogenic foci may exist in the deepseated grey matter of cerebral sulci, making ictal analysis of conventional frequency ictal patterns confusing. High-frequency oscillations (HFOs) in the range of 80 to 500 Hz may be seen as a new biomarker for focal epilepsy. There has been literature reporting its detection in the interictal states, but much less is known about the appearance of ictal HFOs. We have found that ictal HFOs are affiliated with radiological lesion, conventional frequency ictal patterns and interestingly, hyperexcitability. We have demonstrated that the proportion of resected channels containing ictal HFOs is higher among patients with Engel Class I/ II outcomes compared with those with Engel Class III/IV outcomes. In particular, we have shown that by using ictal HFOs and hyperexcitability, a higher sensitivity and specificity may be achieved than if only one modality is used alone. In conclusion, the analysis of intracranial EEG is a subject with evolving new evidence and research is aiding clinicians in refining the technique needed for the determination of epileptogenic foci and resection margin among patients with difficult-to-treat epilepsy.

# The Prognostic Value of Evolutionary Electroencephalography Features in Encephalopathy

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**Objective:** Many studies indicated that various electroencephalography (EEG) patterns may predict outcomes among encephalopathic patients. There is a relative lack of research regarding the changing characteristic or evolution of these patterns. This study investigated the clinical value of evolutionary EEG and explored the possible relationship between the different patterns and prognosis.

*Methods:* We retrospectively reviewed the EEG raw data and electronic medical records of patients with encephalopathy, all of whom with two or more EEGs performed during the period January 2010 to December 2014. The first EEG was initiated according to internal medicine physicians, neurologists, or intensive care physicians. The duration between the two tests was at least 24 hours. Interpretation from the American Clinical Neurophysiology Society's standardised critical care EEG terminology 2012 was adopted. Permanent transition was defined as a total change in morphology, EEG frequency, or location of discharge. Fluctuation was defined as short-term change in frequency and morphology, or permanent change in amplitude only. Outcome was assessed by mortality from admission to post-discharge at 6 months of follow-up.

**Results:** Forty-seven patients (median age, 65 years) were included with a mean of three EEGs performed per patient. Of them, 16 (34.0%) patients were subsequently diagnosed as central nervous system infection, 11 (23.4%) patients had hypoxic encephalopathy, 10 (21.3%) patients had structural causes, and 8 (17.0%) with metabolic/toxic disorders. The initial level of consciousness was coma in 20 (42.6%) patients, lethargic or stuporous in 26 (55.3%), and alert in one (2.1%). Use of sedative agents was found in 21 (44.7%) patients, antiepileptic drugs only in 15 (31.9%), and no psychotropic medication in 11 (23.4%). Generalised period discharges (GPD) underwent permanent transition in 81.3% (13/16). Lateralised periodic discharges (LPD) were found to have permanent transition in 77.8% (7/9). The figures for generalised rhythmic delta activity (GRDA), diffuse slow activity, discontinuous background, and generalised fast wave activity were 80%, 16.7%, 100%, and 33.3%, respectively. Permanent transition was associated with a statistically significant outcome of mortality using the Fisher's exact test (21/29; 72.4%) whereas fluctuation was associated with survival (15/18, 83.3%) [P<0.05].

**Conclusion:** EEG patterns dynamically change over time and each pattern can evolve to different EEG patterns or fluctuate in space and time. Aside from epileptiform discharges, lack of reactivity and burst suppression, permanent transition on interval EEG appears to be another risk factor for prediction of poor clinical outcome among encephalopathic patients. Continuous or repeated EEG monitoring could lend clinical utility in such circumstances.

Ρ1

## Neuropsychiatric Symptom Clusters in Stroke by Cognitive Status and Stroke Subtype

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Background: Neuropsychiatric symptoms are important sequelae of stroke. The objective of this study was to examine the frequencies of neuropsychiatric symptom clusters in patients with stroke or transient ischaemic attack (TIA) by cognitive status and stroke subtype.

Methods: This was a hospital-based cross-sectional study. A total of 518 patients with stroke and TIA were administered the Neuropsychiatric Inventory (NPI) at 3 to 6 months poststroke. Based on a confirmatory factor analysis of the 12 NPI items, symptoms were classified into four symptom clusters: behavioural problems, psychosis, mood disturbance, and euphoria.

Results: Overall, 50.6% of the whole sample exhibited one or more NPI symptoms. Frequency of symptoms increased with severity of cognitive impairment (cognitively normal 28.7%, mild cognitive symptoms 66.7%, dementia 85.7%) but was largely similar between stroke subtypes, except that patients with cardioembolic strokes and intracranial haemorrhage had more frequent mood disturbance compared with patients with TIA. Across stroke subtypes and cognitive levels, the most frequent symptom cluster was mood disturbance, followed by behavioural problems, psychosis, and euphoria. Stroke severity was positively associated with severity of neuropsychiatric symptoms independent of cognitive performance.

*Conclusion:* Over half of the patients exhibited neuropsychiatric symptoms 3 to 6 months after stroke and TIA. Frequency increased with cognitive impairment but was largely similar between stroke subtypes. In general, more severe strokes are associated with more frequent occurrence of neuropsychiatric symptoms independent of cognitive performance. These findings should be considered in screening and risk identification for neuropsychiatric disturbance in patients with stroke and TIA.

## The Non-motor Symptom Profile of a Parkinson's Disease Clinic in a Tertiary **Hospital in Hong Kong**

**P** 3

HF Chan, YF Cheung, A Leung, V Kwok, CS Fong, I Chan, C Li, T Fung, A Wang, WC Fong Queen Elizabeth Hospital, Hong Kong SAR

Background: Although non-motor symptoms were found to be common and disabling in Parkinson's disease (PD) patients, they were seldom reported by health care professionals. Therefore, we conducted a crosssectional study to evaluate the non-motor symptom profile of PD patients in a tertiary hospital.

Methods: All Chinese PD patients of all stages and ages referred to the multidisciplinary PD clinic of Queen Elizabeth Hospital were recruited. Those who had severe dementia and failed to give a valid consent were excluded. The demographic information of all subjects was documented. All subjects were asked to complete the Non-Motor Symptom Scale (NMSS). In order to obtain more information of non-motor symptoms, they had to finish the following assessment: (1) Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) for evaluation of cognitive decline, (2) Modified Parkinson's Disease Sleep Scale (PDSS-2) for assessment of sleep dysfunction, and (3) Hospital Anxiety-Depression Scale (HADS) for evaluation of mood problems.

Results: We recruited 131 patients between May 2014 and June 2015. All subjects had at least one non-motor symptom. The mean MMSE score was  $51.10 \pm 34.16$ . The commonest non-motor symptom in our cohort was urinary symptom, followed by sleep dysfunction, gastro-intestinal problems, mood disorders, and cognitive problems. With further assessment, 26.7% of our cohort were found to have dementia. They were found to have executive dysfunction and impaired visuospatial function, which was compatible with PD dementia. As for sleep problems, our PD cohort had a mean of  $6.88 \pm 1.94$  hours of sleep every night; 39.1% reported sleep disorders. Nocturia was the most distressing sleep symptom. As for mood disorder, 37% were found to have anxiety symptoms while 41% had depressive symptoms which required medical attention.

*Conclusion:* With the use of a comprehensive assessment, non-motor symptoms were found to be common in Chinese PD patients.

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