**NUS-01 Chondroitinase ABC promotes axonal regeneration of Clarke’s neurons beyond the spinal cord injury scar**

Leung-Wah Yick1,2, Pik-To Cheung1, Kwok-Fai So1 and Wutian Wu1, 1Department of Anatomy and 2Department of Paediatrics, Faculty of Medicine, The University of Hong Kong, Hong Kong.

**Introduction:** We have previously shown that enzymatic digestion of chondroitin sulfate proteoglycan (CSPG) at the injury scar promotes the axonal regeneration of Clarke’s nucleus (CN) neurons into a peripheral nerve graft after spinal cord hemisection. The present study examined whether digestion of CSPG using chondroitinase ABC promoted the regeneration of CN neurons across the scar into the rostral spinal cord in neonatal and adult rats.

**Method:** Following hemisection of the spinal cord at T11, either vehicle or chondroitinase ABC was applied onto the lesion site. The postoperative survival periods were 2 and 4 weeks. Regenerating CN neurons were retrogradely labeled by Fluoro-Gold injection at spinal cord level C7.

**Results:** In the sham group, there was no regeneration of injured CN neurons in both neonatal and adult rats. Treatment with chondroitinase ABC in neonates resulted in 11.8% and 8.3% of the injured CN neurons regenerated into the rostral spinal cord, 2 and 4 weeks respectively. In adults, there were 9.4% and 12.3%, 2 and 4 weeks respectively, of the injured CN neurons regenerated their axons to the rostral spinal cord. After chondroitinase ABC treatment, the immunoreactivity for CSPG was dramatically decreased around the lesion site in both neonatal and adult animals.

**Conclusion:** Our results show that degradation of CSPG with chondroitinase ABC can promote the axonal regeneration in the spinal cord. These results further support the hypothesis that CSPG is inhibitory to the regeneration of neurons in the spinal cord after traumatic injury.

**Acknowledgement:** This work was supported by grants from the Hong Kong Research Grants Council and the University of Hong Kong.

**NUS-02 Early release of mitochondrial cytochrome c and the subsequent activation of caspase-3 are involved in the apoptotic death of neonatal motoneurons after injury**

Yuen-Man Chan1, Leung-Wah Yick1, Kwok-Fai So1, Ronald W. Oppenheim2 and Wutian Wu1, 1Department of Anatomy, Faculty of Medicine, The University of Hong Kong, Hong Kong and 2Department of Neurobiology and Anatomy and the Neuroscience Program, Wake Forest University School of Medicine, Winston-Salem, North Carolina 27157, USA.

**Introduction:** We examined the mode of spinal motoneuron (MN) cell death after peripheral nerve injury in neonatal rats.

**Method:** Following root avulsion at C7 spinal segment in neonatal day 1 rats, either PBS or caspase inhibitors was applied onto the lesioned area. The postoperative period was 1, 2, 4, 6, 18, 24 and 48 hours. The time course of apoptosis was assessed by using TUNEL, nuclear staining and expression of cytochrome c and active caspase-3.

**Results:** Apoptotic features were first recognized in degenerating MNs by 6 hours after root avulsion. This was confirmed by both TUNEL and nuclear staining. Cytochrome c was released from the mitochondria into the cytosol as early as 1 hour following the lesion. Cytochrome c was localized preferentially in a diffuse pattern 1 hour after root avulsion whereas near the plasma membrane in normal motoneurons. By 6 hours after the injury, the active form of caspase-3 was first visualized by immunohistochemistry. Treatment with a caspase inhibitor Ac-DEVD-CHO could not completely block the activation of caspase-3 and the release of cytochrome c, whereas the administration of a pan caspase inhibitor Boc-D-FMK delayed the release of cytochrome c for more than 48 hours. These results implied that besides caspase-3, other caspase family members should be taken into account.

**Conclusion:** Because the release of cytochrome c and the activation of caspases play crucial roles in the apoptotic pathway, these results suggest that the mechanism of spinal motoneuron death after root avulsion in developing animals is apoptotic. Accordingly, inhibition of caspases may be a potentially important mean for rescuing immature MNs from injury.

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NUS-03 Reducing calcium-mediated endoplasmic reticulum stress could attenuate beta-amyloid peptide neurotoxicity

Ka-Chun Suen, Jacques Hugon, Kwok-Fai So, Raymond Chuen-Chung Chang, Department of Anatomy, Faculty of Medicine, The University of Hong Kong

Introduction: Beta-amyloid peptide (Ab) has been proposed to play an important role in the pathogenesis of Alzheimer’s disease. Exposure of Abeta could trigger disturbance of cellular calcium homeostasis in cultured neurons. Calcium depletion in the endoplasmic reticulum (ER) is one of the major causes of calcium toxicity. Since Ab could trigger ER stress in neurons, we hypothesize that modulation of calcium-mediated ER stress could protect neurons from Abeta neurotoxicity.

Methods: Primary cultures of cortical neurons from 17-day-old embryos of Sprague-Dawley rats were set up. The neurons were pretreated with three ER calcium release modulators, 2-aminoethoxydiphenyl borate (2APB), Xestospongin C (XeC) or FK506 for 2 hours, followed by the treatment with Abeta. In order to assay their neuroprotective effects against Abeta, the release of lactate dehydrogenase, quantification of apoptotic nuclei stained with 4’,6’-diamidino-2-phenylindole (DAPI) and assessment of PARP cleavage were examined. Intracellular free calcium levels, expression of ER stress proteins and caspase-3 activity were also monitored so as to understand the mechanism underlying the neuroprotective effects of the three drugs.

Results and Conclusion: Our results showed that 2APB, XeC and FK506 significantly attenuated Abeta neurotoxicity. These drugs could reduce calcium depletion-induced ER stress and subsequent caspase-3 activation. Taken together, these results reveal that the modulation of ER calcium release may be a pharmacological target in future therapeutic approaches of Alzheimer’s disease.

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NUS-04 Delayed application of GDNF can decrease the NOS expression and rescue injured motor neurons in adult rat with C7 spinal root avulsion

LH Zhou, WT Wu, Department of Anatomy, University of Hong Kong, Hong Kong

Introduction: Our previous studies have shown that spinal motoneurons express neuronal NOS and then die following root avulsion injury. Expression of nNOS and death of spinal motoneurons due to root avulsion can be prevented if GDNF is applied intrathecally on the lesion site immediately after avulsion. It is unknown whether delayed treatment with GDNF could still prevent the death of motoneurons after root avulsion. This hypothesis is examined in the present study.

Method: At 2 weeks after avulsion of C7 spinal root, the laminectomy was made at the C-7 segment and a small piece of gelfoam pre-soaked in the solution of 2 microliters normal saline or GDNF at 10 microgram/microliter was placed in contact with C7 segment. At different surviving days, the nNOS expression rate and motor neuron survival rate were detected by NADPH-histochemistry and neutral red counter stain.

Results: NOS expression rate of the motor neurons was 36.46%, 56.49%, 32.73% or 15.13% at 2 weeks, 3 weeks, 4 weeks or 6 weeks after avulsion. With a single dose GDNF, started at 2 weeks after avulsion, the NOS expression rate was markedly reduced to 7.30%, 7.99% and 9.24% at 3 weeks, 4 weeks or 6 weeks. In lesion animals, the motor neuron survival rate was 85.95%, 80.5%, 59.66% or 36.32% at 2 weeks, 3 weeks, 4 weeks or 6 weeks after avulsion. But in lesion animals treated with GDNF, the survival rate was increased to 94.33%, 93.75% or 91.83% % at 3 weeks, 4 weeks or 6 weeks.

Conclusion: Our data show that during a 6 week process of neurodegeneration a single dose GDNF treatment, though delayed up to 2 weeks, can still inhibit the expression of nNOS and allow substantial rescue of injured motor neurons.
NUS-05 Diffusion tensor imaging in the evaluation of Wallerian degeneration in paediatric stroke: work-in-progress

LJ Zhou1, VCN Wong2, BHY Chung2, CGC Ooi2, RTF Cheung1, PL Khong1. Departments of Diagnostic Radiology1, Paediatrics2 and Medicine2, The University of Hong Kong, Queen Mary Hospital, Hong Kong

**Introduction:** Wallerian degeneration, the anterograde degeneration of axons and myelin sheaths after proximal axonal or cell body injury, is known to occur after cerebral infarction. In this pilot study, we aim to evaluate if diffusion tensor imaging (DTI), using the indices of fractional anisotropy (FA) and mean diffusivity (MD), can detect and quantify Wallerian degeneration in paediatric middle cerebral artery (MCA) strokes and to compare the findings with conventional MR imaging.

**Methods:** Nine children with unilateral MCA infarctions were studied. Axial T1-weighted, proton density and T2-weighted images, as well as DTI were performed using a Signa 1.5 Tesla imager. Quantitative values of FA and MD were obtained by manually placing regions-of-interest (ROI) in the infarction, and selected areas along the ipsilateral corticospinal tract, i.e. the posterior limb of the internal capsule (PLIC) and cerebral peduncle (CP). Identical ROIs were placed in the matched contralateral regions. The corticospinal tract FA was derived by the mean value of PLIC FA and CP FA. The presence of signal intensity changes in the internal capsule and cerebral peduncles on T2-weighted images were recorded. Statistical comparisons between two sides were performed using the Student’s t-test.

**Results:** WD was detected on conventional T2-weighted imaging by hyperintense signal in the PLIC in 4 children and CP in 1 child. The FA of the infarction, PLIC and CP were reduced, and the MD of the infarction and PLIC were increased on the ipsilateral side compared to the contralateral side in all children, whilst the MD of the CP was increased in six children. The mean FA ratio of the ipsilateral to the contralateral side in the infarction, PLIC, CP was 0.45, 0.77 and 0.79 respectively and the differences were statistically significant in all sites (p=0.029, p=0.014 and 0.008 respectively). The mean MD ratio of the ipsilateral to the contralateral side in the infarction was 2.55 and this difference was statistically significant (p<0.001). The differences in MD in the other sites were not statistically significant.

**Conclusion:** DTI is more sensitive than conventional MRI and can be used to detect and quantify WD. Further studies are required to determine if the measurement of FA in Wallerian degeneration can be used as an indicator of neuromotor outcome.

NUS-06 Diffusion tensor imaging for the evaluation of treatment-induced neurotoxicity in childhood medulloblastoma

PL Khong1, LHT Leung1, GCF Chan2, DLW Kwong1, LJ Zhou1, CGC Ooi1. Department of Diagnostic Radiology1, Paediatrics2 and Oncology3, The University of Hong Kong, Queen Mary Hospital, Hong Kong

**Introduction:** We propose the use of diffusion tensor MR imaging (DTI) to evaluate treatment-induced white matter (WM) injury in childhood medulloblastoma survivors and also aim to determine if fractional anisotropy (FA) can be used as an index for evaluation of treatment-induced neurotoxicity.

**Methods:** 13 medulloblastoma survivors who were treated with surgery, cranial irradiation and chemotherapy were evaluated. Conventional MR imaging and DTI were performed using a 1.5 Tesla imager. FA maps were generated using the FUNCTOOL software. Voxel-based comparison between the patient and control groups was performed with SPM99. Contrasts (1 –1) and (–1 1) were employed for the detection of positive and negative activations. FA of selected supratentorial WM sites (frontal periventricular WM, parietal periventricular WM and corona radiata) were also measured by placement of regions-of-interest (ROI). ROIs of similar size were placed on identical sites as far possible in the healthy age-matched controls. FA (sum of frontal and parietal WM and corona radiata FA) was compared with age at treatment, time interval after treatment and intellectual outcome (deterioration of school performance). Two-tailed paired t-test was used for detection of statistical significance.

**Results:** Patients were between 3 -17 yrs of age at treatment (mean: 8.2 yrs) and time-interval between treatment and MR imaging ranged between 1—11 yrs (mean: 3.7 yrs). Voxel-based comparison showed areas of activation in the periventricular WM, especially parietal WM, and corona radiata. Using ROIs, mean FA of patients was reduced in all sites compared to controls, with a reduction of between 15.6% and 19.2%. The reduction was statistically significant in the parietal WM and corona radiata (p=0.011 and p=0.040 respectively) FA reduction of the groups £ 5 years (n=5) and > 5 years of age (n=8) at treatment was 61.1% and 34.8% respectively and FA reduction in the group with < 5 years (n=8) and ≥ 5 years interval (n=5) since treatment was 35.4% and 60.3% respectively. These differences were however, not statistically significant. Comparing school performance, FA reduction of those with mild deterioration (n=5) and those with moderate/severe deterioration (n=8) was 19.9% and 60.6 % respectively and this difference was statistically significant (p=0.041).

**Conclusion:** Loss of anisotropy occurs in the periventricular white matter of post-treatment medulloblastoma survivors and this loss is significantly greater in those with poor intellectual outcome. DTI is therefore useful in detection and monitoring of treatment-induced neurotoxicity.
**NUS-07 Postictal psychosis related lateral temporal hyperperfusion**

GCY Fong, §WY Ho, *TH Tsoi, KY Fong, SL Ho. Division of Neurology, University Department of Medicine, The University of Hong Kong, § Nuclear Medicine Unit, Queen Mary Hospital, Hong Kong and *Department of Medicine, Pamela Youde Nethersole Hospital, Hong Kong.

**Introduction:** Postictal psychosis is a rare complication of epileptic seizure characterized by reversible psychotic symptoms after flurries of seizure attack. It was attributed to a phenomenon similar to Todd’s paralysis without definite proof. We hypothesis regional hyperperfusion cerebral SPECT defect is associated with postictal psychosis complicating epileptic seizure. Two years ago, we reported our preliminary data of 99mTc-HMP AO cerebral SPECT findings in two patients with PIP. This study is an extension of our previous work.

**Methods:** We prospectively recruited patients with postictal psychosis and performed 99mTc-HMP AO SPECT scan during PIP. Intercital scans were performed at least 4 weeks apart from the PIP and taking off from anti-psychotic medications, if any. No specific treatment, other than simple analgesic, was prescribed for HA during the study period.

**Results:** HA comorbidity was found in 157 patients with EP. Among which, 61 of them could not achieve a seizure free state after a 12 months period. In contrast, only 68 of 315 epileptic patients without HA comorbidity failed to achieve a seizure free state. (p< 0.000, Odd ratio = 2.308, 95% Confidence interval 1.519 – 3.507).

**Conclusions:** Headache is a common co-morbidity for patients with epilepsy and associates with a poor seizure control state. This indicates that monitoring headache comorbidity of patients with epilepsy is equally important. Further study is needed to determine if modification of headache comorbidity could improve seizure control.

**Acknowledgment:** This study was supported, in part, by University Department Medicine research grants from University Department Medicine, The University of Hong Kong (to GCYF).
A large Chinese kindred with familial ALS without SOD1 mutation

**Introduction:** Amyotrophic lateral sclerosis (ALS) is a lethal neurodegenerative disorder with progressive muscle weakness and wasting. About 10% of familial ALS (FALS) cases have SOD1 mutations.

**Methods:** We ascertained a large Chinese kindred with autosomal dominant FALS. All consented family members underwent detailed clinical, electrophysiological and, if indicated, pathological examination.

**Result:** A total of 16 members (12 living) were classified as affected. Eighteen living (eight affected and ten unaffected) members were available for study. Historical review of the clinical features, and clinical, electrophysiological and pathological assessments showed a phenotypic spectrum in this family, from typical ALS (N=8), who rapidly deteriorated with progressive muscle wasting, weakness and respiratory failure to a group (N=8) with very slowly progressive predominantly lower motor neuron lesion. The clinical features of a member from each group appear to lie between the two ends of this spectrum. Mutation screening for SOD1 mutation were all negative in all 5 exons.

**Conclusion:** The interesting phenotypic spectrum observed in this family is distinctive although similar FALS families with heterogenous phenotypes were reported within the same pedigree. Further studies to identify the causative gene/s in this ALS kindred are indicated.

**Acknowledgment:** This study was supported, in part, by Liu Po Shan/Dr Vincent Liu Endowment Fund for Motor Neurone Disease, Faculty of Medicine, The University of Hong Kong (to GCYF/SLH).

A prevalence study of epilepsy in HKSAR, China

**Introduction:** Epilepsy is a common disorder. Epidemiological data is crucial for physicians and health care administrators for taking care patients with epilepsy. In this communication, we report the the epidemiology data of the Hong Kong West (HKW) region of Hong Kong Special Administrative Region (HKSAR).

**Methods:** With the implementation of clustering system in our clinic since 1996, the epilepsy clinic of Queen Mary Hospital is managing a vast majority of adult patients (> 15 years old) with chronic seizure disorders resided in the HKW region where hosted an adult population of 475,900. Seven hundred and thirty-six patients [female 42.9%, male 57.1%, mean 40.8, SD 13.6] with epilepsy were recruited. All patients underwent EEG examination and each subject was independently assessed by two epileptologists for diagnosis and classified according to ILAE recommendations.

**Results:** The prevalence rate of active epilepsy at or above 15 years of age was 1.54 in 1,000 at the prevalent date (January 1, 2002). 285 (38.8%) had idiopathic epilepsy syndromes, 100 (13.6%) had cryptogenic, and 285 (38.8%) had a remote symptomatic etiology. Seizure type was partial in 408 patients (55.4%) and generalized in 285 (38.8%). Thirty-one patients (4.2%) had positive family history. Interestingly, common idiopathic generalized epilepsy syndromes like juvenile myoclonic epilepsy (0.68%) and childhood absence epilepsy (0.95%) were uncommonly encountered.

**Conclusions:** In summary, this clinic based epidemiological study provides crucial data for epilepsy service development and research in HKSAR. Further hospital based or, preferably, door-to-door population based epidemiological study is indicated to ascertain the population based epidemiologic data for epilepsy with patients resided in HKW of HKSAR.

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**NUS-11 Gene mapping of familial amyotrophic lateral sclerosis**

GCY Fong*, TS Cheng*, PWL Ho*,, ATC Chan†, W Mak*, CM Cheung‡, CC Mok*, KH Chan*, KL Tsang*, MHW Kung*, LSW Li†, TH Tsol†, DB Ramaden†, RTF Cheung‡, SL Ho‡. *Division of Neurology, University Department of Medicine, The University of Hong Kong, Queen Mary Hospital; †Liu Po Shan Memorial Unit (for Motor Neurone Disease), Tung Wah Hospital; ‡Computer Center, The University of Hong Kong; §Department of Medicine, Pamela Youde Nethersole Hospital; †Department of Medicine and Geriatrics, Tuen Mun Hospital, Hong Kong; ‡Department of Medicine, University of Birmingham, Birmingham, United Kingdom.

**Introduction:** Amyotrophic lateral sclerosis (ALS) is a lethal neurodegenerative disorder characterized by gradual death of motor neurons in cerebral cortex, brain stem, and spinal cord. The pathogenetic mechanism remains unclear for the vast majority of cases. About 10% of ALS cases are familial (FALS). Cu/Zn superoxide dismutase (SOD1) gene accounts for about 10% of autosomal dominant FALS and the gene(s) responsible for the rest of ALS/FALS remain(s) to be found.

**Method:** We recruited a large Chinese kindred without SOD1 mutation for linkage analysis. Peripheral blood samples were collected and DNA were extracted from peripheral lymphocyte. We screened the family with ~ 400 polymorphic microsatellite markers. The genotyping data were subjected to model-based and model-free linkage analysis.

**Result:** Using MLINK of LINKAGE (Ver 5.2) package, we found a maximum LOD score of 4.357, ?[m=f]=0.0 at a microsatellite marker located at distal long arm of chromosome 8. Multipoint analysis by GENEHUNTER (Ver 1.2) revealed a maximum multipoint LOD score of 3.909 and NPL score 9.209. Haplotype analyses revealed a critical region which spanned 10.18-cM on chromosome 8.

**Conclusion:** We identified a 10.18-cM critical FALS region on chromosome 8. Further analyses using positional cloning and candidate gene approach are indicated to delineate the underlying genetic defect for FALS in this family.

**Acknowledgment:** This study was supported by Liu Po Shan/Dr Vincent Liu Endowment Fund for Motor Neurone Disease, Faculty of Medicine, The University of Hong Kong (to GCYF/SLH), by the University Department Medicine, The University of Hong Kong (to GCYF and TS Cheng), and by the Neurology Donation Fund.

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**NUS-12 Magnetic resonance imaging and diffusion tensor imaging in Chinese neonates with hypoxic ischemic encephalopathy**

G Li†, RTF Cheung‡ & ES Yang‡. *Division of Neurology, University Department of Medicine and ‡The Jockey Club MRI Engineering Centre, The University of Hong Kong, Hong Kong.

**Introduction:** Several studies have suggested the potential utility of diffusion tensor imaging (DTI) in the evaluation of brain injury in the asphyxiated neonates.

**Method:** We present our initial experience with DTI in Chinese neonates (gestational age 37 to 41 weeks, age 1 to 9 days of which there were 3 females) who were diagnosed as having hypoxic injury on clinical examination and the severity of the insult was graded using Apgar scores and Sarnat staging. Magnetic resonance imaging (MRI) with DTI was performed in eighteen neonates (eight with hypoxic ischemic encephalopathy [HIE] and ten with no cerebral pathology). The specific areas of interest were chosen in selected white matter (WM) areas: the posterior limb of the internal capsule, frontal WM, occipital WM, central WM, and temporal WM. The apparent/average diffusion coefficient (AADC) and relative anisotropy (RA) were compared between neonates with HIE and those without cerebral pathology using One-Way ANOVA.

**Results:** Abnormality on MRI was noticed in 3 of 8 neonates with HIE of different clinical stages. One neonate in Sarnat stage I and Apgar score of 10 showed periventricular changes as the MRI abnormality. Of the 2 neonates in Sarnat stage II and Apgar score of 3, one had periventricular changes and another showed thalamic abnormality. In contrast, DTI abnormality was noticed in all 8 neonates. A marked decrease of the AADC values was found in the posterior limb of the internal capsule, frontal WM and occipital WM in neonates with HIE. In addition, the RA values were marked reduced in HIE-affected neonates over the frontal WM and occipital WM.

**Conclusion:** The lower AADC in the capsule indicates active myelination and the presence of myelin, while the lower RA in the cerebral WM (e.g. frontal WM and occipital WM) over the site of injury indicates reduced directionality of diffusion in these brain areas and suggests that central fiber tracts have been destroyed or their subsequent development would be impaired. Based on our initial experience, we conclude that the DTI is potentially useful in understanding the basis of the neurologic deficits and DTI has a better correlation with the Sarnat staging and Apgar scores than MR imaging.
The fractional anisotropy of cerebral gliomas on diffusion tensor magnetic resonance imaging

G Li1,2, RTF Cheung1 & ES Yang2. 1Division of Neurology, University Department of Medicine and 2The Jockey Club MRI Engineering Centre, The University of Hong Kong, Hong Kong

Introduction: Unlike conventional diffusion-weighted magnetic resonance imaging (MRI), diffusion-tensor imaging (DTI) permits the calculation of an apparent average diffusion constant (AADC) and fractional anisotropy (FA). DTI characterizes diffusive transport of water and provides additional structural information of the brain tissue. Several studies have described the DTI abnormalities of brain tumors, including an increase in AADC within the tumoral tissue and a decrease in FA within and around the tumor.

Method: We used DTI to describe deviation or distortion of fibers in normal white matter (WM), tumoral WM, peritumoral WM and WM adjacent to the brain tumor in a cohort of ten patients with confirmed cerebral gliomas. MRI scanning was performed using a 1.5 T GE Signa system with version 9.1 software. The FA from the specific areas on the side of brain tumor was compared to that of the corresponding WMs over the contralateral hemiphere using student’s t test and compared among the specific areas using one way ANOVA

Results: The median age was 53 years old, and there were 5 females. The FA was reduced in the tumoral and peritumoral brain tissue (P<0.001). The abnormal FA in the tumor was much lower than that in peritumoral brain tissue (p<0.001). In the apparently distorted WM adjacent to the tumor, there were no difference in the FA between the two sides.

Conclusion: DTI maps may provide useful information about WM architecture and its alteration due to the tumors. FA provided details of anatomic information on relationships between tumors and nearby WM tracts, which may assist the interpretation of neurological findings and preoperative planning.

Visual cortical activations on functional magnetic resonance imaging upon stimulation of vision-implicated acupoints

G Li1,2, RTF Cheung2 & ES Yang1. 1The Jockey Club MRI Engineering Centre and 2Division of Neurology, University Department of Medicine, The University of Hong Kong, Hong Kong

Introduction: Cho and colleagues previously reported very close correlations between the visual cortical activations on functional magnetic resonance imaging (fMRI) following stimulation with visual light and those following conventional acupuncture.

Method: In this study, we compared the brain activations on fMRI obtained during visual stimulation using light-emitting diodes (LED) flashing at 8 Hz with that obtained during conventional or electro- acupuncture (at 2 or 20 Hz) applied to 4 vision-related acupoints (BL60, BL65, BL55, and BL67) over the lateral aspect of the right foot in 18 healthy volunteers. fMRI was performed using a 1.5 T magnetic resonance scanner with standard scanning parameters. Activation periods of 30 s were alternated with rest periods of 30 s. First, fMRI was performed with visual stimulation. Next, fMRI was repeated with conventional and then electro- acupuncture.

Results: When compared to positive activations on fMRI over the visual cortex upon LED stimulation, similar activations were seen in 10 subjects during conventional acupuncture and in 8 and 7 subjects, respectively, during electro-acupuncture at 2 and 20 Hz. Negative activations were also seen bilaterally in the occipital lobes and temporal gyri in 13 subjects during conventional acupuncture.

Conclusion: Acupuncture may exert its effects via modulating the activity of relevant brain sites. Our results also show that electro-acupuncture is useful for future studies.
A functional magnetic resonance imaging study comparing brain activations during language task with activations during electrical stimulation of language-implicated acupoints

G Li1,2, RTF Cheung2 & ES Yang1. 1The Jockey Club MRI Engineering Centre and 2Division of Neurology, University Department of Medicine, The University of Hong Kong, Hong Kong

Introduction: Functional magnetic resonance imaging (fMRI) can visualize brain activations during various task states. Acupuncture may mediate its effects via modulation of brain activities.

Method: We compared the brain activations on fMRI during a word generation task with the activations during electrical stimulation of two language-implicated acupoints in 17 healthy Mandarin-speaking male Chinese volunteers aged between 19 and 26 years. All subjects were strongly right handed according to a handedness inventory.

Results: Using a standard fMRI protocol and a word generation paradigm, significant activation was seen in the left and right inferior frontal gyri (Brodmann’s area [BA] 44, 45) as well as the left superior temporal gyrus (BA 22, 42). Stronger activation with a larger volume was seen in the left hemisphere. Bipolar electrical stimulation of the language-implicated acupoints, SJ8 (11 subjects) or DU15 (6 subjects), without the word generation paradigm in the same cohort produced significant activation in the right inferior frontal gyrus (BA 44, 46) and in the left and right superior temporal gyrus (BA 22, 42), respectively. In contrast, bipolar electrical stimulation of the adjacent non-acupoints failed to produce any significant brain activation.

Conclusion: Ability of acupuncture over SJ8 or DU15 in selective activation of the language-implicated cortical sites may be related to the benefit of acupuncture on SJ8 or DU15 in language disorders. Nevertheless, stimulation of SJ8 or DU15 failed to activate the main cortical sites for language (left BAs 44, 45, 46); only subsidiary language areas are activated.

Implications of hydrocephalus upon presentation of tuberculous meningitis

K H Chan, RTF Cheung, W Mak, CY Fong, KL Tsang, SL Ho. Division of Neurology, University Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong.

Introduction: Tuberculous meningitis (TBM) is a serious disorder and hydrocephalus is a known complication of TBM that may occur early or late. The clinical implications of hydrocephalus upon initial presentation of TBM are uncertain.

Methods: From January 1997 to September 2001, adults patients diagnosed as TBM in our hospital were studied. Patients referred from other centers for management of hydrocephalus with TBM were excluded. Patients with hydrocephalus on initial or subsequent CT scans were assessed by surgeon and operated if necessary. A standardized regime of anti-TB therapy guided treatment. Patients were followed up regularly for at least 1 year after commencement of anti-TB drugs. A modified Barthel index of 12 or less at 1 year after treatment and mortality were criteria for poor prognosis. Clinical, radiological, microbiological data were analyzed.

Results: A total of 31 patients had TBM diagnosed during the study period. Nine of the 31 had hydrocephalus on CT scan upon presentation, and 8 of the 9 required urgent neurosurgical intervention. Of the 22 patients without hydrocephalus on presentation, only 1 developed hydrocephalus subsequently. Age, sex, duration of presenting symptoms and CSF parameters were indifferent between patients with or without hydrocephalus on presentation. Unsteady gait and ataxia (p=0.001) were more common in patients with hydrocephalus. Despite having similar Glasgow coma scale on presentation (p=0.838) , patients with hydrocephalus on presentation were more likely to develop into stage 2 or 3 disease (p=0.045) and more likely to develop complicating strokes (p=0.012) due to cerebral infaracts (p=0.007), with poorer prognosis compared with patients without hydrocephalus on presentation (p=0.004).

Conclusion: Hydrocephalus upon presentation is common in local TBM patients (29%). This is unrelated to late diagnosis or delayed presentation, suggesting possible abrupt intense inflammatory response to MTB. It seems to be a marker of severe TBM with high risk factor complicating cerebral infaracts associated with poorer prognosis. TBM must be considered for patients who present with hydrocephalus.


**NUS-17 Seronegative myasthenia gravis in Hong Kong Chinese**

K H Chan, KL Tsang, W Mak, CY Fong, TS Cheng, RTF Cheung, SL Ho. University Department of Medicine, The University of Hong Kong, Queen Mary Hospital, Hong Kong.

**Introduction:** Acquired myasthenia gravis (MG) is an autoimmune disease due to anti-acetylcholine receptor antibodies (anti-AChR) that damage nicotinic acetylcholine receptors on neuromuscular junctions. Variable proportions of generalized MG patients were reported to have undetectable serum anti-AChR level, designated as seronegative MG (SNMG) but without clear definitions of SNMG. One group reported that antibodies against muscle-specific kinase was the pathogenetic basis of SNMG. The exact pathogenesis of SNMG is not yet certain and genuine frequency is unknown.

**Methods:** Patients with MG in neurology clinic were studied with clinical, radiological, serological, electrophysiological and histological data reviewed. Patients with initial negative anti-AChR had the assay repeated at least 12 months apart from the first one, together with anti-striational antibody test. Patients with family history of MG had EMG results repeated in details to exclude congenital MG. Patients with repeatedly negative anti-AChR binding assays had serum tested for anti-AChR modulating antibodies (a bioassay using cultured muscle cells) and P/Q type calcium channel antibodies to look for Lambert-Eaton myasthenic syndrome. Only patients with repeatedly negative anti-AChR binding and anti-striational antibodies, negative for anti-AChR modulating and calcium channel antibodies, and with congenital MG excluded were defined as SNMG.

**Results:** A total 52 MG patients were studied, 21 had pure ocular MG and 31 had generalized MG. Three had turned seropositive upon repeated assay and 1 had positive test for modulating antibodies only. One patient with family history had congenital MG upon detailed EMG. Only 2 of the 31 generalized MG patients (6.5%) were SNMG. One of the 2 generalized SNMG patient had thymic hyperplasia. No SNMG patients had thymoma. SNMG is more common in pure ocular MG patients.

**Conclusion:** Generalized SNMG is rare. Strigent criteria are required for diagnosis of SNMG. Thymic hyperplasia, but not thymoma, can occur in SNMG. We postulate that a subgroup of SNMG patients may have low titer of high affinity anti-AChR undetectable by current assays.

**NUS-18 An epidemiological study of motor neuron disease in Hong Kong**

TS Cheng, GCY Fong, W Mak, KH Chan, RTF Cheung, SL Ho. Division of Neurology, Department of Medicine, University of Hong Kong, Queen Mary Hospital, Hong Kong

**Background:** In a previous epidemiological study conducted in 1990s, the incidence and prevalence of motor neuron disease (MND) in Hong Kong Chinese were found to be low compared to the worldwide figures. Moreover, the incidence of MND had been reported to increase steadily over the last few decades in other parts of the world. In this communication, we reported our epidemiological data of MND in the Hong Kong West region of Hong Kong Special Administrative Region of China and compared the results with that of the previous study.

**Method:** We identified the subjects from the Hospital Authority Database by searching the admission records of Queen Mary Hospital, between 1997 and 2001, using ICD-9 codes of 335. Each retrieved case record was reviewed independently by at least two neurologists. The clinical diagnosis and classification of MND were based on the revised El Escorial criteria.

**Results:** Of 50 identified subjects, 27 subjects were recruited in the present study. Among which, 22 (81%) were definite MND and 5 (19%) were probable MND. Among definite MND, 15 (68%) were limb onset. The male to female ratio was 2.8:1. All subjects were Chinese. The number of new cases from 1997 to 2001 was 22. Thirteen cases were died in this period, and 14 patients were surviving as of December 31, 2001. Therefore, the annual incidence was 4.4 with an incidence rate of 0.77/100,000/year, the point prevalence at December 31, 2001, was 2.4/100,000, the average annual mortality was 2.6, and the mortality rate was 0.46/100,000/year. The mean survival time was 27.1 months (range: 7 to 65 months, SD 17.9). The mean age of onset was 51.5 years (range: 30 to 77 years, SD 11.7), with a peak observed between 55 and 59 years. Eleven cases (40%) had their disease-onset before 50 years of age.

**Conclusion:** In this study, the incidence and prevalence of MND among Hong Kong Chinese remained low compared with the worldwide figures. However, comparing to the previous epidemiological data of MND collected between 1989 and 1992, we noticed a trend of increase in the overall incidence (148%) as well as prevalence (152%) over the last decade. Moreover, the incidence of MND among the younger age group was also increased. Our data warrant a territory wide epidemiological study to document the changes in MND epidemiology in Hong Kong over the last decade.

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**NUS-19 A study of hemiplegic shoulder pain at Tung Wah Hospital**

TK Kwok, L Li, KP Leung. Rehabilitation Unit, University of Hong Kong, Tung Wah Hospital, Hong Kong

**Introduction:** Hemiplegic shoulder pain was reported in 30-40% of stroke patients in Western literature and found to be more common during the spastic phase of motor recovery. It is our impression that the incidence of hemiplegic shoulder pain in Hong Kong is not as high. This study aims to investigate the incidence, diagnosis and association factors of shoulder pain in stroke survivors at Tung Wah Hospital, one of the regional rehabilitation centre of the Hong Kong West cluster.

**Method:** Retrospective case note review of all 114 stroke patients who were admitted into Tung Wah Hospital Stroke Rehabilitation Unit from March to June 2002. Hospital notes were meticulously scrutinised including prescription details for any consumption of analgesics and all records of the doctors, nurses, physiotherapists and occupational therapists.

**Results:** As on September 30, 2002, all patients were followed for at least 3 months. Nine of 114 of patients were found to have hemiplegic shoulder pain giving an incidence of 7.8%. The occurrence of shoulder pain was not significantly related to the motor power or muscle tone of the hemiplegic arm. There were also no relations with age/sex of patients; the type/side of strokes and other medical comorbidities. Causes of shoulder pain were mainly adhesive capsulitis, impingement syndrome, biceps tendinitis and glenohumeral subluxation. Most shoulder problems responded to simple analgesics and physical modalities.

**Conclusion:** The incidence of hemiplegic shoulder pain is rather low as compared with that reported in other Western countries but the pattern of shoulder problems is quite similar. We postulated that the low incidence of shoulder pain could be related to our active prevention programme during rehabilitation through staff, patient and caregiver training and education on proper positioning and handling of the hemiplegic arm. Furthermore, the Chinese culture, which usually values a higher pain tolerance, may be another contributing factor.

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**NUS-20 Reduced susceptibility to ischaemic brain damage following photochemical stroke in transgenic mice overexpressing the amyloid precursor protein**

LY Zou¹, F Tang² & RTF Cheung¹. ¹Division of Neurology, University Department of Medicine and ²Department of Physiology, University of Hong Kong, Hong Kong

**Introduction:** Amyloid precursor protein (APP) is the source of beta-amyloid, the principal component of amyloid plaques in the brain of Alzheimer’s disease. Mice overexpressing APP have an increased vulnerability to brain ischaemia induced by endovascular middle cerebral artery occlusion. In this study, we investigate the role of APP in ischaemic brain damage due to photochemically induced thrombosis of cortical microvessels in transgenic mice overexpressing APP. Non-transgenic mice were used as a control group.

**Method:** The brains of transgenic mice overexpressing APP and non-transgenic mice were illuminated with a cold light source through the intact skull for 15 min or 3 min at 1 min following an injection of 0.1 mL or 0.04 mL of Rose Bengal respectively. Infarct volume was assessed 48 hours later from the triphenyltetrazolium chloride-stained brain slices.

**Results:** The relative infarct volume in the transgenic mice and non-transgenic mice following 15 min of photochemically induced thrombosis was 7.87±1.25% (mean±S.E.M.; n=3) and 14.47±4.16% (n=4), respectively. Thus, the infarct volume in the transgenic mice was reduced by 45.6% (P<0.05). The relative infarct volume in the transgenic mice and non-transgenic mice following 3 min of photochemically induced thrombosis was 1.53±1.36% (n=3) and 3.48±0.64% (n=4), respectively. Thus, the infarct volume in the transgenic mice was reduced by 56.0% (P=0.05).

**Conclusion:** We conclude that the mice brain overexpressing APP is less susceptible to ischaemic damage due to photothrombosis of cortical microvessels. Our results are different from the reported findings when focal ischaemia was induced by endovascular middle cerebral artery occlusion.
**NUS-21 Clinical features and risk factors of cognitive impairment after stroke in Hong Kong Chinese**

LY Zou¹, LSW Li² & RTF Cheung¹. ¹Division of Neurology, University Department of Medicine, The University of Hong Kong and ²Department of Medicine, Tung Wah Hospital, Hong Kong

**Introduction:** Stroke is recognized as an important cause of dementia. The goal of the present study is to examine a series of clinical features and risk factors of cognitive impairment after stroke.

**Method:** A standard protocol was applied to 185 consecutive unselected stroke patients within two weeks after onset of their strokes. Demographic and clinical data were collected. Barthel Index was used to assess the activities of daily living and Mini Mental Status Examination (MMSE) was used to assess the cognitive function. The cutoffs on MMSE score for cognitive impairment were selected according to Crum’s criteria and the education level.

**Results:** Seventy-seven stroke patients (41.6%) had cognitive impairment or worse. Cognitive impairment was unrelated to age, gender, marital status, handedness, type of stroke (ischaemic/haemorrhagic), side of the lesion, location of stroke, smoking habit, drinking habit, diabetes mellitus, and hyperlipidaemia. Low education level, low Barthel Index and hypertension were the independent predictors of cognitive impairment in logistic regression analysis (P<0.05).

**Conclusion:** The local incidence of cognitive impairment after stroke is high. Education level, functional impairment and hypertension may increase the risk of cognitive impairment after stroke.

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**NUS-22 Research strategies in molecular signaling of neuronal apoptosis in Alzheimer’s disease**

Raymond Chuen-Chung CHANG, Ka-Chun Suen, Man-Shan Yu, Jacques Hugon
Department of Anatomy, Faculty of Medicine, The University of Hong Kong

**Introduction:** Neuronal loss is a key issue in the pathogenesis of Alzheimer’s disease (AD). It is evident that neuronal apoptosis is one mode of neurodegeneration. Among all the factors leading to neuronal apoptosis, β-amyloid peptides (β-APP) are the most important toxin in AD pathogenesis. Therefore, the molecular signaling events of neuronal apoptosis receive much attention in AD research.

**Methods:** Different cell culture models were employed to prove the involvement of a particular protein kinase in β-APP neurotoxicity. To verify the involvement of a protein kinase, both the phosphorylation of the kinase and its substrate had to be examined. Having done these experiments, the next step was to elucidate how significance of a kinase in β-APP neurotoxicity by using molecular biology technique to transfect neurons over-expressing wild-type or negatively mutated kinase. Furthermore, neurons from knockout and the wild-type mice were used to prove the findings from genetically manipulated neurons. Apart from these experiments, investigation of whether the kinase involved in real clinical case was another important strategy to show the significance of the kinase in the pathogenesis of AD. Afterwards, it is also essential to show how a particular kinase incorporates into other well-known apoptotic pathways.

**Results and Conclusion:** By using these strategies, we have demonstrated that a novel double-stranded RNA-dependent protein kinase (PKR) is significantly involved in β-APP-induced neuronal apoptosis. It also plays significant roles in the pathogenesis of AD.

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**NUS-23** A longitudinal study on functional decline and health services utilisation in fallers and recurrent fallers in community dwelling Chinese older adults in Hong Kong

LW Chu¹, A Chi¹, I Chi²
¹Division of Geriatrics, University Department of Medicine, Queen Mary Hospital, the University of Hong Kong,
²Department of Physiotherapy, Queen Mary Hospital
³Sau Po Centre on Ageing, the University of Hong Kong, 102 Pokfulam Road.

**Introduction**: Falls and fall-related injuries commonly led to functional decline, disability and increased hospitalizations or other health care services utilization. There was no local data on the functional impact and health services utilization in fallers for Chinese elderly people in Hong Kong. This study investigated the functional decline and health services utilization for fallers in community dwelling Chinese elderly in Hong Kong.

**Method**: A population based elderly sample (age 65 years or over) of 1517 subjects were recruited in 1998. Baseline face-to-face interviews and direct clinical and functional assessment were performed for this cohort. Falls were monitored 2-monthly for one year. Re-assessment of their physical function was performed one year later. Data on the utilization of health care services were also documented for one year.

**Results**: 401 falls occurred over 1 year. The prevalence of falls, single fallers and recurrent fallers were 26.4%, 19.4% and 4.75% respectively. Injuries occurred in 76.6%. Fallers experienced a greater decrease in Barthel Index for basic activities of Daily Living, Instrumental Activities of Daily Living, gait speed and Total Mobility Score. Recurrent fallers experienced the largest degree of decline in all the four functional measures. 216 subjects (14.8%) had been hospitalized. Fallers, recurrent fallers, had greater numbers of visits in clinics, visits at the Accident and Emergency Department and hospitalizations. Based on the current public health care cost data, elderly fallers would consume approximately HK$552 millions more than non-fallers per year for the whole of Hong Kong.

**Conclusion**: Elderly fallers experienced greater declines in their functional ability and utilized much more health care services than the non-fallers in Hong Kong. Interventions which could reduce falls in our elderly would reduce their functional decline as well as saving the health care dollars.

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**NUS-24** Screening tests for Alzheimer’s disease: a comparison of four short tests in the Hong Kong Chinese

LW Chu¹, CP Chung¹, W Mok¹, SL Hui¹, P Lee², ‘Division of Geriatrics, University Department of Medicine, Queen Mary Hospital, the University of Hong Kong; *Clinical Psychology Unit, Queen Mary Hospital and Department of Psychiatry, the University of Hong Kong

**Introduction**: The prevalence of dementia was 6.1% and was predicted to increase significantly with population ageing in Hong Kong. With the availability of symptomatic treatments for Alzheimer’s disease, the current challenge is to find tools to identify patients who had Alzheimer’s disease in the early stage. This study investigated the values of the Delayed Word Recall Test, Mini-Mental Status Examination, Abbreviated Mental Test and Alzheimer’s Disease Assessment Scale - cognitive subscale to discriminate between elderly persons with Alzheimer’s disease and cognitively normal elderly persons in the Hong Kong Chinese.

**Method**: Chinese elderly subjects with Alzheimer’s disease (AD) were recruited from the Queen Mary Hospital Memory Clinic. Cognitively normal elderly persons were recruited from community elderly centres. Every subject underwent a detailed assessment protocol including a detailed history, physical examination and neuropsychological tests as well as the four tests in this study (i.e. Delayed Word Recall Test, the Mini-Mental Status Examination, the Abbreviated Mental Test and the Alzheimer’s disease Assessment Scale-cognitive subscale). These four tests all had Chinese Cantonese versions. The Mini-Mental Status Examination (MMSE), Abbreviated Mental Test (AMT) and Alzheimer’s disease Assessment Scale-cognitive subscale (ADAS-cog) had all been validated previously in Hong Kong. The diagnosis of AD was based on the NINCDS-ADRDA criteria (i.e. probable Alzheimer’s disease). The tests’ scores were analysed by the Receiver Operating Characteristic (ROC) curves. The Area under the Curve (AUC) was computed for each test. The sensitivity, specificity, positive and negative predictive values would be compared using the cut-off criteria derived from the ROC curve analysis.

**Results**: 150 subjects were recruited from Feb. 2001 to Oct. 2002. 52 were AD and 98 were cognitively normal subjects. The cut-off scores for AD were ≤ 8, ≤ 22, ≤ 2 and >13 for AMT, MMSE, DWRT and ADAS-cog respectively. From the AUC analyses, the Delayed Word Recall Test (DWRT) had the best discriminative power (AUC=0.99) among the four tests with a sensitivity of 94%, specificity of 100%, positive and negative predictive values of 100% and 99.6% respectively.

**Conclusion**: The Delayed Word Recall Test is a good screening test with very high sensitivity, specificity, positive and negative predictive values, which is suitable for use in the early detection of Alzheimer’s disease.

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NUS-25 The role of nitric oxide on regeneration of paraventricular nucleus and supraoptic nucleus following hypophysectomy

Q. J. Yuan, W. Wu., K-F, So
Department of Anatomy, Faculty of Medicine, The University of Hong Kong

Introduction: The mammalian neurohypophyseal system exhibits a high degree of structural plasticity and recovery of neuroendocrine function following a broad array of physiological and anatomical manipulations. This study investigates the role of nitric oxide (NO) on neuronal regeneration of paraventricular nucleus (PVN) and supraoptic nucleus (SON) in developing and adult rats.

Methods: NOS expression and neural regeneration on the floor of the third ventricular were detected by using nitric oxide synthase (NOS) histochemistry and scanning electronic microscope (SEM).

Results: Preliminary results have shown that the role of nitric oxide on regeneration of PVN and SON in developing rats seems different from that in the adult. Instead of that the process of regeneration is invariably accompanied by the up-regulation of NOS in the adult, there was no significant increase of NOS activity in SON and PVN neuronal perikarya and neurites in the adjacent median eminence in PN 7, PN 14 and PN 21 rats following hypophysectomy. Despite the fact, large complexes of apparent neurites remained upon the floor of the third cerebral ventricle by SEM in PN 7, PN 14, PN 21 rats by 4 weeks posthypophysectomy as in the adult. It has been also demonstrated that neural regeneration is more robust in the adult than in developing rats by SEM. Most interestingly, we found that the entire process of neurohypophyseal temporary introduction of the antagonist of NOS, L-NAME at 25 or 50 mg/kg per day for ten days immediately after surgery, which is nearly similar in the adult rats those received continuous administration of the NOS inhibitor for 4 weeks after hypophysectomy.

Conclusions: This data suggests that NO is a critical initiator for the process of regeneration and regrowth of magnocellular (SON/PVN) axons into the median eminence regeneration in the adult. Our further study aims at investigating the mechanisms.

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