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SUPPLEMENT 5

29th Annual Scientific Meeting of The Hong Kong Neurological Society

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List of Speakers

Name	Affiliation
Prof Michael Barnett	The University of Sydney, Australia
Prof William Barsan	University of Michigan, United States
Dr Sophelia Chan	Queen Mary Hospital, Hong Kong SAR
Dr Bjorn Falck	University Hospital, Uppsala, Sweden
Dr Michael Fu	Tuen Mun Hospital, Hong Kong SAR
Prof Graeme Hankey	The University of Western Australia, Australia
Prof Rita Horvath	Newcastle University, United Kingdom
Prof Ho Jin Kim	National Cancer Center, Goyang, Korea
Dr Raymand Lee	Queen Mary Hospital, Hong Kong SAR
Dr Richard Li	Pamela Youde Nethersole Eastern Hospital, Hong Kong SAR
Prof Hanns Lochmuller	Newcastle University, United Kingdom
Dr Aidan Neligan	Homerton University Hospital, United Kingdom
Prof Thorsten Steiner	Klinikum Frankfurt Höchst, Germany
Dr Frederick Tsang	Queen Mary Hospital, Hong Kong SAR
Dr TH Tsoi	Hong Kong Sanatorium & Hospital, Hong Kong SAR
Prof Yih-Ru Wu	Linkou Chang Gung Memorial Hospital, Taiwan

SCIENTIFIC PROGRAMME

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

5 November 2016, Saturday

08:15 – 08:30	Registration	Poster Room
08:30 – 09:30	**FREE PAPER PRESENTATIONS** Chairpersons: *Carlin Chang, WK Cheng* Judges: *David Chin, Eric Chan, CM Chang*	**POSTER PRESENTATION**
09:30 – 09:45	Coffee Break	
09:45 – 11:15	**DISSERTATION HIGHLIGHTS** Chairpersons: *Carlin Chang, WK Cheng* Judges: *David Chin, Eric Chan, CM Chang*	
11:15 – 12:15	**BAYER LUNCH SYMPOSIUM** Chairperson: *Yannie Soo* **The Latest Real World Evidence of Non–vitamin K Antagonists Oral Anticoagulants for Stroke Prevention in Patients with Non-valvular Atrial Fibrillation** *Graeme J Hankey*	
12:25 – 12:35	**OPENING CEREMONY** Guest of Honour: *Prof Tai-fai Fok, Vice-President (General Affairs), Hong Kong Academy of Medicine*	
12:35 – 13:10	**BOEHRINGER STROKE SYMPOSIUM** Chairpersons: *PW Ng* **Specific Reversal Agent of New Oral Anticoagulants: Why, Which, and How?** *Thorsten Steiner*	
13:10 – 14:25	**NEUROPHYSIOLOGY SYMPOSIUM** (CO-ORGANISED WITH HKSNMD) Chairpersons: *Winnie Wong, CN Lee* **Sports-related Neuropathies in Upper Body—a Clinical and Electrodiagnostic Overview** *Michael Fu* **Special Neurography Techniques** *Björn Falck*	
14:25 – 14:45	Coffee Break	
14:45 – 16:30	**NEUROMUSCULAR DISORDERS SYMPOSIUM** (CO-ORGANISED WITH HKSNMD) Chairpersons: *Sharon Fung, Amanda Kan* **Diagnosing Neuromuscular Disorders: Are We Doing Better Than Before?** *Sophelia Chan* **Recent Advances in Neuromuscular Disorders** *Hanns Lochmüller* **Introduction on Charcot-Marie-Tooth Disease and Mitochondrial Diseases with Neuromuscular Complications** *Rita Horvath*	
18:00	Faculty Dinner (by invitation only)	

6 November 2016, Sunday

08:15 – 08:30	Registration	Poster Room
08:30 – 10:00	**NOVARTIS MULTIPLE SCLEROSIS SYMPOSIUM** Chairpersons: *KL Shiu, KK Lau*	**POSTER PRESENTATION**
	How to Distinguish Neuromyelitis Optica from Multiple Sclerosis? *HJ Kim*	
	New and Emerging Therapies in Multiple Sclerosis *Michael Barnett*	
10:00 – 10:15	Coffee Break / Poster Viewing Session Judges: *KK Lau, Nelson Cheung, Betty Ng*	
10:15 – 10:50	**ASTRAZENECA STROKE SYMPOSIUM** Chairpersons: *Yannie Soo, KM Leung*	
	Current Clinical Management of Transient Ischaemic Attack? *TH Tsoi*	
10:50 – 11:45	**STROKE SYMPOSIUM** (CO-ORGANISED WITH HKSS) Chairperson: *Yannie Soo, KM Leung*	
	Intra-arterial Thrombectomy for Acute Ischaemic Stroke: Current Status in Hong Kong *Richard Li, CP Tsang, Raymand Lee*	
11:45 – 12:45	**ALLERGAN LUNCH SYMPOSIUM** Chairperson: *SH Ng*	
	The Clinical Applications of Botulinum Toxin in Managing Movement Disorders *YR Wu*	
13:00 – 14:30	**EPILEPSY SYMPOSIUM** Chairpersons: *Gardian Fong, Richard Chang*	
	Advances in the Treatment of Refractory and Super-refractory Status Epilepticus *Aidan Neligan*	
	Advances in the Management of Acute Repetitive Seizures *William Barsan*	
	Management of Epilepsy in Traumatic Brain Injury and Spontaneous Intracerebral Haemorrhage *William Barsan*	
14:30 – 14:45	Coffee Break	
14:45 – 16:15	**MOVEMENT DISORDERS SYMPOSIUM** (CO-ORGANISED WITH HKMDS) Chairpersons: *Jonas Yeung, Ken Yung*	
	Clinical Spectrum of Alpha-synucleinopathies *YR Wu*	
	Translating Parkinson's: Genetic Models for Target Discovery *Richard Wade-Martins*	
16:15 – 16:30	Closing Ceremony and Award Presentations	

FP 1

Congenital Myopathies are a Group of Phenotypically and Genetically Heterogeneous Diseases

Sophelia HS Chan[1], Ronnie SL Ho[2], Angel Chan[2], Janice Ip[3], S Wong[4], Grace Ng[5], Hencher Lee[6], Sandy Cheng[7], KT Liu[8], CN Lee[9], Sharon Fung[10], Sharon Cherk[10], Timothy Chan[11], Wendy Lam[3], T Shek[2], VCN Wong[1]
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Congenital myopathies are a group of childhood-onset neuromuscular disorder diagnosed by specific clinical, pathological, and genetic features. With the phenotypic, genotypic, and pathological heterogeneity of these specific conditions, diagnostic confirmation is often challenging. Among our 16 patients with the pathological findings of congenital myopathies, 11 have confirmed genetic mutations. Four patients have *RYR1* mutations, three patients have *ACTA1* mutations, two patients have *KLHL40* mutations, one patient has *MTM1* mutation, and one patient has *DNM2* mutation. Genetically heterogeneity is well illustrated in the five patients with nemaline myopathy having different mutations including *RYR1* (1 patient), *ACTA1* (2 patients), and *KLHL40* (2 patients). Pathological heterogeneity is nicely demonstrated in the four patients with confirmed *RYR1* mutations but having different pathological features including nemaline rods, central cores, multi-minicores or type 1 fibre predominance. The specific finding of rectus femoris sparing on muscle magnetic resonance imaging provides helpful clues to the underlying *RYR1* mutations. Neonatal onset of severe weakness requiring early ventilation is common in our cohort in patients with *ACTA1* autosomal dominant mutation, *KLHL40* autosomal recessive mutation, *DNM2* autosomal dominant mutation, and *MTM1* X-linked mutation. The missense *RYR1* mutation (c.3523G>A) was found in two patients, and the missense *KLHL40* mutation (c.1516A>C) was found in another two patients, suggesting that these variants could probably be the hot spots mutations among Chinese patients.

FP 2

Delayed-onset Dementia after Stroke/Transient Ischaemic Attack

Bonnie YK Lam[1], Adrian Wong[1], Zhaolu Wang[1], Wenyan Liu[1], Lisa WC Au[1], Eric YL Leung[2], Sirong Chen[2], Anne YY Chan[1], Alexander YL Lau[1], Lin Shi[1], Florence SY Fan[1], SH Ma[1], Vincent HL Ip[1], Yannie OY Soo[1], Thomas WH Leung[1], CL Ho[2], Lawrence KS Wong[1], Vincent CT Mok[1]
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Background: We hypothesised that concurrent cerebral small vessel disease and/or Alzheimer's disease (AD) pathologies predicted delayed-onset dementia after stroke/transient ischaemic attack.
Methods: We followed up 919 dementia-free subjects who were recruited into the STRIDE study for a 3-year period. We investigated the relationship between baseline clinical, neuropsychological, genetic, and imaging measures with delayed-onset dementia using logistic regression. Pittsburg compound B (PiB) positron emission tomography was performed on 31 patients with (n=10) and without (n=21) delayed-onset dementia.
Results: Overall, 40 (4.4%) subjects developed dementia during the study period. Presence of ≥3 lacunes (odds ratio [OR]=2.6; 95% confidence interval [CI], 1.3-5.3) and severe white matter changes (OR=2.6; 95% CI, 1.3-5.1) significantly predicted delayed-onset dementia after adjustment for age, education, and gender. Medial temporal lobe atrophy and apolipoprotein E4 status were not associated with dementia. There was no significant difference in the proportion of subjects having AD-like PiB retention among those with (n=3/10, 30%) and without (n=3/21, 14%) dementia (P=0.30).
Conclusion: Severe small vessel disease, rather than AD, was associated with delayed-onset dementia after stroke/transient ischaemic attack.

FP 3

A Threshold of White Matter Hyperintensity in Predicting Cognitive Decline in Stroke/Transient Ischaemic Attack

Stephanie Cheung[1], Jill Abrigo[2], Lin Shi[1], Bonnie Lam[1], Eugene Lo[1], Adrian Wong[1], Vincent Mok[1], CY Lai[1]
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[2] Department of Imaging and Interventional Radiology, The Chinese University of Hong Kong, Hong Kong SAR

Background: We aimed to determine a threshold of cerebral white matter hyperintensity (WMH) severity in predicting cognitive decline in subjects with stroke/transient ischaemic attack.
Methods: Among 245 subjects recruited into the STRIDE (STroke Registry Investigating cognitive DEcline) study, we investigated the association between WMH severity and cognitive decline. We investigated this association using nine different measures of WMH: (1) visual global score of ≥2 of the age-related white matter changes (ARWMC) scale; (2) visual global score of 3 of the ARWMC scale; (3) highest quartile (ie ≥6) of visual total score of the ARWMC scale; (4) periventricular hyperintensity (PVH) of ≥2 of the Fazekas scale; (5) PVH of 3 of the Fazekas scale; (6) deep white matter hyperintensity (DWMH) of the Fazekas scale; (7) DWMH of 3 of the Fazekas scale; (8) volumetric measure as indexed by the highest quartile of intracranial volume (ICV)–corrected WMH volume ratio (ie >0.91%); and (9) volumetric measures as indexed by the highest quartile of the raw WMH volume (ie >13 mL). We defined cognitive decline as a drop of ≥1 standard deviation (ie ≥3 points) of worsening of Montreal Cognitive Assessment (MoCA) performance over 3 years.
Results: Binomial regression analysis showed the highest quartile of ICV-corrected WMH volume ratio predicted cognitive decline in 3 years (P=0.029, β=2.05), adjusted with gender, age, education, and baseline MoCA scores. Analysis also showed that highest quartile of raw WMH volume was barely associated with cognitive decline (P=0.056, β=1.89). Highest quartile of visual total score, visual global scoring of ≥ 2 or 3, and PVH and DWMH of ≥2 or 3 were not associated with cognitive decline.
Conclusions: Threshold of 0.91% in ICV-corrected WMH volume ratio predicts cognitive decline in subjects with stroke/transient ischaemic attack and is a better predictor than other measures of WMH.

FP 4

Prevalence and Distribution of Cerebral Microbleeds in Atrial Fibrillation Patients

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Background: Cerebral microbleeds (CMBs) are dot-like hypointense signals detected by magnetic resonance imaging (MRI) gradient recalled echo or susceptibility weighted imaging sequences, which predicts future intracerebral haemorrhage (ICH). With the emergence of new stroke prevention strategies for atrial fibrillation (AF), CMBs can potentially help identify patients at high risk of ICH, who may benefit from treatments with better safety profile. The objective of this multicentre study was to evaluate the clinical characteristics of CMBs in AF patients.

Methods: We prospectively recruited patients with AF for 3T MRI brain in IPAAC study (Risk of ICH in Patients Taking Oral Anticoagulants for AF with CMBs) since April 2014. Quantity and distribution of CMBs were evaluated.

Results: A total of 470 patients were recruited. CMBs were identified in 157 (33.4%) patients, which was more common than that reported in previous atherosclerotic stroke cohorts (25%-27%). CMBs were more commonly identified in those with prior stroke or transient ischaemic attack (36.5% vs 27.1%; P=0.042). Lobar areas were commonly involved, 44.6% of patients had pure lobar CMBs, 26.8% had CMBs affecting both lobar and other areas. Only 13.4% of patients had pure deep CMBs. Patients with CMBs were more likely to have underlying hypertension (89.2% vs 81.2%; P=0.026), higher CHA_2DS_2-VASc (4.1 ± 1.6 vs 3.7 ± 1.6; P=0.008) and HAS-BLED scores (2.9 ± 0.9 vs 2.7 ± 1.1; P=0.011).

Conclusion: CMBs are commonly identified in AF patients, regardless of the stroke history. Managing AF patients with CMBs may be clinically challenging as they have high risk of both ischaemic stroke and ICH. The predilection of lobar involvement suggests that hypertension alone cannot fully account for the high prevalence of CMBs in AF patients. Further studies are needed to determine the underlying vascular pathophysiology of lobar CMBs in AF patients, and their clinical risk of ICH with oral anticoagulation.

FP 5

The Registry for Early-onset Dementia and Caregivers in Hong Kong (Reach) Study

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Background: To date, studies to investigate the characteristics of early-onset dementia patients in Hong Kong are very limited despite the region being one of the most densely populated cities in Asia. An early-onset dementia registry was set up to (i) facilitate research and raise public awareness; (ii) investigate the genetic profile and neuroimaging characteristics of Hong Kong Chinese frontotemporal dementia (FTD) patients; and (iii) utilise these characteristics that are specific to the local population to help differentiate FTD from other neurodegenerative diseases.
Methods: Patients were recruited from the cognitive disorder clinic of Neurology division in Prince of Wales Hospital. Inclusion criteria included Chinese ethnicity, cognitive impairment before the age of 65 years, and no clinical history of stroke or brain injury. Detailed clinical assessments, neuropsychological assessments, and brain magnetic resonance imaging were performed. Patients were diagnosed with different types of dementia according to established clinical diagnostic criteria. Patients with FTD were tested for mutation in three genes: progranulin (*GRN*), microtubule-associated protein tau (*MAPT*), and chromosome 9 open reading frame 72 (*C9orf72*).
Results: A total of 69 patients were recruited (age of onset, 58.2 ± 6.2 years; female, 37; education, 8.5 ± 3.8 years). The most common clinical diagnosis of early-onset dementia (<65 years) was Alzheimer's disease (59.4%), followed by FTD (31.9%; 12 behavioural-variant, 6 semantic dementia, and 4 progressive nonfluent aphasia). The youngest patient suffered from dementia at the age of 38 years secondary to Niemann-Pick disease type C (mutation in *NPC1* gene). Among the FTD patients, 22.7% had motor disorders including signs of amyotrophic lateral sclerosis and parkinsonism. Family history of dementia was found in 10.0% of all FTD cases. No FTD patient showed genetic mutation tested on *GRN* (22/22) and *MAPT* (22/22), and *C9orf72* (8/8).
Conclusion: FTD is the second most common early-onset dementia. There is evidence of motor disturbances while no genetic association was found to date in the Chinese FTD subjects but a larger sample size is needed to validate the above observations.

FP 6

Increased Pulsatility Index of the Middle Cerebral Artery Measured on Transcranial Doppler is an Early Marker of Cognitive Decline among Community Older Adults with Vascular Risk Factors

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Background: Pulsatility index (PI) obtained on transcranial Doppler is a measure of distal vascular resistance and associated with burden of cerebral small disease. It is not clear whether PI represents an early marker of cognitive decline in non-demented older adults with vascular risk factors.
Methods: PI of middle cerebral artery (MCA) was obtained in 91 community dementia and stroke-free older adults having ≥1 vascular risk factors. Cognitive function was measured by the Montreal Cognitive Assessment (MoCA). Volume of white matter hyperintensities (WMH) and fractional anisotropy (FA) of the normal-appearing white matter (NAWM) measured on diffusion tensor imaging to reflect microstructural integrity were obtained. Linear regression models were constructed to examine the associations between MoCA scores with PI, WMH volume, and NAWM FA with adjustment for age and education.
Results: Performance on the MoCA was significantly and inversely associated with MCA PI (ß= –0.402, P<0.001). WMH volume (ß=0.02) and NAWM FA (ß=0.026) were not significantly associated with MoCA. In the multivariable model incorporating all three measures, only MCA PI was significantly associated with MoCA total score (ß= –0.207, P=0.031).
Conclusions: In stroke and dementia-free older adults with vascular risk factors, elevated MCA PI, indicating increased cerebrovascular resistance, may represent an early vascular marker of vascular cognitive decline preceding the effects of microstructural alternations of the white matter or appearance of WMH.

DH 1

Cognitive Screening in the Chinese Human Immunodeficiency Virus Population in Hong Kong—a Cross-sectional and Longitudinal Study

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Objectives & Methods: Cognitive impairment is a significant complication of human immunodeficiency virus (HIV) infection. As the first cross-sectional and longitudinal observational cohort in the local Chinese HIV population, 98 adult HIV individuals were assessed cognitively with a screening questionnaire, the International HIV Dementia Scale and the Montreal Cognitive Assessment. Overall, 57 subjects underwent a longitudinal cognitive review.

Results: Baseline cognitive impairment was present in 39% of subjects, and was associated with functional difficulties (odds ratio=4.5; 95% confidence interval, 1.415-14.197; P=0.016). Cognitive impairment was associated with lower education level (P=0.030) and an inpatient HIV diagnosis (odds ratio=2.3; 95% confidence interval, 1.005-5.417; P=0.047). Subjects with inpatient HIV diagnosis had more advanced HIV infection and more severe immunosuppression, but none of these factors had significant association with cognitive impairment individually. There was a small but significant overall cognitive improvement on follow-up (P≤0.001). One-fourth of the subjects improved from baseline cognitively impaired to become cognitively preserved, while the others were cognitively static. No association was found between cognitive change and HIV severity or control, comorbidities, host or social factors. Cognitive change was not associated with whether combined antiretroviral therapy (cART) was used, or the central nervous system penetration-effectiveness (CPE) index of the regimen.

Conclusion: Cognitive impairment is common in HIV individuals, especially in those with lower education level, and is associated with functional difficulties. There was an overall cognitive improvement on follow-up, but the current study found no significant predictor. Neither cART nor its CPE index had any association with cognitive change.

DH 2

Autoimmune Encephalitis in Hong Kong: a Retrospective Study of Clinical Characteristics and Outcomes

Adrian Hui
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Background: Since the discovery of the first onconeuronal antibody, anti-Hu, autoimmune encephalitis has been intensely studied over the past decades. Many antibodies targeting either intracellular peptides or cell membrane antigens have aroused researchers' interests to delineate the pathophysiological mechanism, clinical manifestations, and subsequent outcomes of patients suffering from this disorder. The aims of the study were to compare the clinical manifestations and outcomes of antibody-positive adult patients in local population, and to identify specific features for early diagnosis in each antibody discussed.
Methods: Collaborating with 10 government-funded hospitals in Hong Kong, patients older than 18 years at time of onset and harbouring antibodies of one or more of the following antibodies were recruited: N-methyl-D-aspartate (NMDA), voltage-gated potassium channel (VGKC), alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic (AMPA), gamma-aminobutyric acid (GABA), metabotropic glutamate receptor 5 (mGluR5), and glutamic acid decarboxylase (GAD). The study period was between January 2008 and September 2015. Information of demographics, clinical features, and treatment was collected and analysed for variables to predict treatment outcome.
Results: Thirty patients were recruited in this cohort with a median age of symptom onset at 40 years. Of these patients, 20 had NMDA antibodies, 8 VGKC, 1 GABA(B), and 1 mGluR5. The number of cases was steadily accumulating over the years, with an average of five new cases discovered per year since 2011. Four died within 7 months of symptom onset. The clinical manifestations and outcomes were similar between our cohort and the current literature. Subjects with NMDA encephalitis presented with seizures (25%), psychiatric symptoms (25%) with prodromal symptoms (30%), and the characteristic orofacial or brachial dyskinesia was also frequently seen in our cohort (35%). However, other specific features such as movement disorders (apart from orofacial/brachial dyskinesia), hypoventilation, or dysautonomia were less observed. Subjects with VGKC encephalitis presented with amnesia (63%) and seizure (25%), and the majority (88%) showed hyponatremia compatible with SIADH (syndrome of inappropriate antidiuretic hormone) at onset. One case each was identified for GABA(B) and mGluR5; they presented with refractory seizure with cognitive impairment and acute psychosis with fever, respectively. Our result was also able to show that admission to intensive care unit could predict poor outcome.
Conclusion: Recognising the specific features of each antibody would allow early and aggressive treatment thereby improving the outcome of patients with autoimmune encephalitis.

A Prospective Study on the Risks of Fall in Chinese Parkinson's Disease Patients in Hong Kong

DH 3

YO Lam
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Background: Parkinson's disease (PD) is the one of the commonest neurodegenerative diseases worldwide and the prevalence is growing. The hallmarks of PD including tremor, rigidity, bradykinesia, and postural instability result in motor disability in PD patients and predispose them to fall. Falls in PD are of particular importance as they result in direct injury to patients and secondary consequences with substantial socio-economic implication. The objective of this study was to identify the risk factors for falls in Chinese PD patients which could be potential treatment target in altering disease outcome.
Methods: This was an observational cohort which included a group of idiopathic PD patients regularly followed up in the movement disorder clinic in a regional hospital prospectively for 6 months to observe for the occurrence of fall and associated risk factors. Patients were recruited over a predefined period (December 2014 to March 2015) from one single centre. Apart from collection of baseline demographic data, four additional tests were performed including Mini-Mental State Examination, Montreal Cognitive Assessment, Tinetti Mobility Test, and Multiple Tasks Test. Retrospective fall history and prospective fall occurrence were recorded both for 6 months.
Results: A total of 84 patients completed baseline assessment and provided prospective fall data. Their mean age was 67.8 years, with a mean duration of 7.9 years. The total number of falls occurred was 47. Of the patients, 29 (34.5%) developed at least one fall and were regarded as fallers. Fallers had longer disease duration (P=0.037), higher level of dependence in activity of daily living (P=0.002), higher number of falls before recruitment (1.7 ± 2.2; P<0.001). Fallers had more severe PD with higher total Unified Parkinson's Disease Rating Scale (33.0 ± 18.8; P=0.007), performed worse in both Tinetti Mobility test (total score in fallers 19.8 ± 8.6; P<0.001), and Multiple Tasks Test (score in fallers 3.6 ± 2.1; P <0.001).
Conclusion: Falls are common in Chinese PD patients. Our study identified risk factors of fall including previous history of fall, more advanced stage of disease, motor disability resulting in gait and balance disturbance, and executive dysfunction with impairment on multitasking to be of statistical significance.

Five-year Outcome of Vertebrobasilar Territory Ischaemic Stroke Attributed to Large Artery Disease

DH 4

SH Ma
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Background: Vertebrobasilar (VB) territory infarct with large artery disease (LAD) is an important subset of ischaemic stroke. While previous studies demonstrated an increased risk of recurrence in the short term, data regarding the long-term prognosis are lacking.
Methods: We conducted a retrospective analysis in a cohort of 282 patients with VB territory infarct. We evaluated the 5-year restroke rate, functional outcome and mortality, and assessed the effect of an optimal control of conventional risk factors. Optimal risk factor control was defined as a combination of low-density lipoprotein of ≤1.8 mmol/L, systolic blood pressure of ≤140 mm Hg, and glycosylated haemoglobin of ≤6.5%.
Results: The 5-year restroke risk was 21.4% for the LAD group versus 11.8% in the non-LAD group (odds ratio [OR]=2.03; 95% confidence interval [CI], 1.05-3.91; P=0.032). The LAD group was also associated with a poor functional outcome (OR=2.19; 95% CI, 0.97-7.13; P=0.05) and a higher mortality rate (OR=2.41; 95% CI, 1.26-4.76; P<0.01). Optimal risk factor control was associated with a significant risk reduction (20.9% vs 6.1%, OR=0.24; 95% CI, 0.61-0.98; relative risk=3.42, P<0.01). Absolute risk reduction was 24.7% and the number needed to treat was 4.
Conclusion: LAD in VB territory ischaemic stroke portends a poor long-term prognosis with a high recurrence. Optimal risk factor control might significantly reduce the recurrent risk.

Antiplatelet Resumption after Antiplatelet-related Intracerebral Haemorrhage

DH 5

KC Teo
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Background: Antiplatelet resumption in survivors of antiplatelet-related intracerebral haemorrhage (ICH) represents an important medical dilemma as these patients are at risk of both recurrent ICH and ischaemic vascular event. This study aimed to investigate whether antiplatelet medicine should be resumed in survivors of antiplatelet-related ICH, and to identify the risk factors for recurrent ICH and vascular death.
Methods: This was a single-centre retrospective longitudinal cohort study involving antiplatelet-related ICH survivors who were admitted to Queen Mary Hospital from July 2002 to June 2013. Antiplatelet exposure and follow-up data were retrieved from the electronic patient record system. The clinical end-points were recurrent ICH, ischaemic vascular event, and vascular death (death due to ICH or ischaemic vascular event). Predictors of recurrent ICH and vascular death were derived using multivariable Cox regression model.
Results: There were a total of 109 survivors of antiplatelet-related ICH. The median follow-up duration was 3.5 years (total time of 518.2 patient-years). Overall, 37 patients were subsequently resumed on antiplatelet medicine. Ischaemic vascular events were more common than recurrent ICHs (6.8 per 100 patient-years vs 2.6 per 100 patient-years; P=0.028). Antiplatelet exposure was not associated with a higher risk of recurrent ICH (hazard ratio [HR]=1.10; P=0.893) or vascular death (HR=0.85; P=0.825). A mean follow-up systolic blood pressure of >140 mm Hg was associated with an increased risk of recurrent ICH (HR=5.18; P=0.034) and vascular death (HR=11.14; P=0.001). Cerebral amyloid angiopathy (HR=28.05; P=0.003) was an independent predictor for recurrent ICH.
Conclusion: Antiplatelet resumption after antiplatelet-related ICH was not associated with a significant increased risk of recurrent ICH. The risks of recurrent ICH and vascular death were increased with inadequate blood pressure control. Antiplatelet resumption should be considered, especially in survivors with low risk of recurrent ICH (non-lobar ICH and patients with adequate blood pressure control). Adequate blood pressure control during follow-up is pivotal to reduce the risk of both recurrent ICH and vascular death.

Effect of Serum 25-Hydroxycholecalciferol Level on the Severity and Prognosis in Acute Ischaemic Stroke Patients

DH 6

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Background: Vitamin D deficiency is a common condition in stroke patients. Serum 25-hydroxycholcalciferol [25(OH)D] level is the best indicator of vitamin D status. Low serum 25(OH)D levels have been reported to be possibly associated with poor neurological outcome in stroke patients. This study aimed to evaluate the effect of serum 25(OH)D level on the initial severity and neurological outcome in acute ischaemic stroke patients.
Methods: From March 2015 to October 2015, consecutive first-ever acute ischaemic stroke patients admitted to the Acute Stroke Unit of Princess Margaret Hospital, Hong Kong, were identified. Serum 25(OH)D levels were measured at baseline. Patients were dichotomised into vitamin D–deficient group and non-deficient group using a cut-off of 25(OH)D level of <50 nmol/L for deficiency. Severe stroke was defined as National Institutes of Health Stroke Scale score of ≥6 upon admission (D0 NIHSS ≥6). Poor neurological outcome was defined as modified Rankin Scale score of ≥3 at day 90 after admission (D90 mRS ≥3). Multivariate analyses were performed using logistic regression to evaluate the associations between vitamin D deficiency with severe stroke upon admission and poor neurological outcome at day 90.
Results: A total of 192 patients were enrolled in this study. Of these patients, 120 (62.5%) were classified into vitamin D–deficient group. The percentages of patients having severe stroke upon admission and poor neurological outcome at day 90 were significantly higher in the vitamin D–deficient group than non-deficient group (38.3% vs 19.4%, P=0.006 and 39.2% vs 19.4%, P=0.006, respectively). In multivariate analyses, a low serum 25(OH)D level of <50 nmol/L was independently associated with both D0 NIHSS ≥6 (odds ratio [OR]=2.25; 95% confidence interval [CI], 1.09-4.66; P=0.028) and D90 mRS ≥3 (OR=2.36; 95% CI 1.13-4.93; P=0.022) after adjustment of covariates.
Conclusion: The results of this study suggest that vitamin D deficiency is associated with higher stroke severity and worse neurological outcome in acute ischaemic stroke patients. Whether vitamin D supplementation can improve the outcome of stroke patients has not yet been proven and warrants further research.

DH 7

Occurrence of Multiple Sclerosis and Its Investigations: a Retrospective Observational Study

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Background: The prevalence of multiple sclerosis is rising and new therapies are becoming available, with a number of drugs undergoing clinical trials.
Methods: We performed a retrospective observational study in the West Midlands region, United Kingdom, looking into the occurrence of multiple sclerosis, and the investigation modalities involved in making the diagnosis. Comparison is made with the findings of an observational study in a regional population in Hong Kong.
Results & conclusion: We concluded that the incidence in the West Midlands was 4.5 in 100 000, and the prevalence in Wan Chai was 5.7 in 100 000, both comparable to the respective national average. Anti-nuclear antibody titre had a tendency to be positive in multiple sclerosis patients, but it was not significantly useful as a diagnostic tool. Further studies on true incidence and prevalence and use of disease modifying therapy would help in planning service provision for the future. The latest investigations and management are discussed.

S 1

The Latest Real World Evidence of Non–vitamin K Antagonists Oral Anticoagulants for Stroke Prevention in Patients with Non-valvular Atrial Fibrillation

Graeme J Hankey
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The global burden of stroke is substantial and increasing. The major cause of stroke is ischaemic stroke and the major cause of disabling and fatal ischaemic stroke is atrial fibrillation (AF). Oral anticoagulation with vitamin K antagonists (VKA) such as warfarin can reduce the risk of AF-related stroke by two thirds if the international normalised ratio (INR) can be maintained between 2.0 and 3.0. However, achieving steady INR control is challenging. Hence, the implementation of effective thromboprophylaxis with VKA for stroke prevention in AF (SPAF) remains suboptimal.

The direct acting, non-VKA oral anticoagulants (NOACs) provide predictable anticoagulation without the need for routine coagulation monitoring and have proved as effective and safe as VKA in preventing stroke, systemic embolism, and major bleeding among patients with AF in large phase III clinical trials.

Recent evidence from several retrospective post-marketing surveillance studies and prospective observational studies of the NOACs for SPAF in real world clinical practice settings complement the evidence from clinical trials of NOACs for SPAF and support the external validity (generalisability) of the results of the clinical trials in real world clinical practice.

S 2

Specific Reversal Agent of New Oral Anticoagulants: Why, Which, and How?

Thorsten Steiner
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Preventing stroke is the primary goal of anticoagulant treatment in patients with atrial fibrillation (AF). Non-vitamin K antagonist oral anticoagulants (NOACs) are increasingly used for this purpose.

NOACs have demonstrated both efficacy and safety in randomised clinical trials. While NOACs are beneficial to AF patients, their usage might increase the complication for AF patients when emergency situations arise.

While there are established measures to manage NOAC-treated patients in emergency situations, the benefits of current treatment options are still unclear and there are certainly still unmet needs.

Recently the first reversal agent is now available for the rapid reversal of dabigatran offering an alternative approach to effectively manage AF patients in cases of emergency.

This lecture discusses:

- current strategies for management of NOACs-treated patients in emergency situations, eg intracranial haemorrhage using both non-specific and specific reversal agents
- real world experiences with administering specific reversal agent prior to thrombolysis

Sports-related Neuropathies in Upper Body—a Clinical and Electrodiagnostic Overview

S 3

Michael Fu
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Sports-related neuropathies may affect both professional and amateur players. They are relatively specific for the types of sports activities. Nerve traction and compression are the usual mechanisms of injury in noncontact sports. In upper body, true neurogenic thoracic outlet syndrome in swimmers and supraclavicular neuropathy affecting the dominant arm of volleyball players are the well-known examples for overhead athletes. Long thoracic nerve palsy or ulnar neuropathy with entrapment at elbow region is seen primarily in throwers and weight lifters. Racquet sports may predispose players to various compressive neuropathies at or below elbow, eg radial tunnel syndrome, posterior interosseous nerve palsy, and carpal tunnel syndrome. Constrictive wrist bands and repeated direct contact by volleyball can cause pressure lesion at the superficial sensory branch of radial nerve. In the hands, ulnar neuropathy at the wrist is most commonly seen in long-distance cycling, ie "cyclist's palsy". Knowledges of the typical neuropathies in the specific sports, the differential diagnoses, and the electrodiagnostic approach are the keys to the correct diagnosis and the subsequent management.

Special Neurography Techniques

S 4

Björn Falck
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In the diagnosis of focal peripheral neuropathies needle electromyography (EMG) and electroneurography (ENG) are essential tools that complement each other. In most laboratories ENG is done with surface electrodes. Many clinically relevant nerves can be studied with surface electrodes. There are, however, a number of common neuropathies that cannot be studied with surface electrodes for several reasons: (1) nerve is too deep to be stimulated or recorded with surface electrodes, (2) the responses are too small to be picked up with surface electrodes, or (3) two nerve branches are close to each other resulting in stimulation or recording of both nerves. These problems can be solved with near nerve needle electrodes. I will present special ENG techniques that are useful in many commonly encountered patients.

Neurography with near nerve electrodes—The needle electrodes used are 30-50 mm long, shaft is insulated, area of active recording surface is 5 mm^2. The electrodes are placed close to the nerve, which can be done in different ways: (1) using anatomical landmarks, (2) by stimulating with the active electrode and using the motor or sensory response as a guide, (3) with ultrasound. The most common nerves are: (1) plantar digital nerves (Morton's metatarsalgia, tarsal tunnel syndrome), (2) lateral cutaneous nerve of the thigh (meralgia paresthetica), (3) inferior alveolar nerve, and (4) the inferior patellar nerve.

Short segment studies—In some focal neuropathies, particularly the ulnar nerve at the elbow, the nerve can be studied across the affected segment in 10-mm segments. This method is in the clinical routine useful in precise characterisation and localisation of ulnar neuropathies at the elbow and peroneal nerve lesions at the knee.

Nerves for which no published methods are available—Sometimes we are asked to study nerves for which there are no published methods. The measurements can usually be improvised, using either surface electrodes or near nerve electrodes.

Future challenges—There are some nerves that cannot be tested with ENG. The most important are the palmar branch of the median nerve, iliohypogastric, ilioinguinal and genitofemoral nerves.

Summary—Many simple focal peripheral neuropathies can be studied with surface electrodes. Electromyographers dealing with more challenging problems should be able to use advanced techniques. Special ENG techniques are easy to learn and can readily be applied in the clinical routine.

Diagnosing Neuromuscular Disorders: Are We Doing Better Than Before?

S 5

Sophelia Chan
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Diagnosing a neuromuscular disorder is a multi-step process and often involves several tests. When considering the differential diagnosis, often the patient's clinical symptoms and signs, and family history, give an important clue. The most important diagnostic tests include biochemical testing, nerve conduction study and electromyography, muscle imaging, muscle biopsy, and molecular genetic study. How each of these diagnostic modalities helps in the confirmation of both rare and more common neuromuscular disorders will be illustrated through the following examples: collagen VI-related congenital muscular dystrophy, congenital myopathy, congenital myasthenic syndrome, Duchenne muscular dystrophy, and spinal muscular atrophy. How a confirmed diagnosis helps the management of our patients with these different neuromuscular conditions will also be highlighted.

Recent Advances in Neuromuscular Disorders

S 6

Hanns Lochmüller
John Walton Muscular Dystrophy Research Centre, Institute of Genetic Medicine, Newcastle University, United Kingdom

The international neuromuscular network TREAT-NMD (www.treat-nmd.eu) was established to address the bottlenecks that have held back translational research and therapeutic development in the neuromuscular field. The network has developed partnerships across the world to help prepare the neuromuscular field for clinical trials and implement best practice in patient care. Specific tools have been developed to overcome the challenges that researchers and clinicians face and to improve international collaboration.

New developments in neuromuscular research have promoted interest from the pharmaceutical industry. However, because of the rarity of the conditions, locating the investigators and the sites with the expertise to run clinical trials and the patient cohorts to enrol into them is still a challenge. By collaborating on an international level, TREAT-NMD has created global registries of patients with the genetic and clinical data necessary for trial recruitment. These bring many benefits to registered patients, and many benefits to industry. The TREAT-NMD DMD registry has more than 10 000 patients in 50 countries and the SMA registry more than 2500 patients in 41 countries. As with the patients themselves, biomaterial samples of rare NMD patients are very limited. The international biobank network EuroBioBank (www.eurobiobank.org) is part of TREAT-NMD and is the first operating network of biobanks in Europe providing human DNA, cell and tissue samples as a service to the scientific community conducting research on rare diseases. More than 400 000 samples are available to researchers worldwide via the online catalogue. The TREAT-NMD Alliance is interested in developing partnerships and supporting neuromuscular specialists and patients worldwide and encourages patient organisations, researchers, and clinicians to join.

Neuromics and RD-Connect are new projects funded by the European Union that build on the foundations of TREAT-NMD, but include additional rare diseases such as rare neurodegenerative diseases or rare kidney diseases. Overall, so-called rare diseases are anything but rare. 6% to 8% of the European population—between 27 and 36 million people—are affected by one of the 5000-8000 distinct rare diseases. Neuromics (www.rd-neuromics.eu) studies 10 rare neurodegenerative and neuromuscular diseases with the aims to find novel disease-causing genes, improve diagnostics, and develop novel therapies for these disorders using -omics technologies. RD-Connect (www.rd-connect.eu) is a unique global infrastructure project that links up databases, registries, biobanks and clinical bioinformatics data used in rare disease research into a central resource for researchers worldwide. It will develop an integrated research platform in which complete clinical profiles are combined with -omics data and sample availability for rare disease research, in particular research funded under the International Rare Diseases Research Consortium (IRDiRC; www.irdirc.org).

Introduction on Charcot-Marie-Tooth Disease and Mitochondrial Diseases with Neuromuscular Complications

S 7

Rita Horvath
John Walton Muscular Dystrophy Research Centre, Institute of Genetic Medicine, Newcastle University, United Kingdom

Inherited peripheral neuropathies (Charcot-Marie-Tooth disease, CMT) and mitochondrial disorders are a heterogeneous group of diseases affecting different organs like brain, muscle, liver, and heart. The severity of the disease is very variable and many patients require surveillance follow-up over their lifetime often involving multiple disciplines. Our understanding of the genetic defects and their pathological impact underlying CMT and mitochondrial diseases has significantly improved over the past decade, however this has not been paralleled with regard to treatment. Currently pharmacological treatment exists only for a very small number of patients due to rare metabolic defects. However several new pharmacological agents with potential benefit for a wider group of mitochondrial diseases are currently being investigated in vitro (in human cells) and in vivo (in animal models). Management is primarily aimed at minimising disability, preventing complications, and providing prognostic information and genetic counselling based on current best practice.

How to Distinguish Neuromyelitis Optica from Multiple Sclerosis?

S 8

HJ Kim
Department of Neurology, Research Institute and Hospital of National Cancer Center, Korea

Neuromyelitis optica (NMO) has long been considered as a variant of multiple sclerosis (MS). This concept changed with the discovery of disease-specific autoantibodies directed against aquaporin-4 (AQP4). NMO was originally considered a disease of the optic nerve and spinal cord, with limited involvement of the brain. But AQP4 antibody has enabled us to define a wider spectrum of disorders called NMO spectrum disorders (NMOSD), such as inflammation limited to the spinal cord or the optic nerve, or even just brain. Now NMOSD is considered an AQP4 antibody-mediated autoimmune astrocytopathic disease in which clinical and neuroimaging findings, and therapeutic responses are distinct from those observed in MS patients. However, some patients, who have overlapping features of both diseases and are tested negative for AQP4 antibody, may be difficult to definitely diagnose. This raises important practical issues, since NMOSD and MS respond differently to immunomodulatory treatment and have different prognoses.

In this talk, I will discuss the contrasting features of two diseases, which help differentiate NMOSD from MS.

New and Emerging Therapies in Multiple Sclerosis

S 9

Michael Barnett
Brain and Mind Centre, University of Sydney, Australia

The multiple sclerosis (MS) treatment landscape has, over two decades, been transformed by the introduction of a range of disease-modifying therapies (DMTs) that seek to redress an imbalance in adaptive immune regulatory networks by targeting lymphocyte proliferation, selectively depleting T and/or B lymphocytes, impeding lymphocyte trafficking both into the central nervous system and from peripheral lymphoid tissue, and altering the expression of downstream pro-inflammatory molecules. The mechanism of action of DMTs dictates not only their efficacy, but also their safety; and critically informs consideration of 'disease risk versus treatment risk' in individual patients with MS. The recent introduction of effective oral immunosuppressive therapies (fingolimod, dimethyl fumarate, and teriflunomide) has improved medicine tolerability and patient adherence; and the advent of highly efficacious 'induction' therapies, including alemtuzumab and AHSCT (autologous hematopoietic stem cell transplantation), has fundamentally altered treatment approach in patients with highly aggressive disease. However, these advances have been accompanied by treatment-related risks that mandate the development of a long-term 'treatment contract' with individual patients, encompassing both stringent disease and DMT-specific monitoring protocols. When appropriately delivered, the benefits of a broad, immune-directed therapeutic armamentarium are clear. The emergence of novel neuroprotective and pro-remyelinating therapies over the next decade will likely herald a further paradigm shift in MS therapeutics and offers real hope that disability can be both prevented and, in some instances, reversed.

Current Clinical Management of Transient Ischaemic Attack

S 10

TH Tsoi
Neurology Centre, Hong Kong Sanatorium & Hospital, Hong Kong SAR

Transient ischaemic attack (TIA) was first described as a medical disease more than one century ago. The concept of TIA as transient ischaemia causing reversible neurological dysfunction without permanent brain damage was proposed by Miller Fisher in the 1950s. The duration of most typical TIAs had been recognised as less than 1 hour ever since the condition was accepted as a disease entity. The classical definition of TIA adopting a 24-hour time point was proposed in 1964 and has been prevailing in clinical practice as well as clinical trials in the past 5 decades. Recently many authorities strongly advocate using a tissue-based definition for TIA in view of better understanding of the pathophysiology of stroke and advancement in acute stroke imaging. TIA is accordingly defined as a transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischaemia, without acute infarction.

Many recent studies consistently showed that the stroke risk after TIA is very high ranging from 10% to 15% within 3 months with half of them occurring in the first 48 hours. Urgent assessment and treatment in a dedicated TIA clinic has reduced the stroke rate by 80%. TIA is a medical emergency requiring immediate admission or referral to a dedicated TIA clinic. The first step in management is awareness and correct diagnosis. The symptoms of TIA are largely similar to ischaemic stroke including motor weakness, sensory symptoms, visual disturbances, speech difficulties, walking difficulties, dizziness, and abnormal movements etc, and of highly variable duration from seconds to minutes or even hours. As the symptoms have mostly resolved by the time the patients are seen, they are frequently evaluated based on patients' subjective reports only. Diagnosis of TIA as the cause of the reporting symptoms sometimes can be very challenging even to the experienced neurologists as many of these symptoms can be produced by a wide variety of non-vascular diseases.

In the past few years, many important landmark studies on treatment and prognosis of TIA have been published which provide strong evidences for guiding clinical management. The results and their impact on clinical practice will be discussed.

Intra-arterial Thrombectomy for Acute Ischaemic Stroke: Current Status in Hong Kong

S 11

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In Hong Kong, there are approximately 15 000 new or recurrent stroke cases each year. In addition to the major impact on patients' lives, stroke also places a significant burden on their families and the society, with an estimated cost of more than 1.6 billion per annum. The fight against this devastating disease requires teamwork, from pre-hospital care to the acute management upon hospital arrival, which involves the collaboration between neurologists, radiologists, neurosurgeons as well as nursing colleagues. Rehabilitation is also crucial to help stroke survivors strive towards regaining independence and attaining the best quality of living.

The results of the landmark trial MR CLEAN, the Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands, has shown that acute ischaemic stroke (AIS) patients with large vessel occlusion (LVO) are more likely to have good clinical outcome (defined as having a D90 modified Rankin score of 0-2) when treated with intra-arterial (IA) thrombolysis (32.6%), as compared with medical management alone (19.1%). This opened up a new chapter in the treatment of AIS with LVO. Several other ongoing randomised controlled trials—including EXTENDED-IA, SWIFT PRIME, and ESCAPE—have been halted for early analyses. Their results were all in favour of endovascular therapy, which supported the fact that mechanical thrombectomy has an overwhelming benefit in treating AIS patients with LVO (Level 1a).

In this session, we would like to share our experience in IA therapy for AIS cases with LVO, including interesting findings on patient demographics; whether IA therapy should be offered to specific patient age-groups (eg octogenarian); the screening workflow; imaging logistics; comparison between monitoring anaesthetic care and general anaesthesia; differences in the technical aspect of local IA procedures (aspiration vs stentriever); complication management; and medico-legal aspects. Our speakers—including a neurologist, a neurosurgeon, and a radiologist—would share the viewpoints of their respective specialties, who are all key players in our goal to improve the local AIS service.

The Clinical Applications of Botulinum Toxin in Managing Movement Disorders

S 12

YR Wu
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Botulinum neurotoxin (BoNT) acts as the blockade of releasing acetylcholine transmitters at peripheral nerve endings. BoNT has proved to be a significantly effective treatment for some movement disorders such as blepharospasm, oromandibular dystonia, cervical dystonia (CD), writer's cramp and hemifacial spasm, as well as post stroke spasticity. Three types A BoNT (BoNT/A) and one type B BoNT (BoNT/B) products are currently available. OnabotulinumtoxinA (BotoxVR, Allergan Inc, Irvine [CA], US) has been used to treat focal dystonias for more than 20 years.

CD is the most common form of focal dystonia characterised by involuntary muscle contractions causing abnormal movements and posturing of the head and neck, and is usually accompanied with significant pain. BoNT is considered the first-line therapy in the treatment of CD. Two Cochrane reviews concluded that BoNT/A are effective and safe for treating CD. Blepharospasm is an abnormal contraction of the eyelid muscles, which is a form of focal dystonia leading to episodic closing of the eyelids bilaterally. Symptoms usually begin as mild and infrequent spasms that progress to forceful and frequent contractures of the eyelids, in advanced cases causing functional blindness from inability to temporarily open the eyes. One treatment of choice for blepharospasm is a periodic injection of BoNT into the orbicularis oculi muscle.

In this talk, I will focus on the following issues. First, the role of BoNT within CD and blepharospasm treatment options. Second, patient perspectives and desires for treatment. Third, assessment and goal setting. Fourth, treatment with BoNT/A. Five, follow-up sessions, including management of side-effects and management of non-response.

Advances in the Management of Acute Repetitive Seizures

S 14

William Barsan
Department of Emergency Medicine, University of Michigan, United States

This talk will address research performed by the Neurological Emergencies Treatment Trials (NETT) network in the management of status epilepticus. The RAMPART (Rapid Anticonvulsant Medication Prior to Arrival Trial) will be described in detail including the design, primary outcomes, inclusion and exclusion criteria, and results. The presentation will also discuss the treatment of established status epilepticus and describe the design, primary outcomes, inclusion and exclusion criteria for the ESETT (Established Status Epilepticus Treatment Trial). This trial utilises a unique adaptive trial design which will be described.

S 15

Management of Epilepsy in Traumatic Brain Injury and Spontaneous Intracerebral Haemorrhage

William Barsan
Department of Emergency Medicine, University of Michigan, United States

This presentation will discuss the incidence and significance of seizures both in the acute phase of traumatic brain injury (early post traumatic seizures) and the frequency and risk of post traumatic epilepsy (late post traumatic seizures). The significance of early post traumatic seizures on traumatic brain injury outcomes will be discussed as well as the recommendations for prophylactic treatment. Recommendations regarding monitoring and treatment will be given.

The incidence and treatment of seizures in patients with spontaneous intracerebral haemorrhage (ICH) will be discussed. The use of continuous electroencephalography monitoring in ICH patients and its potential impact on outcome will also be discussed.

S 16

Clinical Spectrum of Alpha-synucleinopathies

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It has long been recognised that several neurodegenerative diseases of the central nervous system are characterised by the presence of intracellular inclusion bodies. The core proteins underlining these pathologies have been defined. One of these proteins is alpha synuclein, which was found to be the main component of Lewy bodies or Lewy neurites in the late 1990s. After this discovery, alpha synuclein was found to link with the pathology of Parkinson's disease (PD) and dementia with Lewy bodies (DLB) and multiple system atrophy (MSA). These three disorders constitute the majority of patients with an 'alpha synucleinopathy'. In addition, there are a number of rarer conditions that can also cause this pathology, including inherited metabolic disorders such as Gaucher's disease.

In this talk, I will focus on the natural history and clinical presentations of PD, the commonest alpha synucleinopathy, and its associated dementia (PDD) first. Then I will discuss the clinical features of DLB and MSA. At the end, I will discuss whether diagnosing patients with specific clinical conditions is useful, and if we should move towards classifying Parkinsonian syndromes with a pathological basis, to facilitate a combined approach to develop new therapies directed target to prevent alpha synuclein aggregates.

Translating Parkinson's: Genetic Models for Target Discovery

S 17

Richard Wade-Martins
Oxford Parkinson's Disease Centre, Department of Physiology, Anatomy and Genetics, University of Oxford, United Kingdom

Parkinson's disease (PD) is the second most common neurodegenerative disease and a major unmet clinical need in our ageing population. The focus of the Oxford Parkinson's Disease Centre (OPDC; www.opdc.ox.ac.uk) is to exploit the interdisciplinary research environment within Oxford as a leading centre focused on translational research understanding the earliest pathological pathways in PD. Groups with strengths in genetics and genomics, transgenic rodent models, in-vivo neuroanatomy and neuropharmacology of the basal ganglia, magnetic resonance imaging (MRI), and analysis of protein biomarkers, are working closely with experts in epidemiology and clinical neurology to better understand and ultimately target the causes of PD.

In the clinic we have collected 1000 PD patients, plus age-matched controls and 'at-risk' individuals for our longitudinal study. The cohort is being studied to allow biomarker discovery, MRI and fMRI programs, and genetic analysis by exome resequencing and high-density SNP arrays. In the laboratory we have generated >150 induced pluripotent stem (iPS) cell lines to derive dopamine neurons from PD patients and controls to allow us to study cellular phenotypes in an accurate, physiologically relevant model of dopaminergic neurons. We have generated iPS cells from control individuals, from sporadic PD patients and patients carrying mutations in the leucine-rich repeat kinase 2 (*LRRK2*) and glucocerebrosidase (*GBA*) genes. Mature dopaminergic neurons with correct morphology express essential protein markers, exhibit key neurophysiological features, and reveal neurobiological deficits in PD lines. To better understand and model the sequence of events which occurs in vivo in PD we have created BAC transgenic mice and rats expressing mutant or wild-type forms of key genes alpha-synuclein and *LRRK2*. Rodents transgenic for disease genes show age-dependent motor and non-motor phenotypes and deficits specific to those parts of the brain vulnerable in PD.

This translational programme spanning a longitudinal clinical study, human neuronal iPS cell models and transgenic rodents encapsulates the key elements required to better understand and ultimately treat a major disease of our time.

P 1

The Protective Effect of *Gastrodia elata* on Pilocarpine-induced Epileptic Mouse Model

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Introduction: Epilepsy research may not focus only on seizure control but neuroprotection and healing. The development of an epileptic model for biological, pathological, and clinical studies is required. 50 million people from around the world suffer from epilepsy and a third of them have refractory epilepsy. The use of *Gastrodia elata* (Tianma) has been reported since 100AD in China. The number of research on the effects of Gastrodia is limited. This study evaluated the protective effect of *Gastrodia* on status epilepticus with a view to future development of drugs for refractory epilepsy.

Methods: Male C57BL/6 mice aged 8-10 weeks were obtained from the Laboratory Animal Services Center of the Chinese University of Hong Kong. The animal dosage was converted from human dosage using US FDA formula: human dosage (166.7 mg/kg) x mice conversion factor (12.3) x extraction yield (43.1%). Both Tianma extract (833.7 mg/kg) and carbamazepine (200 mg/kg) were dissolved in distilled water and pretreatment given to three groups: Tianma, carbamazepine, and control. Pretreatment might be accomplished by intragastric administration to mice daily from day 1 to 14. Status epilepticus was induced on day 14 with the following protocol: 127 mg/kg of lithium chloride (intra-peritoneal [ip]) followed by 1 mg/kg of scopolamine (ip) on day 15 and 320 mg/kg of pilocarpine (ip) 30 minutes later. 10 mg/kg of diazepam (ip) was used at 2 hours for abortion of seizure when Racine stage 3-4 was reached.

Results: A total of 12 individual mice comprised each treatment group (n=36). After pilocarpine injection, 1 mouse from Tianma group, 2 mice from carbamazepine group, and 2 mice from control group died. Using the Racine scale, the time to development of status epilepticus was determined. There was a significant prolongation in Tianma group for level 1 seizure ($P<0.05$). There was a significant prolongation in Tianma and carbamazepine group for level 2/3 seizures ($P<0.05$). For level 4 seizures, the carbamazepine group had the most significant prolongation effect ($P<0.001$). The average time of status epilepticus development was 61.5 minutes for control, 92.9 minutes for Tianma, and 107 minutes for carbamazepine. The Kaplan-Meier analysis of time of status epilepticus was significant between control and each of Tianma and carbamazepine group ($P<0.05$).

Conclusion: In the present study, 320 mg/kg of pilocarpine showed a reproducible status epilepticus induction. The mice treated with 883.7 mg/kg of Tianma had longer latent period of developing status epilepticus compared with control. This may be due to the neuroprotective and antiepileptic effect of Tianma.

P 2

Lower Extremity Predominance Spinal Muscular Atrophy Caused by *DYNC1H1* Mutation: a Case Report

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We report a 17-year-old girl characterised by congenital club feet, delay walking, and predominant proximal lower-limb weakness with progressive distal wasting. Her creatine kinase level was normal. Needle electromyography showed persistent chronic denervation. *SMN1* mutation study was negative. Magnetic resonance imaging of muscle showed diffuse involvement of quadriceps with relative sparing of adductors, short head of biceps femoris and semitendinosus in the thighs, and diffuse involvement of soleus and gastrocnemius with sparing of anterior and medial muscles in the calves. Whole-exome sequencing showed a heterozygous mutation [p.Arg251Cys (c.751C>T)] in the tail domain of the *DYNC1H1* gene encoding the cytoplasmic dynein heavy chain 1. The case demonstrates the power of whole-exome sequencing in the discovery of rare lower-extremity predominant spinal muscular atrophy.

Myofibrillar Myopathies: a Clinicopathological Study of 13 Cases

P 3

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Myofibrillar myopathies (MFM) are a group of neuromuscular disorders sharing common histological features. We report 13 patients from nine families with MFM. Eleven patients have adult onset of weakness between 40 to 59 years of age and most of them had lower limb weakness as initial presentation. Two paediatric patients had disease onset at 6 and 11 years old. One-third of the patients have cardiac complications. Four patients needed respiratory support eventually. All have progressive muscle weakness. In general, typical pathology of MFM was noted in all patients. The muscle fibres showed variation in size and shape, with eosinophilic inclusions noted. The numbers of fibre with inclusion varied from abundant to very scanty, requiring diligent search in some cases. Ultrastructural examination was done in all 13 cases. Disorganisation of myofilament was noted in general. The granulofilamentous and filamentous inclusions can be focally present and scanty. In one case with *FLNC* mutation, inclusions were not found in the specimen. Abnormal mitochondria with paracrystalline inclusions were seen in three cases, two with *FLNC* mutation. In five patients out of four families c.8129G>A (p.Trp2710*) was detected in *FLNC*, while in one patient c.626C>T (p.Pro209Leu) and c.772C>T (p.Arg258Trp) were detected in BAG3. In essence, MFM is a slowly progressive disease with onset mostly after 40 years old. However, paediatric age of onset is also possible. There is a spectrum of pathology in MFM, from subtle to full-blown histomorphological alterations. High index of suspicion is required for the pathological diagnosis. Mitochondrial abnormalities should alert the pathologist to consider the diagnosis of MFM. The missense variant c.8129G>A (p.Trp2710*) in *FLNC* appeared to be a recurrent mutation in the Hong Kong Chinese population.

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A Man with Orbitocranial Injury Resulting from Transorbital Chopstick Penetration

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Penetrating brain injury often results in significant morbidity and mortality. Sometimes it may only produce minimal neurological symptoms. We encountered a patient with self-inflicted orbitocranial injury and no neurological deficit was detected. A 56-year-old man was admitted for acute psychosis. He used plastic chopsticks to inflict injury to both of his eyes, resulting in marked periorbital swelling and bruises. There was bilateral subconjunctival haemorrhage, but the eyeballs were intact and the ocular movements were full. Urgent head computed tomographic (CT) scan showed two linear parallel hyperdense haemorrhagic contusions extending posterosuperiorly from bilateral inferior frontal lobes near orbital roofs to involve part of the caudate and lentiform nuclei, sparing the internal capsules. Reformatted images showed tiny defects in both orbital roofs, indicating fractures. No retained foreign body was detected. Psychotic symptoms resolved with treatment and there was no clinically detectable residual neurological deficit. This case illustrates that the apparent severity of cerebral trauma on CT scan may not actually correlate with patient's degree of neurological deficit.

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Sequential Patterned Repetitive Transcranial Magnetic Stimulation for Post-stroke Aphasia—Preliminary Analysis

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Background: Controlled trial of sequential patterned repetitive transcranial magnetic stimulation (theta burst stimulation, TBS) in post-stroke aphasia was scarce. We aimed to investigate the potential therapeutic effect of consecutive suppressive-facilitatory TBS on language outcome after stroke.
Methods: Overall, 21 right-handed aphasic stroke patients with left hemispheric infarction were allocated into three interventional groups: (1) continuous TBS (total, 600 pulses) over right hemisphere followed by intermittent TBS (total, 600 pulses) over left hemisphere, plus 30-minute conventional one-to-one speech therapy (group A: TBS + ST); (2) continuous TBS over right hemisphere followed by intermittent TBS over left hemisphere (group B: TBS only); or (3) 30-minute conventional one-to-one speech therapy (group C: ST only). The intervention was performed once a day. The Chinese version of Western Aphasia Battery was adopted to assess their language ability at baseline and after 10 sessions of intervention.
Results: Language ability was improved significantly in all three groups after intervention (P_a=0.028, P_b=0.005, P_c=0.043). No difference in treatment effects was found among three groups.
Conclusion: Sequential TBS individually is as effective as treatment by ST only and combining it with ST in Chinese post-stroke aphasic patients.

AUTHOR INDEX

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