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## KEYNOTE SESSION

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### Mild Cognitive Impairment: an Epidemiological Perspective

**K1****R.C. Petersen***Alzheimer's Disease Research Center, Mayo Clinic College of Medicine  
Rochester, Minnesota, USA*

With increased emphasis on making the diagnosis of dementia and Alzheimer's disease (AD) at the earliest point in the disease spectrum, mild cognitive impairment (MCI) has become an important construct. Mild cognitive impairment represents a transitional state between the cognitive changes seen in normal aging and the very earliest clinical features of dementia and AD. Since MCI is a relatively new clinical construct, few epidemiological studies have been conducted to estimate its incidence and prevalence. Most of the original studies constituted a retrofit of criteria to pre-existing datasets, and consequently, the estimates of the rates of MCI were quite variable. However, more recently, new epidemiology studies of incidence and prevalence are beginning to emerge. There are several European studies and a few from the United States and other parts of the world designed to generate rates in a prospective fashion. These studies are providing rates for MCI and its subtype in the range of 8-15% for individuals aged 65 years and older, and incidence studies are demonstrating rates in the 0.75-1.25% per year range. When these figures are projected onto the worldwide population, the implication for the magnitude of the problem of impending dementia is enormous. These studies emphasize the importance of prevention strategies for public health purposes.

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### Holistic Care for Dementia Elderly in Asian Chinese Communities

**K2****N. Chow***Chair Professor, Department of Social Work and Social Administration, The University of Hong Kong, Hong Kong SAR*

The presentation aims to explore a holistic care model for dementia elderly living in Asian Chinese communities. It is argued that the task of taking care of the dementia elderly in Chinese communities is often shared by a number of parties, including the family, the community where the elderly live, and the government. As a result, dementia elderly often fail to obtain the help they need, and even when assistance is available, it is fragmented and seldom meets their needs in a holistic manner. It is suggested that while the contributions of the various parties have to be recognized, ways must be found to put together their efforts, so that each is complementing and supplementing one another, to offer the dementia elderly the most appropriate help they need, and in a way which is congruent with the values of a Chinese society.

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## PLENARY SESSION

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### Mixed Dementia

**P1****P. Sachdev***School of Psychiatry, University of New South Wales, and Neuropsychiatric Institute, Prince of Wales Hospital, Sydney, Australia*

**Background:** Older individuals with dementia often have multiple pathologies, with clinical uncertainty regarding the salience of one or more pathologies. These individuals are often referred to as having a 'mixed dementia'. **Methods:** An overview of the current literature, and an examination of the concepts relating to the pathogenesis of distinct pathologies. **Results:** On post-mortem examination, the most common overlap is between Alzheimer's disease (AD) and vascular dementia (VaD). However, there is considerable overlap between the various neurodegenerative disorders, in particular AD and dementia with Lewy bodies (DLB), and AD with frontotemporal dementia (FTD), corticobasal degeneration (CBD), and progressive supranuclear palsy (PSP). The clinical presentation is often 'mixed'. Some pathogenetic

factors are shared by these disorders. There has been a special interest in the shared risk factors for AD and VaD. **Conclusions:** The overlap presents a challenge to clinicians as new and more specific drugs are being developed. The overlap also presents a challenge to the nosological status of the various disorders, and warrants a re-examination of this along other lines such as the proteins involved or genetic abnormalities. The overlap of AD and VaD has prompted the examination of AD as a vascular disorder.

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### Molecular Biological Basis of Future Therapy of Alzheimer

**P2****E. Giacobini***Department of Rehabilitation and Geriatrics, University of Geneva, Medical School, Geneva, Switzerland*

Following the introduction of cholinesterase inhibitors in 1986 and its 20-year long successful application in mild, moderate and more recently in severe patients, the treatment of AD has reached a turning point toward disease modifying approaches. The most promising treatment is based on the reduction of beta-amyloid in the brain of patients with mild-to-moderately advanced disease by means of active or passive immunization. Several types of vaccines are presently available. Three large international immunization trials are in progress in US and Europe on mild-to-moderate AD patients. The most advanced in time is the humanized antibody trial. Drugs aiming to reduce tau phosphorylation (GSK3 inhibitors) are entering in clinical phase. On the other hand, due to intrinsic difficulties, the development of gamma- and beta-secretase inhibitors is still at an initial preclinical phase with no drugs on sight. Anti-amyloid aggregation therapies are being developed but only one of them, based on aminoglycan compounds, is still in clinical trial. Anti-APO-E approaches are being evaluated but only one is at a clinical stage. Stem cell therapy and gene-replacing therapy are being applied only at the experimental stage and are still far from clinical application. Prolonged protection of the central cholinergic system has been attempted by means of growth-factor therapy, either directly through i.c.v. infusion of NGF, with genetically modified fibroblasts or indirectly by means of gene therapy. NGF treatment could double the clinical effect of ChEI in time. It is expected that within the next 5 to 10 years a new therapy for AD will emerge. This therapy will allow long-term stabilization of at least 5 years, block disease progression or be preventive if applied at preclinical stages of the disease.

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### Neuropsychology of Mild Cognitive Impairment and Dementia

**P3****G.E. Smith***Professor of Psychology, Department of Psychiatry and Psychology, Mayo Clinic, USA*

Simultaneous progress in the normative neuro-psychology of aging and the neuropsychology of early Alzheimer's disease (AD) have led the dementia field to focus on the boundary zone between normal aging and dementia. Mild cognitive impairment (MCI) has gained acceptance as a concept and diagnosis to capture this boundary zone. The focus on early detection of AD and MCI has provided hope that we may be able to identify risk factors for AD years before people develop the devastating cognitive impairments characteristic of the disease. These risk factors may themselves include cognitive markers. More is being learned about how biomarkers and cognitive markers interact. This talk will briefly discuss normative neuropsychology, the neuropsychology of MCI and AD, and the use of cognitive measures in dementia differential diagnosis.

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### Neuropsychological Profile of Mild Cognitive Impairment

**P4****T.P. Wong<sup>1,2</sup>, C.S. Yu<sup>1</sup>, K.H.Y. Wat<sup>1</sup>, G. Li<sup>3</sup>, E. Yang<sup>3</sup>, T.M.C. Lee<sup>2</sup>**<sup>1</sup> *Psychogeriatric Team, Kwai Chung Hospital, Hong Kong SAR*<sup>2</sup> *Laboratory of Neuropsychology, The University of Hong Kong, Hong Kong SAR*<sup>3</sup> *Jockey Club MRI Centre, Li Ka Shing Faculty of Medicine, The University of Hong Kong, Hong Kong SAR*

Increased life expectancy of mankind is associated with an increase in the prevalence of age-related diseases such as dementia, which has imposed tremendous burden on the society: the financial investment on the provision of medical and institutional care for those suffering from dementia and also the toll on the psychological well-being of the caregivers. The recent discovery of a long preclinical phase of the Dementia of the Alzheimer's Type (DAT) of up to 7 years, has led to an enhanced research interest in identifying and establishing early diagnostic indices of dementia for possible pharmacological treatment for slowing down the clinical course of DAT. This preclinical phase is commonly known as mild cognitive impairment (MCI). In this presentation, we shall present the findings of a cross-sectional study launched to the neuropsychological profile of people diagnosed of MCI. Significant neuropsychological indicators identified will be discussed.

## The Neuropsychiatry of Dementia

P5

P. Sachdev

*School of Psychiatry, University of New South Wales, and Neuropsychiatric Institute, Prince of Wales Hospital, Sydney, Australia*

**Background:** It is estimated that about 90% of patients with dementia will develop significant behavioural or emotional problems at some stage of their illness. These problems can present a major challenge in the optimal management of dementia and cause considerable distress to patients and support personnel. **Methods:** An overview of the literature, and personal experience in the management of these problems. **Results:** Behavioural and emotional symptoms in dementia are common and quite heterogeneous, which present a challenge to their classification. They include disturbed mood, delusions, altered perception, agitation, aggression, anxiety, withdrawal and altered appetitive behaviours. They do not often meet criteria for discrete psychiatric disorders. They do however occur in clusters and rational diagnostic and management strategies are possible. There is mounting evidence that they have a neurobiological basis, but contributions of unmet emotional needs, inappropriate environment, sensory impairment, altered social circumstances and comorbid medical conditions are important. The type of dementia is also important. A rational plan for management can lead to much reduction in distress, delaying of institutionalization, and improved quality of life. **Conclusions:** The neuropsychiatric symptoms of dementia deserve careful assessment and management to improve the quality of life of sufferers and their supporters. Some simple strategies, including drug management, will be discussed.

## Future of Cholinergic Therapy in Dementia

P6

E. Giacobini

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Twenty years after the first report of Summers in 1986, several million Alzheimer disease (AD) patients have been treated with cholinesterase inhibitors (ChEI) with no evidence of severe side-effects. There is no evidence that treatment is not cost-effective. The time limit in long-term clinical effects is at least 3 years, this term has now been extended to severe patients (MMSE<10). The recent discovery of the role of butyrylcholinesterase (BuChE) in brain points to this enzyme as a new target for AD treatment in advanced AD cases. Selective BuChEI should be tested in more severe cases. Based on the functional role of the cholinergic system, indication for ChEI treatment should be extended to those diseases or syndromes showing a cholinergic deficit such as Lewy body disease, vascular dementia, Parkinson dementia, delirium, brain injury, attention deficits and HIV dementia. Bifunctional ChEI are being developed to add non-cholinergic to cholinergic effects such as APP synthesis inhibition, anti-oxidation, MAO inhibition, A-beta anti-aggregation, 5HT uptake inhibition. ChEI will continue to play an important role in AD therapy for many years to come. The possibility of rescuing forebrain cholinergic cells from degeneration is being attempted with NGF therapy directly, through gene therapy or through genetically modified stem cells. This approach may double the effect-length of ChEI.

## Advances in Neuroimaging for Dementia

P7

C.R. Jack

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**Background:** Improved noninvasive methods are needed to identify the risk of developing dementia and to measure its progression. Imaging has emerged as a prime candidate to fill this role. Major advances have been made recently in this area in labeling of plaques and/or plaques and tangles with nuclear medicine-based probes. In addition to nuclear medicine-based techniques, however, magnetic resonance imaging (MRI) and associated modalities provide useful information about the stage and longitudinal progression of neurodegeneration. **Methods:** The literature pertinent to advances in neuroimaging for dementia will be reviewed under several different categories. These are cross-sectional detection of prevalent disease, imaging-autopsy correlation, detection of incident disease—i.e. prediction of dementia, and longitudinal studies of the ability of serial imaging to detect concurrent disease progression. **Results and Conclusions:** Although improvement in imaging based biomarkers for detection of prevalent and incident disease as well as measuring longitudinal progression is needed, major progress has been made toward this end in recent years. The most significant advances have been the development of nuclear medicine-based probes for amyloid plaques and/or plaques entangles. Opinions as to the appropriate role of various imaging modalities for diagnosis and measuring progression are in a state of flux. However, the most likely outcome would seem to be that non-overlapping roles will be identified for various imaging modalities and that the ultimate approach to imaging of dementia will incorporate multiple modalities each contributing complementary information.

## Behavioural and Psychological Symptoms of Dementia

P8

H. Brodaty

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Behavioural and psychological symptoms of dementia (BPSD) are a heterogeneous group of non-cognitive symptoms that occur in over 90% of persons with dementia at some time during the course of their illness. Depression occurs in over 20% of persons with dementia, delusions in over a third, hallucinations in 16% and physical aggression in 20%. With some exceptions most BPSD come in the later stages of the dementia and have a time-limited course.

The main causes of BPSD are pathological changes in the brain, interpersonal interactions and environmental factors. Behavioural and psychological symptoms of dementia are very distressing to families, nurses and other professional carers, co-residents in nursing homes and to people with dementia themselves. They are major determinants of caregiver depression and predictors of institutionalisation.

Management is challenging and usually requires a multi-dimensional approach. The presentation will review: the effectiveness of pharmacotherapy in particular the newer agents: novel (atypical) antipsychotics, anticonvulsants, antidepressants and cholinergic agents; psychological and environmental strategies; and planning of services.

## Sleep Disorders and Neurodegenerative Diseases

P9

C.N. Chen

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In the 19th century and up to the first third of the 20th century, interest in sleep centred on pathology of sleep and arousal. From mid-20th century onwards, clinical aspects of sleep have become the focus of attention following the discovery of rapid-eye-movement (REM) sleep. Interest in sleep was no longer restricted to a few isolated research laboratories in the western world. In addition, it has also attracted clinicians from many clinical disciplines including psychiatrists, neurologists, otorhinolaryngologists,

anaesthetists, pulmonary physicians, cardiologists, endocrinologists, etc. In the second half of the 20th century it led to the growth of clinical sleep societies all over the world. In the United States, sleep medicine has become an independent discipline in its own right. About the same time, neuroscience research has advanced from microscopic studies to studies in molecular biology. The latter developments have contributed to further understanding of the mechanisms of sleep and arousal as well as the genetic and molecular basis of neurodegenerative diseases.

From the phenomenological point of view, sleep disorders among patients with neurodegenerative diseases are similar to other clinical disorders. That is, they are manifested with difficulty maintaining sleep, frequent awakening at night, excessive daytime sleepiness, behaviour disorders during sleep, breathing disorders during sleep, etc. However, recent research findings have paved the way to understanding the problems of sleep and arousal in neurodegenerative diseases with their underlying pathology. They may even help in making positive diagnoses of the latter.

In recent years, Alzheimer's disease, Pick's disease, progressive supranuclear palsy, cortico-basal degeneration, frontotemporal dementia with Parkinsonism linked to chromosome 17 are considered as 'tauopathies' (Malliot et al, 1998; Spillantini MG and Goedert M, 1998); and Parkinson's disease, multiple system atrophy, and dementia with Lewy bodies are considered as alpha-synucleinopathies (Litvan, 1999). The former pathology involves microtubule-associated protein tau that makes up filaments within neurons and glial cells; and mutations of tau lead to tangles and cause tauopathies such as Alzheimer's disease and frontotemporal dementia. On the other hand, Parkinson's disease and dementia with Lewy bodies involve mutations of alpha-synuclein, which is also the protein that makes up the filaments inside the microtubules, and lead to Lewy bodies and cause alpha-synucleinopathies.

In general, albeit with exceptions, the tauopathies tend to manifest with symptoms of sleep disruptions, whereas alpha-synucleinopathies tend to show rapid-eye-movement sleep behaviour disorder (RSD). Some even suggest that the occurrence of RSD is a diagnostic, or even premonitory, sign for alpha-synucleinopathies (McKeith IG et al, 2005; Olsen et al, 2000). However, it may be safer to suggest that the manifestations of sleep disorders depend more on the sites of neuropathology. Thus, among patients with multiple system atrophy with its involvement of brain stem and respiratory neurons, sleep-breathing disorders and RSD are common. Sleep-breathing disorder may be related to thalamic cholinergic deficits (Gilman et al, 2003b) and RSD to nigrostriatal dopaminergic deficits (Gilman et al, 2003a).

## Treatment of Alzheimer's Disease and Mild Cognitive Impairment

P10

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Most investigators believe that the earlier we treat dementias such as Alzheimer's disease (AD), the more likely we will be able to preserve viable brain tissue. Thus far, most of the emphasis on treatment has focused on symptomatic AD. These studies will be reviewed. With the recent recognition of mild cognitive impairment (MCI) as an early clinical presentation of dementia and AD, there has been increasing attention paid to the treatment of the disease process at this stage. Several randomized clinical trials on MCI have been conducted in recent years, and the results of these will be reviewed. The most successful trial was the study performed by the Alzheimer's Disease Cooperative Study evaluating subjects with amnesic MCI. This trial enrolled 769 subjects with amnesic MCI and randomized them to donepezil or vitamin E and followed them for 3 years. Results demonstrated that the donepezil group had a reduced risk of developing AD over 12 months in all subjects and up to 24 months in the Apolipoprotein E4 carrier subset. Vitamin E had no effect. Several other trials involving galantamine, rivastigmine, and rofecoxib failed to demonstrate significant beneficial effects, however trends were seen in several of the studies. In all of the studies, the subjects with MCI had an accelerated rate of developing AD over the course of the trials. Methodological differences among the studies accounted for the variable results, and these will be discussed.

## Ageing in the Asia Pacific: Trends and Priorities with Special Reference to Chinese Communities

P11

A. Chan

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The ESCAP region, with 53 member states and nine associate member states, is diverse in population composition and social development. The region already has about 55% of the world's population aged 60+ (mid-2006) and has a number of important demographic features which warrant setting policy priorities, these include: (1) China and India, together accounted for 34.6% of the older population in the world. The rest of Asia accounted for another 19.9%; (2) The Asia-Pacific region in particular has countries with the world's lowest total fertility rates and the longest life expectancy; (3) Whereas in the West it took 80-150 years for older populations to double from 7 to 14%, here it will take just 25-50 years; (4) Japan, currently with 27% of its population aged 60 years or over, has already has an inverted population pyramid. Other "older societies" (e.g. Hong Kong, Singapore and Korea), currently with 15% of its population aged 60+, will have as many as 40% by 2050, level with Japan; (5) The oldest-old population (aged 80+), one of the fastest growing segments, is expected to increase by almost 5-fold by 2050, accounting for about 20% of the older population in many countries; (6) Across countries, women commonly outlive men by a few years; and (7) Across Asia, persons aged 60 or over are expected to outnumber those aged below 15 before 2050.

The present paper will address to ESCAP's proposal in setting three priority areas, namely Older Persons and Development, Advancing Health and Well-being into Old Age and Ensuring Enabling and Supportive Environments, for the upcoming challenges. Examples will be drawn mainly from Confucian (i.e. Chinese) communities.

## Endoplasmic Reticulum Membrane Ubiquitin Ligase Hrd1 Mediates Tau Degradation in Proteasome-dependent and Independent Manner

P12

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Abnormal accumulation of hyperphosphorylated tau protein in intracellular inclusions is a recognized pathological feature in a number of dementias, which is collectively called tauopathies. To explore the molecular mechanism by which tauopathies are regulated, we investigated the effects of human Hrd1, an endoplasmic reticulum (ER) membrane ubiquitin ligase (E3) with RING finger domain, on tau degradation in mammalian cells. We found that overexpression of Hrd1 reduced the levels of non-phosphorylated and phosphorylated tau in 293T cells when cotransfected with tau, which was partially blocked by MG132, a reversible proteasome inhibitor. The reduced level is due to increased degradation of tau mediated by hHrd1 as revealed by cycloheximide chase analysis. Meanwhile, inhibition of proteasome increased high molecular weight forms of polyubiquitinated tau in the cells cotransfected with hHrd1 and tau, compared with tau alone. Consistently, a mutation of Hrd1 with E3 activity inactivation cancelled the impact of Hrd1 on tau degradation. Double immunostaining reveals that there is a colocalization of Hrd1 and tau in cytosol. Unexpectedly, we observed that tau, expressed in 293T cells, was degraded rapidly in vitro when transfected with Hrd1, which was inhibited by an additional amount of protease inhibitor cocktail (PIC). If phosphorylated by GSK-3 $\beta$ , tau was degraded more when coexpressed with Hrd1, which only partially was inhibited by additional amount of PIC. Therefore, Hrd1 may function as an ubiquitin ligase for tau and targets tau for proteasome-dependent degradation and also involves in proteasome-independent tau degradation. This suggesting that hHrd1 may be a potential therapeutic target for tauopathies.

### Neuroprotective Composition Effective for Ameliorating Mental Decline: Volume MR and Histological Images in vivo

S1.1

G. Li

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In the last several years there has been an increasing interest in the possible role of oxidative stress in Alzheimer's disease (AD). Antioxidants are believed to be important in health maintenance through the modulation of oxidative processes in the body. Oxidative damage with the unregulated production of reactive oxygen species (ROS) such as hydrogen peroxide and hydroxyl radicals has been implicated in a growing number of clinical disorders such as atherosclerosis, stroke, Parkinson's disease, and AD. Mechanisms responsible for the ROS-mediated injury to cells and tissues mainly include lipid peroxidation, oxidative DNA damage, and protein oxidation, but there is also evidence that ROS can induce the process of cell death. Indeed, unbalance in the endogenous antioxidant system can modulate cellular proliferation, either in a positive or a negative way, respectively leading to stimulation in cell proliferation at low levels of peroxides or to apoptotic/necrotic cell death at higher concentrations. Based on this background, it is clear that investigating compounds able to counteract this oxidative damage may have a relevant clinical impact for MCI and AD.

We invented a new antioxidant composition composed of coenzyme Q<sub>10</sub> (CoQ<sub>10</sub>), acetyl-L-carnitine, D-ribose, lecithin, vitamin E and grape seed extract, which, when administered daily, at a particular dosage level, has broad neuroprotective efficacy, and has been demonstrated to be effective to delay brain atrophy in double transgenic amyloid precursor protein (APP)/presenilin 1 (PS1), single transgenic APP and PS1 as well as wild type mice by volume MR and histological images in vivo.

### The Impact from Understanding the Biological Mechanisms of Neurodegeneration in Alzheimer's Disease to the Development of Neuroprotective Agents

S1.2

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**Background and Objectives:** Alzheimer's disease (AD) is a chronic neurodegenerative disease, affecting not only patients themselves. As the incidence rate increases with age, our society will receive great economical and health care burden in 30 years because the nature of our population becomes an aging society. Although medical treatment is to preserve the level of acetylcholine for cholinergic neurons, the level of neurotransmitter will diminish if neurons have committed to demise. Therefore, our laboratory aims to elucidate the biological mechanisms of neurodegenerative processes. **Methods:** We used in vitro cell culture and post-mortem human brain tissues for our studies. **Results:** Neuronal apoptosis (programmed cell death) is one of the modes of neurodegeneration. We are among the first to discover that one stress signaling pathway, namely double-stranded RNA-dependent protein kinase (PKR), plays significant roles in  $\beta$ -amyloid peptide induced neuronal apoptosis. We have investigated its molecular pathways of activation and its downstream effects on protein translation. When we investigate deeply about the signaling pathways of protein translation control, we surprisingly discovered that these stress pathways also play important roles in other modes of neurodegeneration such as autophagy (self-eating) and synaptic degeneration. Molecular signaling of translational control becomes a prominent and effective biological target for the development of neuroprotective agents. Using the molecular machineries as pharmacological target, we have successfully recruited them as screening platform and disclose the neuroprotective effects from several Chinese medicinal herbs. **Conclusion:** Our experience shows the significance of hand-in-hand for basic and applied science research.

### Axonal Leakage: a Novel Axon Lesion and its Implications in Alzheimer's Disease

S1.3

J.P. Dai, A.W. Xiao

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**Background and Objectives:** It has been noted for a long time that the various pathologies seen in Alzheimer's disease (AD), including senile plaques (SP), neurofibrillary tangles (NTF) and dystrophic neurites, etc, have been difficult to link together in a convincing framework. Recently, some studies have indicated that axonopathy and axonal transport deficits may play an important role in the pathogenesis of AD. However, how axonopathy and axonal transport deficits contribute to the classic neuropathological changes, and cognitive deficit in AD is unclear. **Methods:** Using an in vitro postmortem tracing technique, we analyzed the morphological changes of axons and terminals of neurons in the different brain areas including cortex, hypothalamus and hippocampus, etc, from 41 postmortem human brains, 26 of which were AD. **Results:** We identified a new neuropathological change—"axonal leakage" in the brains of AD patients. Axonal leakage was clearly present in the brains of AD patients, with variability depending on the affected brain areas. Axonal leakage was usually accompanied by swellings of varicosities or axons, but also occurred in normal-sized axons and varicosities. Axonal leakage showed different profiles from a diffusion dark spot attaching to the axon, a broken swollen varicosity, to an "AD like-plaque" appearance, etc. The leakage profiles were also found in the swollen terminals. The further analysis showed that the number of axonal leakage was related to the amount of SP and NTF in the prefrontal and temporal cortex. Axonal leakage was a few or rare in non-demented aged subjects. **Conclusion:** Our findings suggest that axonal leakage might be a key neuropathological change to link various pathologies together, probably lead to the formation of plaques and neurofibrillary tangles, and may also play a causative role in the cognitive deficit in AD.

### Metallothioneins, Anti-Aging and Alzheimer's Disease

S1.4

B.G. Ru

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The world is becoming older. The problem of aging and its relevant diseases, such as cancer, coronary diabetes, diabetes and specially senile dementia, senile depression, parkinsonism and Alzheimer's disease (AD) etc, have appeared to be a great challenge to humans. According to some reports, more than 5 to 7 percent of people older than 65 have some degree of senile dementia. These senile diseases have brought great harm to many individuals, families and our whole society. Therefore, more and more researches focus on aging and its relevant diseases.

Metallothioneins (MT) are widely distributed in nature, especially in the liver and kidney of human and mammalian. Dr. Margoshes and Dr. Valley discovered the MT in horse urine which was poisoning by Cd<sup>2+</sup> in 1957, at first. Metallothioneins are a family of low-molecular-weight (6-7kDa), cysteine-rich and metal-binding proteins. Whole molecule contains two parts:  $\beta$  domain and  $\alpha$  domains, it contains seven bivalent metals or 20 mono-valent metals. Such metals include some rare metal elements (Zn, Cu, Co, etc) and heavy metals (Cd, Hg, Pb, etc). Metallothioneins is a collective name for a super family. All vertebrates examined contain two or more distinct MTs (MT-1 to MT-4 in mammals), MT-1 and MT-2 are found in liver tissue, whereas MT-3 is expressed mainly in brain and MT-4 is most abundant in certain stratified tissues.

Metallothioneins are synthesized in liver by induction with metals, some hormones, etc. Their main functions include: (1) Participate the transportation, storage and metabolism of some trace elements in vivo (Zn, Cu, Co, etc); (2) Participate the detoxification of heavy metals in vivo (Cd, Hg, Pb, Cr and Ni, etc); (3) Participate radiation protection, especially to repair DNA damage by radiation in vivo; (4) Scavenge free radicals, especially hydroxyl free radicals (Over 100 times compared to SOD); (5) Promote cell growth, development and energy metabolism, etc; and (6)

Strong anti-oxidation and anti-ageing in vivo.

So, it is shown that MTs have biological anti-oxidation and as anti-ageing agents. During 1985-2003, the research of MTs in our group is interesting in MTs (MT-I, MT-II, MT-III) and anti-ageing field: (1) Anti-radiation (Co<sup>++</sup>, UV) function: to repair the damage of DNA by radiation, and its mechanism (molecules, cells and animals level); (2) Scavenge free radicals: to repair the damage of DNA and its mechanism, especially on anti-hydroxyl free radicals is stronger than SOD (molecules, cells and animals); (3) Anti-ageing effects of MT on D-galactose-injected mice (animals); (4) Anti-oxidation: to increase GSH, GSH-PX, SOD, and to decrease MDA etc in vivo (animals); (5) The research of drosophila that finds MTs can extend the lifetime of drosophila; (6) Metallothioneins can inhibit the toxicity of  $\beta$ -amyloid (related with AD); (7) Metallothioneins can mediate Zn<sup>++</sup> concentration, anti-aggregation of  $\beta$ -amyloid and anti-apoptosis of neurons (related with AD). **Conclusions:** On molecules, cells and animals levels, the all results of research show that MTs (MT-I, MT-II, MT-III) are a stronger native anti-oxidation agent, stronger native anti radiation and free radical scavenger in vitro or vivo. So, MTs can be used as natural anti-ageing agents to prevent or treat some diseases. GIF participates in gene expression regulation, neuron signal transduction, inhibition to apoptosis, anti-oxidative stress, so as to protect neurons from damage and prevent neuro-degenerative disease.

### Prevalence Study on Very Mild and Mild Dementia in the Community Living Older Persons in Hong Kong

S2.1

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**Background and Objectives:** Early detection of dementia is essential for effective health care planning but there is limited information on the local prevalence of dementia. The main objective of this study is to estimate the prevalence of very mild and mild dementia (VMD and MD) in community dwelling Chinese older persons in Hong Kong and study the associations between demographic health factors and dementia. **Methods:** This was a two-phase study. In Phase 1, elders would be screened by two screening tools, namely the Cantonese version of the Mini-Mental State Examination (MMSE) and Abbreviated Memory Inventory for the Chinese (AMIC). Screened positive subjects would be invited to Phase 2 assessment. Diagnosis and severity of clinical dementia were determined by the DSM-IV classification and global Clinical Dementia Rating (CDR) respectively. Mild dementia was defined as CDR=1; and VMD if CDR<1 and the memory and three or more subscales in CDR were 0.5. **Results:** In Phase 1, 6100 elders aged 60 and above completed assessment and 2073 (33.9%) were screened positive. Seven hundred and thirty-seven (35.6%) agreed to Phase 2 assessment. The overall prevalence of VMD and MD for persons of 70 years and above was 8.50% and 8.88% respectively. Women had a higher prevalence. Logistic regression showed that for the VMD group, age and educational levels were significant risk factors and strenuous and mind-body exercise had significant protective effects. For MD group, age, lower educational level and cardiovascular risk factors were significant risk factors while the practice of regular physical exercises was protective. **Conclusion:** The prevalence of VMD and MD among the local population are 8.50% and 8.88% respectively among elders aged 70 and above.

### Early Detection of At-Risk Older Hong Kong Chinese Adults for Probable Dementia

S2.2

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**Background and Objectives:** According to a recent report, Hong Kong has about 59 700 older Hong Kong people suffering from dementia, with around 18 500 new cases every year. These two figures will rise to 109 000 and 32 600 respectively in 2020. Hong Kong Alzheimer's Disease Association has launched an Early Detection Project since August 2005

aiming at (1) early identification of older people who are at risk of dementia or mild cognitive impairment (MCI), and (2) promoting public awareness on brain health. **Methods:** Recruitment was done in the community. Participants who were screened as at-risk cases (AMT>6) were invited to receive further assessments in areas of daily task performance, mental state, memory, attention, and mood. **Results:** Around 250 older adults, with a mean age of 75 years, completed the assessments. A majority of them were females (70%) and received little education (80%). Preliminary data analyses showed that 54% had MCI and 36% had signs of dementia (early to middle stages). Seventy-three percent of participants with MCI were still able to handle complex instrumental daily living but only 26% with signs of dementia demonstrated this ability. Cognitive impairments were found among participants with MCI and probable dementia in aspects of information recall, attention, and working memory. Older age and low level of education were associated with MCI and dementia. Participants with probable dementia were recommended for further medical investigation. **Conclusion:** The early detection program has proven its timely significance in identifying older people with probable dementia in the community and public education on brain health.

### Assessment of Mild Dementia in Community Living Chinese Older Adults in Hong Kong

S 2.3

C.W. Lam

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Although it is estimated that the greatest proportional increase in dementia population of the coming decades will come from developing countries, the preparation for early detection are inadequate. Dementia is a chronic degenerative disorder when clinical presentations occur late in the disease course. For any intervention to assume maximal benefits in symptom modification, early detection of disease will be the key. However, it is also well known that demented patients present only when significant impairments and complications occur. This is especially apparent in societies with lower acceptance and awareness of dementia. In a recent population survey conducted in Hong Kong, it is identified that about 10% of the community living Chinese older persons suffered from mild dementia. For subjects with mild dementia, a significant impairment in cognitive function and instrumental activities of daily living was identified. Depression, anxiety and apathy were the common psychological symptoms associated with cognitive decline. Old age, female gender and lower educational levels are demographic risk factors associated with diagnosis of dementia. Of those with clinically diagnosable dementia, only 11% had been informed by medical professionals of the diagnosis. The results showed that a comprehensive clinical assessment is useful in detecting mild dementia. More work should be done to enhance awareness and knowledge of this disorder in the local community.

### 軍隊老年人輕度認知損害的發病率及向癡呆和 Alzheimer病的轉化率：基於人群的佇列研究

S 2.4

于寶成、田京利、歐陽荔莎、王玉敏、王成章、崔欣、王雪麗、齊麗娟、潘志剛、魏士賢、高義  
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**目的：**研究軍隊老年人輕度認知損害(MCI)的發病率及向癡呆和 Alzheimer病(AD)的轉化率，為進一步研究AD提供依據。**方法：**以2001年石家莊市26個部隊休幹所MCI患病率調查的2674名60歲及以上的離退休幹部為研究物件，對患病率調查時診斷為MCI的216例患者和2302名認知正常受試者進行為期3年的佇列研究，比較MCI患者和認知正常受試者癡呆和AD的平均年發病率。**結果：**認知正常的老年人MCI的發病率為4.8/百人年，癡呆和AD的平均年發病率分別為1.3/百人年和0.8/百人年；MCI患者癡呆和AD的平均年發病率分別為8.1/百人年和5.6/百人年；男性和女性MCI患者癡呆和AD的平均年發病率差別無顯 性意義( $P > 0.05$ )；隨 文化程度的提高MCI患者癡呆和AD的平均年發病率有降低的趨勢( $P < 0.05$ )；隨着年齡的增長，MCI患者癡呆和AD的平均年發病率有增高的趨勢( $P < 0.01$ )。MCI轉化為癡呆或AD的相對危險性分別為認知正常者的6.4倍和7.4倍。**結論：**軍隊老年MCI患者轉化為癡呆的危險性遠遠大於認知正常的老年人。應加強對老年MCI患者這一癡呆高危人群的監測。

## A Study on Attentional Function in Patients with Mild Cognitive Impairment

S2.5

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**Objective:** To investigate whether the sustained and selected and divided attentional functions are affected in patients with mild cognitive impairment (MCI). **Methods:** Several tests designed to test attentional functions were given to patients with MCI as well as to normal control elderly subjects: Continuous Performance Task (CPT) for assessing sustained attentional function, Stroop test for selected attentional function, dual task test for divided attentional function. **Results:** Mild cognitive impairment group did as well as the normal control group in the CPT test and the dual task test, but poorly in Stroop test. In Stroop test, MCI group made more errors during the whole test. **Conclusion:** The MCI patients were impaired in selected attentional function compared with normal control group with sustained and divided attentional function intact.

## Memory Training Program for Older People with Early Memory Loss

S3.1

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Memory loss is a common phenomenon occurred in the natural course of ageing but can also be an indication for a dementing disease. In psychogeriatric field, the diagnosis of mild cognitive impairment (MCI) is a controversial issue so far. It is known that around 8-15% of people with MCI will turn into Alzheimer's disease each year. Early intervention is highly indicated for slowing down the disease deterioration. People with early memory loss or mild cognitive impairment have dominant features of memory deficit, instrumental self-care problems and depressed mood. Development of memory training program is necessary for memory enhancement and maintenance of quality of life.

Memory training is a structured drilling program through various methods to enhance memory function. We have developed a training program based on five memory elements of attention, registration and recall, perception, verbal fluency and problem solving skill. The program consisted of 36 sessions. To test the effectiveness of the program, we selected eight sessions for 28 participants in three groups. We adopted Mini-Mental Status Examination in Chinese version, Memory Symptoms Score, Mattis Dementia Rating Scale (DRS) and Personal Wellbeing Index in Chinese version (PWI) for assessing the participants' functions. Up to the end of November, we processed 16 participants' results and all indicated positive effects in overall scores of the DRS and PWI. We have therefore designed the program into a more systematic training kit for further promotion of this program.

## Determinants of Burden Among Informal Caregivers of Dementia Persons in Hong Kong

S3.2

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**Background and Objectives:** As the prevalence of dementia doubles every 5 years after the age of 65, a rapidly ageing local population has made dementia a pressing healthcare issue. The impact of dementia goes far beyond the affected individuals. In developed countries, numerous studies have illustrated its deleterious effects, both psychological and physiological, on caregivers. Nevertheless, there is a paucity of information about the experience of local caregivers of dementia persons. This study aims at investigating the determinants of burden among informal caregivers of dementia persons in Hong Kong. **Methods:** Two hundred and fifty-two consecutive new attendants of a multidisciplinary memory clinic were assessed using validated instruments. Their cognitive, behavioural and functional profiles were evaluated by Mini-Mental State Examination (MMSE), Neuropsychiatric Inventory (NPI), Cohen-Mansfield Agitation

Inventory (CMAI), and Disability Assessment for Dementia (DAD). The severity of dementia was determined by Clinical Dementia Rating (CDR) Scale. When available, their major informal carers were interviewed by Relative Stress Scale (RSS) to ascertain their levels of burden. **Results:** One hundred and forty-three key carers were interviewed. Of them, 36% were elderly spouses, 33% daughters, 15% sons, 8% daughters-in-law, and 8% other relatives or friends. Their mean age was  $53.8 \pm 14.7$  y with a female preponderance. On average, they have provided care for their family members with dementia for  $3.0 \pm 2.2$  y, and 70.7% of them were live-in caregivers. The level of carer stress as exemplified by RSS scores was highest for those looked after persons with moderate dementia (CDR 2). Using stepwise multiple regression analysis, only three factors (NPI total score, CMAI total score, and carer age) were found to significantly predict the level of stress among carers. Together, they constituted a multiple R of 0.457. **Conclusions:** The findings confirm that caregiving careers in Hong Kong are as demanding and challenging as reported in other developed communities. Neuropsychiatric symptoms of dementia and carer age predict stress among carers. Tailor-made training and interventional programs targeting at the management of behavioural and psychological symptoms should be developed to help relieve their burden.

## The Integration Care Model of Dementia Patients

S3.3

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**Background and Objectives:** Currently the incidence of the dementia patients in Taiwan is over 4% among the elderly. The number is still growing. These patients diagnosed with dementia may have not only the cognition disturbance but also abnormal behavior which is troublesome for their families. It will be the most painful experience for them when the immediate family member turns to be a broken-down stranger. We located a dementia nursing home with 40 beds. We devoted ourselves to take care of dementia patients to help them rebuild body and soul in every operation of software and hardware. **Methods:** (1) The hardware of the dementia unit; (2) The integration care model: the complete medical team—family doctors take care of patients' chronic problems; psychiatric doctors evaluate patients' psychotic syndromes; neuro-doctors diagnose patients if there is vascular dementia; and rehabilitation doctors enhance physical and mental rehabilitation. The specialists are well cooperated and have care plans regularly. In addition to social workers, dietitians and volunteers are included in the integration care team; (3) The tailor-made activities, including tactile, sense, hearing, smell, pet and gardening therapy; (4) Measurement form: MMSE, GDS, caregiver burden, family satisfaction questionnaire. **Results:** Cognition function increased; depression scale and caregiver burden decreased; family felt more satisfied about this care model. **Conclusion:** The Integration Care Model of Dementia Patients Based On Patient centered is the trend of the future.

## Special Care Unit—Helping Hand Zhaoqing Home for the Elderly: A Place to Bring "Happiness" to Cognitive Impaired Individual and Their Caregiver

S3.4

C.M.W. Lee

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**Background:** As people are getting old, changes in their personal competencies would most likely to occur. They will most likely experience a decrease in cognitive function especially for those people with dementia (PWD) that in turn not only influencing how they react to their environment, but also affecting their level of self-care ability. As PWD progress in their disease, it is often accompanied by high care dependency and behavioral disturbances, resulting in an increased burden and frustration for the caregiver. Design of the physical environment and provision of special features is increasingly recognized as an important aid in the care of PWD and is also regarded as a therapeutic resource to promote well-being and functionality among them. **Method and Results:** The Special Care Unit (SCU) of the Helping Hand Zhaoqing Home for the Elderly is a segregated unit that accommodate only cognitively impaired individuals. It offers special features including dementia-appropriate activities, consistent daily

routine, reduced over-stimulation, and specialized physical design such as non-institutional setting, small size unit, increased lighting, camouflaged doors/exits, provision of orientation signage/landmarks, allowing for safe wandering and access to secured outdoor therapeutic garden. Such features together with special/fixed staff selection and training showed improvement in PWD's communication skills, self-care skills, orientation ability, social function, mobility and affective response. Additionally, reduction in behavior disturbances and apathy among residents was also shown. **Conclusion:** The SCU that incorporated specially designed physical environment and features is important not only in 'fitting' with PWD's functionality and enabling them to stay independent longer, but also useful in reducing emotional and physical strain among caregivers. And most importantly, it brings "Happiness" to cognitive impaired individual and their caregiver.

### Investigation on the Needs of Caregivers for Dementia Patients Living at Home

S3.5

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**Objective:** The purpose of this study was to investigate on the needs of caregivers for patients with dementia living at home. **Methods:** A convenience sample of 108 caregivers of dementia were studied. A cross-sectional design was employed, using questionnaires to measure the needs of caregiver. **Results:** The needs were higher in caregivers of dementia patient; patients' factors such as age, marital status, drugs, the time of diagnosis and identification, were associated with the needs. Numbers of caregivers and their education were also correlated with. **Conclusion:** During caring for patients with dementia, the needs of caregivers should be paid with special attention in order to alleviate their strain.

### Integrated Day Care Centre for Dementia People

S4.1

O.S.K. Sin

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Dementia is a progressive degenerative brain syndrome which affects memory, thinking, behavior and emotion which affects all facets of life. Care needs of dementia people are much different from those frail elderly with physical disability. Day centre for dementia people serves more than a respite function for the carers. It can also be a non-medical treatment to enhance the remaining abilities of demented people.

For increasing the longevity, approximately 60 000 of the elderly population over 65 years old are suffering from the disease in Hong Kong. More and more demented cases were found in day care centers for the elderly (DE) setting. As dementia is a chronic illness, the requirement of care is for the long-term maintenance and monitoring of the people with dementia. The aim of the study is to point out six essential areas, including physical setting, staff training, assessment, day operation and activities, discharge policy and carer support when operating a dementia-specific day centre or modifying the existing DE setting to meet the needs of dementia people and their family so as to provide a good quality of dementia care. These six essential areas were common factors when setting up a day care centre. The study used observation and staff interview as methods to compare with day care centers for the elderly and dementia-specific day centre.

### In-home Training for Elders with Dementia

S4.2

M.N.Y. Lee

*Occupational Therapist, Hong Kong Alzheimer's Disease Association, Hong Kong SAR*

**Background:** There are many elders with dementia still living in the community with their family or even living alone. Elders and their carers may be suffered from similar problems, including limited meaningful activities and cognitive stimulation at home, unable to manage elder's behavioral and psychological symptoms, etc. At the end, the worst result

of faster deterioration and higher caring stress will occur. **Methods:** An in-home training session lasting for 1 to 1.5 hours was provided to 25 elders with dementia every week. Training session was implemented at elder's home by occupational therapist or trained assistants. The content of training focused on different functional aspects based on the initial assessment done by therapist, including ADL and IADL, cognitive functions (i.e. memory, attention, problem solving, judgement, etc) and physical functions (i.e. strength and tolerance, mobility, balance, etc) according to elders' performance and functional levels, the training would be modified at any moment. After 1 year implementation of training, elders' functions and performance were reviewed in terms of different assessment methods, including MMSE, Behavioural Rating Scale, Barthel Index and Lawton IADL Scale and physical assessment, etc. At the same time, caring stress and competency were reviewed as well. **Results:** Most of the elder's cognitive function was maintained and orientation towards living environment and people was improved but no significant changes in orientation towards dates. Obvious improvement was found in elder's performance in terms of initiation, concentration, level of response and following instruction. Caring stress of carers was relieved by means of enhancement in caring skills and caring competency. **Conclusions:** In-home training could provide good opportunities to elders with dementia to benefit from cognitive stimulation. Effectiveness was increased because the training was based on elder's home environment and life style and also goal of 'everyday training' could be achieved through increasing the training skills of carers.

### Carer Support and Mentorship

S4.3

T. Tsien, M. Wong

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Dementia affects not only the people who suffered from the illness but also their families. With the deterioration of cognitive and mentally abilities, many daily activities, such as bathing, feeding and toileting need assistance by the carers. The informal care always shifted to the family members, mostly their older spouse or the children. However, the caregiving tasks become heavier and more demanding with the development of the illness. Unexpected behaviors of the patients, such as wandering, confusion and delusion also cause more stress and distress to the carers on the heavy caring duties. Concerning the mental and physical health of the carers is the main objective of the carer support service in the dementia care setting.

To relieve the stress caused by misunderstanding, formal training workshops, enquiry hotline and publications, such as leaflets, carer handbooks provide knowledge to the families on both the illness and caring techniques. Counseling service helps those families to retrieve their caring situation. Regular carer support group meetings help to build up a rapport system among the carers that they are not alone in the situation. To strengthen the mutual help to achieve the objective of carer support service, 'Carer Mentorship programme' was held from 2005 which had two parts. First part was the training workshops to provide basic knowledge to the mentors and mentees. Second part was to pair up mentors and mentees in groups. Telephone contacts and home visits were made to mentees by mentors to provide support and experience sharing. Feedbacks of mentees were positive after the programme.

### Art, Mind and Brain

S4.4

S.O.S. Ting

*Occupational Therapist, Hong Kong Alzheimer's Disease Association, Hong Kong SAR*

The Brain Health Center of the Hong Kong Alzheimer's Disease Association is serving around 50 clients in our day programme, among which most are suffering from Alzheimer's disease (AD), followed by vascular dementia (VAD). We report a mid-aged lady suffering from a commonly misdiagnosed type of dementia: frontotemporal dementia (FTD).

The patient, being a previously non-artistic lady, developed skill in art during the course of her illness. Aged 58, with primary education, she owned a shop selling textile with her husband before their retirement 6 years ago. It was first discovered by therapist in a drawing session that

she could copy pictures very well with very neat outlines, precise details, and also in right proportion. Her family was amazed by the fact that she had never shown any interest or talent in any kind of artistic work before she had had the illness. A painting can be a window into mindset, mood, skills, perceptions, preoccupations, and training of the artist. People with FTD can develop new artistic skills in the setting of their illness (Miller et al, 1996). Meanwhile, her language function was severely affected, particularly in expression, and the use of correct words, such as naming objects and in expression of her ideas.

Artwork of the client and others will be shown. The application of non-medical intervention such as art therapy in dementia care will be discussed.

## Calligraphy for Dementia Care and Rehabilitation S4.5

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Chinese calligraphic training could facilitate cognitive functioning, calm down emotions and improve behavioural and clinical disorders. Three studies are reported:

(1) Cognitive facilitation: The first experiment assigned 66 normal aged (60-74 years) to a directional-character writing group, a non-directional character writing group, each for writing for 45 minutes, and a resting group. Assessed by DAT-Spatial Ability and Clinical Memory Scale, their spatial ability and pictorial memory improved after writing the directional characters, while their pictorial memory also improved after writing the non-directional characters. No change existed in the controls. In the second experiment, 20 AD patients (59-82 years) wrote Chinese characters for 25 minutes, while 10 AD controls (60-80 years) rested for the same duration. The MMSE-Chinese assessment showed that its total score improved significantly from the pre-test to the post-test, as well as the subscales on Short-term Memory, Language and Drawing tasks in the experimental group, but not in the controls.

(2) Psychological health: Using the SCL-90, the second study compared one group of normal aged elderly (n=18) with over 7 years and another group without any calligraphy experience (n=19). The results showed that the experienced had better health in eight SCL-90 Scales, excepting Phobic Anxiety.

(3) Personality change: The third study compared professional calligraphers (n=209) with over 15 years and ordinary practitioners (n=445) with less than 9 years of calligraphy practice by 16PF-Chinese. Professional calligraphers significantly differed from the ordinary practitioners in lower Anxiety, better Mental Health, higher Creativity and more Efficient Learning.

## Study on the Current Status and Family Caregivers' Attitude to the Characteristics of Physical Environment for Patients with Dementia S4.6

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**Objective:** To determine the current status and family caregivers' attitude to the characteristics of physical environment for the homebound patients with dementia. **Methods:** Direct observation and interviews were used to assess the characteristics of safety, stability and appropriate stimulus of physical environment, as well as family caregivers' attitude in 121 homebound dementia patients. **Results:** More than 2/3 of families possessed the characteristics of safety and stability in physical environment, 1/3 possessed the characteristics of appropriate stimulus. Respectively 86.8%, 59.5% and 50.4% of the family caregivers regarded safety, stability and appropriate stimulus as important to dementia patients. **Conclusions:** Most of the family caregivers paid close attention to the safety of physical environment for dementia patients, but showed relative deficiency to the importance of stability and appropriate stimulus. Because family tends to remain a naturally stable environment, which is helpful to the dementia patient, it is necessary to provide supervision in the arrangement of physical environment and try to maintain the dementia patients to be cared at their own home.

## Cognitive Rehabilitation: From Theory to Practice S5.1

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**Background and Objective:** The potential of ecologically valid and specifically computer-assisted cognitive rehabilitation (CACR) for people with cognitive decline is increasingly being recognized. **Methods:** A review of neuroplasticity, the interaction effect between human and computer, advantages/limitations of CACR for persons with cognitive deficits will be outlined. The global trends of CACR, namely: compact and customizable; internet-based; be intelligent; virtual-reality-based; and client-led will be illustrated with examples of cultural-relevant, customized software (developed by Visual Basic, Flash and C++ languages, etc): (1) Attention training for persons with brain injury; (2) Communication board downloadable/customizable from web-server for language disorders; (3) Chinese character writing for dysgraphia; (4) Use of artificial intelligence (expert system) in memory rehabilitation; (5) Virtual-reality-based supermarket shopping for community orientation; (6) Tele-rehabilitation, including (i) tele-assessment using examples of Neurobehavioral Status Examination (NCSE) or Rivermead Behavioral Memory Test (RBMT); and (ii) tele-cognitive training for persons with memory (e.g. in recalling object locations within a kitchen or bedroom) and problem-solving difficulties (daily problem-solving skills); and (7) The application of Flash Com (a kind of net meeting) to individual and group of 3-4 members (e.g. in group-learning of tailor-made training content and strategies). **Results:** Initial findings of preliminary studies indicated that CACR have shown significant improvement in memory, problem-solving and functional skills like writing, reading following treatment. Computer-assisted cognitive rehabilitation's usability and feasibility has been supported by clients' feedback. However, our findings need more support in differentiating efficacy of a CACR and non-CACR programs in different cognitive processes, especially people with mild cognitive impairment and dementia.

## Intelligent Cognitive Assessment System—a Better Way to Assess? S5.2

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**Background and Objectives:** Traditional standardized cognitive assessments require special assessment tools and interpretation of the norm-referenced result may be complicated and time-consuming. Though administration procedures are standardized, administrators might make errors and underestimate or overestimate the actual abilities of the test-taker. The objective of this study was to develop an intelligent cognitive assessment system (ICAS) which is a computerized assessment system equipped with rich multimedia, simulated real situations that considers both test item difficulty and test-taker's ability. The core of the ICAS based on the item response theory that pulls different cognitive aspects into a linear scale and the artificial neural network helps to predict the functional outcomes accordingly. **Methods:** The ICAS were constructed and under review of an expert panel group to ensure the construct validity. Trial run of the ICAS on 15 subjects suffering from stroke that fulfilled the selections criteria as a pilot testing. In addition of the ICAS, Mini-Mental State Examination (MMSE), Neurobehavior Cognitive State Examination (NCSE) and the demographic data of the subjects were collected. Correlation of scores among ICAS, MMSE and NCSE were used to demonstrate the concurrent validity of the ICAS. **Results:** Eleven males and three females with age ranged from 60 to 86 years participated in the study. The score of ICAS respectively correlated with MMSE ( $r=0.676$ ,  $P=0.011$ ) and with the repetition, naming, construction and calculation sub-cores of NCSE. For the content validity, the ICC(2,k) among the panel members was 0.972 ( $P<0.01$ ). **Conclusion:** Although the sample size was small, the content and concurrent validity of ICAS

were established and significant correlated with both MMSE and NCSE. The result was encouraging to guide further development of the ICAS.

### Virtual Reality-Based Cognitive Intervention—Fact or Fad? S5.3

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**Background and Objectives:** Acquired brain injury (ABI) is one of the major causes leading to long-term cognitive and functional deficits. Managing community living tasks would be the ultimate goal targeting for functional independence. In contrast to traditional cognitive rehabilitation approaches, a non-immersive virtual reality-based learning environment has been developed to improve the related skills. The objective of this pilot study was to evaluate the effectiveness of this newly developed VR-based community living skills training program, which was proposed as a cost-effective, ecologically valid, by means of skills acquisition in the program, behavioral performance in real-life setting and self-efficacy. **Methods:** Five people with ABI had been recruited for a single case A-B-A experimental study before group comparative study to be launched in future. In the treatment phase (B), subjects were provided with an 8-session VR community living skills training. Apart from session-based scores for A-B-A evaluation, outcome measures documenting client's performance in pre- and post-treatment phase included Neurobehavioral Cognitive Status Examination (NCSE), Hong Kong Lawton Instrumental Activities of Daily Living Scale, self-efficacy questionnaire, behavioral checklist for community integration as well as self-awareness of deficits interview. **Results:** Improving trend and slope in data points were observed through visual analysis. Initial results demonstrated positive changes in performance and self-efficacy. Further VR-based cognitive rehabilitation development would also be discussed.

### Community-Based and Group Rehabilitation Program in Cognitive Rehabilitation—Sharing Experience and Evidence of a Local Example of Community Program for Cognitive Enhancement S5.4

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**Background and Objective:** The Occupational Therapy Department of Kwai Chung Hospital collaborated with community partners to launch community-based and cognitive rehabilitation program to promote the cognitive functioning of elderly clients so that they could lead a happier and more meaningful late life. **Methods:** Elderly persons from Shamshuipo, Kwai Chung areas and Lantau Island in Hong Kong were invited voluntarily to join cognitive rehabilitation program and after the screening program for dementia using the Chinese Version of Mini-Mental Status Examination (CMMSE). Identified elderly persons would then attend therapeutic groups organized by occupational therapists and evaluated with a pre- and post-test quasi-experimental design. Results were also generated from focus group discussion. **Results:** One thousand one hundred and forty-three elderly persons attended a total of 14 sessions of community educational talk and eight sessions of outreaching exhibition respectively. Among 247 elderly persons who were screened for the study, their mean CMMSE score was found to be 20.99 (SD=5.26). Among them, 26 persons attended cognitive training groups which had incorporated memory strategies, etc. Pre- and post-group CMMSE was 17.54 (SD=4.235) and 20.04 (SD=4.485) respectively; while pre- and post-group Chinese Dementia Rating Scale was 94.50 (SD=21.593) and 104.04 (SD=16.624) respectively. Both measurements showed improvement in cognitive functioning ( $P<0.005$ ). Besides, an explorative case study on application of errorless-based cognitive training would also be implemented. **Conclusion:** Findings seem to suggest positive results in early cognitive screening and training program for the elderly. Occupational therapists and

staff of rehabilitation team should adopt innovative and tailor-made intervention program to meet different needs of the elderly living in the community.

### 州市城鄉養老院及以上人群痴呆患病率調查 S5.5

唐牟尼、馬崔、韓海英、郭揚波、黃杏梅  
中 州市精神病 院老年科

背景与目的：目前養老院患病率報道較少，本課題調查 州市城鄉養老院≥60歲人群痴呆的患病率。方法：采用分層 机整群抽 方法，將 州地區的養老院按規模及地關係分為五層，各層 机抽取一 養老院進行調查。應查者為抽中養老院的全部入住者，年齡≥60歲。查1105人，失訪12人，失訪率1.07%。按美 精神障 診斷与 計手冊第4版的標準診斷痴呆。結果：(1)查出痴呆患者324例，痴呆患病率為29.3%。其中AD 225例、血管性痴呆(VD) 85例、混合性痴呆 5例、帕金森痴呆3例、其他 型器質性痴呆6例，他們的患病率分別為20.4%、7.7%、0.5%、0.3%、0.5%。(2)女性痴呆患者235例，患病率(31.8%)高于男性(89例，24.3%； $P<0.01$ )。(3)痴呆患病率 年齡增 而上升。結論： 州地區養老院年齡0歲老人的痴呆患病率為29.3%，AD患病率高于VD。

### Regulatory Effects of Heart Benefiting Recipe on the Neurotoxicity of $\beta$ -amyloid Induced AD Rat Model S6.1

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The regulatory effects of TXR (調心方) on the neurotoxicity of  $\beta$ -amyloid induced AD rat model were explored. The results showed that (1) TXR could improve the spatial learning and memory ability, enhance ChAT activity and Rt value of M receptors; (2) TXR could down-regulate the expression of A $\beta$  and hyperphosphorylated tau protein in cortex and hippocampus. The mechanism of reducing A $\beta$  expression may be partly due to the inhibition of astroglial reaction, reducing inflammatory cytokines which in turn decreases App mRNA level, preventing A $\beta$  driven inflammatory AD cascade. Decrease of hyperphosphorylated tau protein possibly be related to the down-regulation of GSK-3 $\beta$  and P38 MAPK mRNA expression; (3) TXR could up-regulate bcl-2 and down-regulate bax expression proceed through caspase-3, suppress hippocampal neuronal apoptosis; (4) TXR could enhance brain mitochondrial respiratory function and the enzyme activity of respiratory complex, up-regulate the expression of cytochrome oxidase (CO)II mRNA, increase the capacity of eliminating free radicals, decrease the cellular Ca<sup>2+</sup> level in neurons; (5) TXR could increase synaptophysin expression in hippocampal neurons. All the results revealed that the mechanisms of the curative effect of TXR on AD might be through the regulation in multi-level and multi-links.

### “三焦氣化失常與衰老”理論及其防治針法研究 S6.2

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初步闡釋“三焦氣化失常與衰老”相關學說和該學說指導下確立的“益氣調血，扶本培元”針法。

對於人體衰老機制的認識：伴隨生命進程，臟腑氣化功能日趨低下，無論上焦心肺、中焦脾胃、下焦肝腎中的任何一個臟(腑)氣化功能出現異常，都可最終導致三焦整體氣化失常，氣血津液升降出入的通道不暢，從而內生風、火、濕、熱諸邪及痰、瘀、濁毒等病理產物。這種失常的氣化狀態因而成為許多老年期疾病發生的根源，疾病的存在又進一步加重三焦氣化失常，促進機體衰老，如此形成“因衰老而易病，因病而加速衰老”的惡性循環。三焦氣化失常正是衰老的根本機制和諸多老年病(如：老年癡呆、老年骨質疏松症等)的關鍵病機。

“益氣調血，扶本培元”針法的確立：在“三焦氣化失常與衰老”相關學說的指導下，主張從調理三焦氣化角度延緩衰老和防治老年病。穴位組方以膻中、中腕、氣海分別調理上、中、下三焦，配以外關通調三焦，佐以足三 補益後天，血海調血和血。臨牀及基礎實驗研究都已證實，該針法對於腦老化和骨老化具有確切療效。

## Modified Wendan Decoction Cerebrospinal Fluid in Protection Against $\beta$ -Amyloid25-35-Induced Injury in NG108-15 Cells S6.3

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**Objective:** To explore the effective mechanism of modified wendan decoction in treating AD with "Cerebrospinal Fluid Pharmacology in Chinese Materia Medica". **Methods:** NG108-15 cells were cultured in vitro. Detecting the action of modified wendan decoction in protection against A $\beta$ 25-35-induced injury in NG108-15 cells. **Results:** Both of p-JNK and p53 are obviously up-regulated in the model group and both are dose-dependently down-regulated after treated. The high-dose group has significant difference with the blank and the model group ( $P < 0.01$ ). The cells are arrested in S phase. **Conclusions:** The JNK signal pathway involved in the cell apoptosis process induced by the A $\beta$ 25-35 fragment. Modified wendan decoction cerebrospinal fluid can down-regulate the level of p-JNK and p53, promote cells transferring from S phase to G2 phase. It can neutralize the cytotoxicity in some degree. Its possible mechanism maybe relevant to the activation of JNK signal pathway and down-regulation of p53.

## 滋補脾陰方藥對谷氨酸損傷神經元中樹突棘的保護作用及機制研究 S6.4

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背景：突觸是神經元進行信息傳遞的重要結構，它的破壞和丟失對神經系統的功能將產生重大影響。突觸功能障礙及缺失是發生於阿茲海默病(Alzheimer's disease, AD)早期的病理過程，是AD疾病過程中的重要神經病理改之一，並且是與認知功能下降最為密切的病理表現。樹突棘是存在於哺乳動物大腦神經元樹突干上的小突起，它構成中樞神經系統興奮性突觸傳的原始位，是學習和記憶活的生物基礎。在AD病人腦中，現有樹突棘丟失及密度的少，樹突退化等現象。樹突棘內含有多種細胞表面受體、肌蛋白細胞骨架、手架蛋白等多種成分，它們對樹突棘的發育成熟以及結構的穩定起調節作用。其中以樹突棘相關的Rap-特异性GTPase-活化蛋白(spine-associated Rap guanosine triphosphatase [GTPase] activating protein, SPAR)為代表，它與樹突棘成熟及形態的維持密切相關。在神經元活化時SPAR可被血清誘導激(serum-inducible kinase, SNK)降解，而導致樹突棘結構的失穩定。目的：探討滋補脾陰方的神保作用與樹突棘形態調節的相關分子機制。方法：將增綠螢光蛋白表載體(pEGFP-N2)通過離子脂質體轉染法轉染至原代培養的大鼠海神經元內，用谷氨酸處理細胞，通過螢光顯微鏡觀察樹突棘的形態結構的變化；免疫螢光細胞化方法觀察與樹突棘形態相關的分子SNK、SPAR在谷氨酸處理後的變化，並觀察在使用滋補脾陰方含血清預理後對SPAR和SNK表達的調節作用。結果：谷氨酸對原代培養的海神經元的樹突棘結構有明顯的損傷作用：表現在樹突干斷裂，樹突棘呈靜曲張改變，樹突棘結構的退化、消失等；谷氨酸可以引起血清誘導激SNK蛋白表上調，並引起樹突棘內肌蛋白調節蛋白SPAR蛋白表下調並在細胞內重新分布，2%濃度的滋補脾陰方含血清預理能明顯抑制SNK和SPAR的蛋白表化，改善谷氨酸對樹突棘結構的損傷。結論：滋補脾陰方的神保作用與維持樹突棘正常的形態和結構有關。

## Effect of GETO Extract on Expression of ChAT and NGF in the Hippocampus CA1 Area of AD Model Induced by A $\beta$ <sub>42</sub> Peptide S6.5

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**Background:** Central cholinergic neurons are all dependent on nerve growth factor (NGF), a neurotrophin differentially enhance acetylcholine release, acetylcholine content and choline acetyltransferase activity (ChAT) in basal forebrain neurons. Whether GETO, an herbal extract, effective in the improving memory of patients with mild cognitive impairment (MCI) influences NGF and ChAT is unknown. **Objectives:** To observe effect of GETO on expression of ChAT and NGF in the brain with AD model. **Methods:** Rat model of AD was prepared by A $\beta$ <sub>1-42</sub> 5 $\mu$ l (A $\beta$ <sub>1-42</sub> 2g/L) injection into hippocampus of rats, and was screened by Morris Water maze test after 4 weeks of the injection. The brains of the rats were cut off after 12 weeks of oral administration of GETO extract, and ChAT or NGF in hippocampus CA1 were immunohistochemically stained differentially using ChAT or NGF antibody. **Results:** The numbers of positive neurons with ChAT (23.2 $\pm$ 13.4) and NGF (34.5 $\pm$ 21.4) in hippocampus CA1 in AD model rats were significantly decreased than those of normal rats. The numbers of positive neurons with ChAT (46.5 $\pm$ 17.1) and NGF (63.1 $\pm$ 28.3) in hippocampus CA1 individually significantly increased in GETO compared to AD models, but not significantly different with Donepezil group (39.1 $\pm$ 12. and 43.5 $\pm$ 21.2). These data indicate that GETO extract increase expression of ChAT and NGF in hippocampus CA1 of AD models, suggesting the effect of GETO extract on memory of patients with MCI may be associated with maintaining cholinergic nerve function. This work was supported by a National 973 project of China (No. 2003CB517104).

## Tiaoxin Recipe of Chinese Medicine Treatment Alzheimer's Disease: a Randomized Controlled Trial S6.6

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Clinical study on treatment of 115 patients of Alzheimer's disease (AD) from five hospitals. The treatment time is 12 weeks. Tiaoxin recipe (TXR) can increase score of MMSE, FOM, RVR, DS, and decrease score of ADL with significant difference ( $P < 0.01$ ), but no significant difference among TXR and Aricept ( $P < 0.05$ ). After stop TXR on 3 months, TXR group are stable on treatment effect.

## Huperzine A Add-on Therapy Improves Cognitive Functions in Patients with Treatment-resistant Schizophrenia: an Open-Labeled Trial S7.1

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Enhancement of central cholinergic function is thought to be an effective strategy for the treatment of cognitive impairments observed in individuals with schizophrenia. Huperzine A (HupA), an alkaloid initially isolated from the Chinese medicine *Huperia serrata*, is a potent reversible acetylcholinesterase (AChE) inhibitor. In this study, 17 hospitalized patients with treatment-resistant schizophrenia openly received 0.3 mg/day HupA as add-on treatment to the existing neuroleptic regimen for 12 weeks. Outcomes were measured using the Scale for Assessment of Negative Symptoms (SANS) and the Mini-Mental State Examination (MMSE). The addition of HupA resulted in significant symptom alleviations as indicated by 32% reduction in mean SANS score and 14% increase in mean MMSE score from baseline to endpoint. Furthermore, 47% of subjects (8/17) had at least 30% improvement on SANS score and 76% (13/17) displayed at least 3-point increase in MMSE scores. These preliminary data suggest that HupA may be a potential adjunctive agent in the treatment of cognitive impairments and negative symptoms in patients with psychotic disorders. A large-scale, controlled trial is needed to further confirm the beneficial effects of HupA.

β淀粉 前体蛋白328-332 (APP5 ) 似物神 S7.2  
養作用的体外 驗研究

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目的: 研究β淀粉 前体蛋白N端328-332 (APP5 ) 似物對人神 母細胞瘤株SY5Y生 的影 , 希望 現可口服的、具有神 營養作用 的小分子多。方法: 合成APP5 和多 5 似物, 以SY5Y為細胞 模型, 以MTT代謝率為篩選標, 并應用胃蛋白 對APP5 和 似物 165進行消化 驗。結果: 1. APP5 及多种 似物均可使MTT代謝率 增高, 似物165的效果最好, 40μmol/L為最佳有效濃度。2. APP5 及 似物165可使LDH漏出率 少, 細胞數增加, P-CREB、Bcl-2蛋 白表 增加。3. 胃蛋白 濃度為40g/L和100g/L時, APP5 和 似物 165的 解率分別為96.4%、99.1%和16.9%、58.6%, 者差异非常顯 著。結論: APP5 及 似物165對SY5Y細胞具有神 營養作用, 而 APP5 似物具有更 的抗胃蛋白 消化能力。

何首烏治療老年期痴呆的臨床研究 S7.3

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目的: 探討何首烏對老年期痴呆患者的治療作用。方法: 對68例AD患 者和70例VD患者, MMSE評分在13-24分之 、進行為期32W的何首 烏治療。療效评价: 采用MMSE、日常生活能力量表(ADL)、Blessed- Roth痴呆量表、臨床療效 評量表(CGI)。在入組時及治療結束後評, 同時測定血清 酯 (ChE)活性。正常對照組入組時進行量表評定 及血清ChE活性測定。結果: (1)治療結束後 組患者MMSE、ADL、 Blessed-Roth、病情嚴重程度(SI)評分均有顯著性改善(P<0.05), 療 效 評(GI)和療效指數(EI)評分均大于1。(2)血清ChE活性: 与對照 組比較, 治療前AD組血清ChE活性顯著增高(P<0.05); 治療后AD組 和VD組血清ChE活性与治療前比較均有所降低, 但 計意 (P>0.05), 与對照組比較亦 顯著性差异(P>0.05)。結論: (1)何首烏可 改善AD患者和VD患者的認知功能、情感人格及日常生活自理能力; (2)AD患者血清ChE活性增高。

Transgenic Mice with Familial Alzheimer's Disease Mutants of APP and Presenilin-1 Show Tau Hyperphosphorylation and the Underlying Mechanisms S7.4

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Alzheimer's disease is characterized by β-amyloid (Aβ) overproduction and tau hyperphosphorylation. Our recent study has shown that Aβ overproduction promotes tau phosphorylation in cell culture and the mechanisms involve glycogen synthase kinase-3 (GSK-3) activation. To further explore the role of Aβ deposits in the generation of cytoskeletal lesions in vivo, we by western blot and immunohistochemistry determined the alterations of phosphorylated tau and the activity of GSK-3β by activity-dependent antibodies in transgenic (Tg) mice overexpressing a mutant form of APP<sup>swe</sup> and a mutant form of PS1 (L235P). We found that phosphorylation of tau at pSer396, Tau-1(S198/199/202), pSer404 and pSer214 epitopes was significantly increased in both young (7-8 months) and aged Tg mice (16-17 months) compared with the wild type mice (wt), and that the level of phosphorylated GSK-3β (S9, inactivated GSK3β) was significantly decreased and the phosphorylated level of GSK-3β at Tyrosine 216 (activated GSK-3β) was significantly increased, while the total GSK-3β did not alter. The colocalization analysis revealed a significant correlation between phosphorylated cy tau at pS396 and pS214 and GSK-3β at both Serine 9 and Tyrosine 216. The current results demonstrate that tau hyperphosphorylation observed in the Tg mice may be a consequence of Aβ-mediated activation of GSK-3β, however, the specific molecular mechanisms leading to GSK-3β activation need further investigation.

Pharmacological Studies of Traditional Chinese Medicine to Treat Alzheimer's Disease S7.5

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**Background:** Shen-wu Capsule (SWC) is a new compound containing 6 kinds of traditional Chinese herbs. TSG is a major effective component of SWC. **Objective:** To investigate the pharmacological effects of SWC and TSG on multiple kinds of AD-like animal models. **Methods:** The drugs were intragastrically administered to the animal models for 1 or 2 months. Morris water maze test was used to detect learning/memory ability; microarray and RT-PCR to measure gene expression. Western blotting and immunohistochemistry to determine related proteins. **Results:** (1) In APP transgenic mice, SWC and TSG improved learning/memory ability, and decreased Aβ content and β-secretase expression; (2) in Aβ brain injection model, SWC and TSG inhibited microglial activation, and decreased IL-1β and tumor necrosis factor α (TNFα) content; (3) in ibotenic acid-induced basal forebrain cholinergic damage rat model, SWC and TSG improved learning/memory ability, increased the ratio of cholinacetyl-transferase (ChAT)/cholinesterase (AChE), or enhanced M-receptor density; (4) in naturally aged rats of 24 months old, SWC and TSG improved learning/memory ability, decreased cholinergic cell death, and increased expression of nerve growth factor (NGF) and its receptor trkA in hippocampus; (5) in D-galactose-induced brain aging mouse model, SWC and TSG improved learning/memory ability, inhibited lipid peroxidation, increased activities of antioxidant enzymes, and enhanced NGF and trkA expression in hippocampus; (6) in dementia rat model induced by mitochondria complex IV inhibitor azide perfusion, SWC improved learning/memory ability, increased the ratio of ChAT/AChE, decreased Aβ and hyperphosphorylated tau content, increased expression of protein phosphatase 2A (PP2A), brain derived neurotrophic factor (BDNF) and its receptor trkB; (7) in diabetic-ischemic model rats, SWC improved learning/memory ability, enhanced long-term potentiation (LTP) in hippocampus, decreased cholinergic cell death, enhanced the expression of neurotrophin-3 (NT-3) and trkC, increased Bcl-2 and Akt protein expression, and decreased the content of Bax, caspase-3 and phosphated cAMP response element binding protein (P-CREB); (8) in hypercholesterolemia-induced dementia rat model, TSG improved learning/memory ability, decreased the content of Aβ and serum cholesterol. **Conclusion:** SWC and TSG act on multiple targets in the complicated pathogenesis of AD, thus may have strong potential to the treatment of AD.

Neuroimaging in Vascular Dementia S8.1

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Vascular dementia (VD) has been a neglected area although it is common, disabling, and potentially preventable. Different from Alzheimer's disease, which is a homogeneous entity, VD is heterogeneous with complexity far exceeds that of AD or the traditional concept of multi-infarct dementia. Findings from imaging studies have contributed significantly to our present understanding and management of VD. It is currently believed that VD may involve complex interactions between vascular etiologies, vascular-related brain lesions, brain atrophy, co-existing dementing diseases, host factors, and vascular risk factors. Basic imaging modalities for the evaluation of VD are computed tomography and magnetic resonance imaging (MRI) [T1-, T2-, proton density, and fluid-attenuated inversion recovery], which can provide relevant imaging variables including vascular-related brain lesions (e.g. size, site, laterality, multiplicity, pattern), extent and site of white matter changes (WMC), and brain atrophy (cortical, subcortical, general, regional). Lesions at other strategic sites (e.g. thalamus, genu of internal capsule, angular gyrus) causing VD are generally less common. The NINDS-AIREN criteria incorporate the most detailed imaging criteria to aid the diagnosis of VD, yet modification is needed to improve its sensitivity and inter-rater agreement. Recent applications of more

advanced MRI techniques including DWI, DTI, MTI, MR perfusion, and MRS, have enhanced early detection of ischemic brain tissue with increased specificity and better understanding on the pathophysiology of WMC. Further study is warranted to evaluate the usefulness of imaging variables (e.g. progression of WMC, cerebral perfusion, and metabolism) as surrogate markers in clinical trials.

### **Development of 3-acetoxymethoxycarbonyl-2,2,5,5-tetramethyl-1-pyrrolidinyloxy as an Electron Paramagnetic Resonance Imaging Reagent for in vivo Mapping Brain Oxygen Distribution and Infarction in Ischemic Brain** S8.2

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Measurement of oxygen concentration and distribution in brain is essential to understanding the pathophysiology of stroke. Although brain oxygen level is critical for brain tissue survival, in vivo non-invasive measurement of brain oxygen distribution and identification of infarction area remain technical challenge. Low-frequency electron paramagnetic resonance (EPR) spectroscopy with application of oxygen sensitive probe is an attractive imaging modality that can potentially map O<sub>2</sub> concentration in the brain. We recently developed a paramagnetic probe, 3-acetoxymethoxycarbonyl-2,2,5,5-tetramethyl-1-pyrrolidinyloxy (AM-CTP), for brain oxygen measurement with EPR spectroscopy. In this study, we demonstrated that after intraperitoneal administration of AM-CTP to mice this nitroxide diffused across the blood brain barrier where, after hydrolysis, 3-carboxy-2,2,5,5-tetramethyl-pyrrolidinyloxy was liberated and entrapped. The probe is sensitive to the changes of oxygen concentration. Pharmacokinetic and pharmacodynamic studies showed that the probe was relatively stable enough for brain imaging study. By using AM-CTP and low-frequency EPR instrument, we obtained EPR brain oxygen map, for the first time, in mice of ischemic stroke. Furthermore, by co-registration with magnetic resonance imaging, we demonstrated that the EPR imaging technology could be potentially used for identification of infarction area in ischemic brain.

### **Clinical Usefulness of Cerebral Perfusion Single-photon Emission Computed Tomography by Technetium-99m Ethyl Cysteinate Dimmer in the Evaluation of Various Types of Dementias** S8.3

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Cerebral perfusion single-photon emission computed tomography (SPECT) is a scintigraphic imaging method to visualize the cerebral perfusion distribution by intravenous injection of Technetium-99m ethyl cysteinate dimmer (ECD). The cerebral perfusion SPECT is an easy and convenient imaging method with no specific patient preparation. The whole examination can be completed within half an hour with almost instantaneous post-data processing. Visual analysis of the perfusion pattern is usually sufficient for clinical diagnosis. The radiation dose is acceptable with a low dosimetry for an adult and no permanent damage to body.

The clinical indications of cerebral perfusion SPECT are various, apart from detection of epileptic focus in seizure and confirmation of brain death, the most valuable way is to classify the various types of dementias by their respective distinguishable perfusion defect patterns of brain. Alzheimer's disease (AD) has a characteristic symmetrical hypoperfusion in temporo-parietal regions whereas fronto-temporal dementia (FTD) has predominant asymmetrical fronto-temporal hypoperfusion pattern. Cortico-basal degeneration (CBD) and progressive supra-nuclear palsy (PSP) have asymmetrical hypoperfusion mainly involving the basal ganglia

and thalamus in addition to various parts of cerebral cortex. Dementia of cerebral Lewis body (DCLB) usually presents with occipital hypoperfusion defects.

Cerebral perfusion SPECT can detect early patho-physiological change of brain well before any structural change such as cerebral atrophy. By using magnetic resonance spectroscopy as an initial screening technique to detect cerebral metabolites changes, patients with suspicious early dementing features can be selected for further evaluation by cerebral perfusion SPECT to confirm the diagnosis.

### **Magnetic Resonance Neuroimaging of Dementing Illnesses** S8.4

P.W. Cheng

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Alzheimer disease (AD) is the most common cause of dementia in the elderly with immense financial implication, not to mention the psychologic burden on patients and their families. With recent development of promising pharmaceutical agents for prevention or slowing disease progression of AD, there is growing need for early recognition and monitoring of early brain changes. To this end, modern neuroimaging emerges as an important adjunct to current clinical and neuropsychologic tests.

Conventional structural computed tomography (CT) or magnetic resonance (MR) imaging used to play a supportive role in the diagnosis of AD with exclusion of treatable clinical mimics of dementia such as normal pressure hydrocephalus. However with the advent of more contemporary structural MR imaging techniques, it is now possible to detect the subtle structural changes in early AD or mild cognitive impairment (MCI) by serial volumetric imaging. High-resolution MR images can be useful to quantify atrophy of the hippocampus and entorhinal cortex, both of which occur early in the disease process. This quantitative approach is useful for monitoring dementia progression and rates of regional atrophy.

In addition to other functional imaging studies such as positron emission tomography (PET) and single photon emission CT (SPECT), functional MR imaging methods (e.g. functional MR-based memory challenge test) are also in development for identification of more subtle changes even earlier during the disease course.

This lecture will address the evolving role of contemporary MR neuroimaging in the evaluation of AD. The current status of structural neuroimaging as diagnostic tools for evaluation of patient with dementia will be described. The potential role of functional imaging will also be highlighted.

### **White Matter Alterations and Gray Matter Loss in Early Alzheimer's disease: a Voxel-Based Whole Brain Analysis** S8.5

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**Objective:** To investigate the relation between white matter microstructural alterations and gray matter loss in early Alzheimer's disease (AD).

**Methods:** We performed magnetic resonance diffusion tensor imaging (DTI) and T1-weighted imaging in 17 patients with mild AD and 23 age-matched healthy elderly controls. Fractional anisotropy (FA) was derived from DTI. The voxel-by-voxel comparisons of white matter FA and gray matter density between the AD patients and elderly controls were performed. Correlation analysis between FA values extracted from the regions showing significantly reduced FA and gray matter density derived from the regions showing significantly atrophy were performed in the AD group. **Results:** Compared with elderly controls, the diffusion anisotropy in the mild AD patients was decreased in the white matter in the prefrontal lobe, temporal lobe and cingulate gyrus, etc. The gray matter loss involved in the medial temporal lobe bilaterally, left posterior cingulate gyrus, etc. The gray matter loss in the MTL bilaterally

significantly correlated with reduced FA in bilateral cingulum in the AD patients group. No correlations were found between reduced FA in the prefrontal and temporal white matter and gray matter loss in the AD patients. **Conclusion:** These findings indicate that neuronal degeneration might be responsible for white matter damage within the limbic system. However, the white matter damage in prefrontal and temporal lobe might implicate in other AD-related pathological process that need further investigations.

## Guardianship

S9.1

C.C.Y. Chiu

Chairperson, Guardianship Board, Hong Kong SAR

This presentation will centre upon the role of a legal guardian in a health care setting. Thus, predominantly, it will focus on medical and health decisions to be made by a guardian. Hong Kong SAR, a common law jurisdiction, is believed to be the first jurisdiction in the whole of Asia to have a guardianship system since 1999.

The Guardianship Board is an independent quasi-judicial tribunal and independent of other Government departments of the HKSAR, empowered to make orders appointing guardians for adults who are unable to make decisions about substantial proportion of matters of their personal circumstances: welfare, residence, medical or financial affairs because they have a mental incapacity (mentally incapacitated persons). It was established on 1st February 1999 under Part IVB of the Mental Health Ordinance (Cap 136). It is a multi-disciplinary Board consisting of the Chairperson and 56 volunteer members, including lawyers (Panel A), doctors, social workers, and psychologists (Panel B), persons having personal experience of the mentally incapacitated (Panel C). It is supported by the Secretariat, which consists of the Chairperson, the Board Secretary, Assistant Board Secretary, and two other staff. The Chairperson is appointed by the Chief Executive of the HKSAR Government. The aim of the guardianship regime is to protect and promote the interests of mentally incapacitated persons. The development of the Board in the past 8 years shows that guardianship clients or subjects are predominantly elders with some form of mental incapacities. As the population in HKSAR is predominantly Chinese by race, the Board issued its first Guardianship Order in Chinese in 27 May 2003.

Regarding medical and health decisions, there is a need to look at Part IVC of the Mental Health Ordinance which is closely related to guardian's power. However, the picture will not be complete without first revisiting the development in United Kingdom. The landmark case *F v West Berkshire Health Authority* (All England Law Reports [1989] 2, 545-571) has laid the very cornerstone of the post-modern medical law, whether relating to mentally incapacitated patients or otherwise. Doctrine of necessity was expounded in no unclear terms. Lord Goff's judgment (562g-571e) explained in detail how this principle could be put into practice particularly in relation to the patient's relatives and significant others. Since the early 1990's, the very series of consultations and issuance of Law Commission Consultation Papers in England and Wales (LCCP No. 128, 129, 130 and 231) as well as in Scotland (Scot Law Com No 151) were consequentially sparkled off in search for new piece of mental health legislation that could hopefully put an end of the rather unclear scene regarding finance, welfare and medical treatment decisions of such patients. In 2005, the new Mental Capacity Act was passed in UK and is due to implement in April 2007. The new Act establishes a new regime of decision-making and a new system of appointment of guardians/deputies. It also made the law of advance directives expressed in written statutes. The draft code of practice, as an official guide to care/service providers, is now in the process of public consultation. The new Act (and the draft code) has detail provisions of what is "Best Interests" and what are the roles of the significant others (including a guardian) in that context.

Locally, the main and only interaction between Part IVB (Guardianship) and Part IVC is regarding medical treatment of the mentally incapacitated person. As mentioned, a guardian can be entrusted with a power to require a mentally incapacitated person to attend at a specified place and time for treatment, and give consent to medical or dental treatment.

Part IVC of the Mental Health Ordinance (Cap 136) gives a doctor the power to provide urgent or non-urgent medical treatment to a mentally incapacitated adult, without his consent, provided that he

does not understand the nature and effect of the treatment. This is what is called the capacity test for consent to treatment. The treatment must also be necessary and in his best interests. Doctors usually only treat all treatments other than a life-saving one, as non-urgent or elective. This may include surgery for a brain tumour, cancer or a broken leg. So the term "non-urgent/elective" may be misleading from a lay person's viewpoint, as it does not reflect the seriousness of the proposed treatment and the pain and suffering of the patient in the meantime.

Consent is an essential element in giving medical treatment, and without it, doctors can be come civilly liable for trespass. In our experience, doctors seem more worried about being sued for trespass than being sued for negligence for the consequences of failing to treat where consent cannot be given by a mentally incapacitated adult.

In this presentation, medical powers of a guardian/deputy will be examined on comparative basis with that of Hong Kong, United Kingdom and Australia through some case examples.

To an extent, the Bournemouth gap or Bournemouth Patient problem will be examined.

## Comparing the Ethical Challenges of Forgoing Tube Feeding in American and Hong Kong Chinese Residents with Advanced Dementia

S9.2

S.M.C. Pang

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The complexity of forgoing tube feeding decisions for persons with advanced dementia (AD) can be characterized by competing views regarding prognostication and clinical outcomes in the context of varying personal, professional, legal and ethical responsibilities as perceived by involving decision-makers. Several broad areas of legal consensus surrounding the withholding of artificial feeding have emerged in North America and Hong Kong over the past few decades. However, what is legally permissible is not always acceptable in practice. Unlike estimating the survival of terminally ill cancer patients, the progression of chronic dementia takes a less definitive course. The lost decisional capacity of AD patients further complicates tube feeding decisions.

Drawing on the findings of two case studies which aimed to develop a cross-cultural dialogue for enriching our understanding of how an ethical environment can be constructed in fostering tube feeding decisions in AD residents, this paper will examine how cultural practices influence the way in which ethical challenges are presented in American and Hong Kong communities. Two layers of culture, medical culture between palliative and conventional and ethnic culture between Caucasian Americans and Hong Kong Chinese, are taken into account for comparing the practices of two long-term care facilities in Boston and Hong Kong respectively.

The decision-making patterns typified in these two contexts and their emergent ethical dilemmas will be expounded. With a broadened understanding of the issue under study, how to meet with the ethical challenges with cultural sensitivity in orchestrating end-of-life care for AD residents by will be proposed.

## Life Sustaining Treatment

S9.3

Y.M. Wu<sup>1,2</sup>

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<sup>2</sup> Honorary Secretary, Hong Kong Alzheimer's Disease Association, Hong Kong SAR

Modern techniques such as cardiopulmonary resuscitation, renal dialysis, artificial ventilation, and artificial nutrition and hydration can considerably benefit the patients. However, life has a natural end and the existence of such techniques presents doctors, patients and their families with dilemmas. Adult competent patients have the right to decide how much weight to attach to the benefits, burdens, and risks of any treatment. They have the right to refuse treatment even where refusal will invariably lead to detrimental result to their health, and doctors are legally bound to respect their decision. Adult patients who have the capacity to make their own decision can express their wishes about future treatment in an advance directive. Any valid advance refusal of treatment—one made when the patient was competent and adequately informed—is legally binding and

must be respected where it is clearly applicable to the patient's present circumstances and where there is no reason to believe that the patient had changed his/her mind. Where adult patients lack capacity to decide for themselves, e.g. dementia patients, an assessment of the benefits, burdens and risks, and the acceptability of proposed treatment must be made on their behalf by the doctor, taking account of their wishes, where they are known. Where a patient's wishes are not known it is the doctor's responsibility to decide in the patient's best interests, taking into account information about the patient from his/her relatives.

## Post-stroke Cognitive Impairment and Dementia

S10.1

W.K. Tang

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**Background and Objectives:** Both dementia and stroke are major health problems in Chinese societies. Stroke is a frequent cause of dementia. Only a few studies have been published on post-stroke dementia, none of which has investigated a consecutive stroke cohort in Asian patient populations. The objective of this study was to examine the prevalence and clinical correlates of post-stroke dementia (PSDE) and post-stroke cognitive impairment (PSCI) in Chinese stroke patients in Hong Kong. **Methods:** Two hundred ninety-seven stroke patients who were consecutively admitted to the medical wards of a university-affiliated regional hospital were interviewed by a psychiatrist 3 months after their stroke. The presence of dementia and vascular dementia were diagnosed according to the Diagnostic and Statistical Manual-Fourth Edition (DSM-IV). Cognitive impairment was determined according to the Mini-Mental State Examination score. In addition, a wide range of demographic and clinical variables were examined. **Results:** Fifty-five participants (18.5%) had PSDE. Thirty-nine participants (21.8%) had PSCI. Univariate analysis found that PSDE was associated with age, level of education, pre-stroke Rankin score, pre-stroke IQCODE score, NIHSS best language score, dysarthria score and total score, urinary incontinence, cortical infarct, leukoariosis, bilateral lesions, number of lesions, involvement of middle cerebral artery circulation, and cerebral atrophy index. Multivariate logistic regression suggested that pre-stroke IQCODE score, NIHSS total score, and cerebral atrophy index were independent risk factors of PSDE. Post-stroke cognitive impairment was associated with age, female sex, level of education, previous stroke, pre-stroke Rankin score, NIHSS dysarthria and total scores, urinary incontinence and cerebral atrophy index. Multivariate logistic regression suggested that female sex, education, NIHSS dysarthria score, urinary incontinence and atrial fibrillation were independent risk factors of PSCI. **Conclusion:** Both PSDE and PSCI are common among Chinese stroke patients in Hong Kong. Their clinical determinants include premorbid level of cognitive function, severity of stroke, and radiological evidence of cerebral atrophy.

## Small Vessel Disease and Cognitive Impairment

S10.2

V. Mok

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Interest in small vessel disease (SVD) has increased in recent years because of its association with cognitive impairment. Small infarcts and white matter change (WMC) are manifestations of cerebral SVD. Small vessel disease is the most common subtype of vascular dementia. Small infarct is found to act synergistically with Alzheimer's pathology in inducing cognitive impairment.

We studied the frequency of cognitive impairment in stroke associated with SVD among Chinese. We noted that varying severity levels of cognitive impairment occur in half of these patients and that executive dysfunction, rather than Mini-Mental State Examination, contributes to the functional outcome of patients. Volume of WMC, frontal lobe atrophy and thalamic infarct all correlate with the severity of cognitive impairment. Results on the long-term cognitive progression after stroke associated with SVD will be presented in this lecture.

Post-hoc analyses on drug studies of vascular dementia have

suggested that drug effects may vary with the subtypes of vascular dementia. Memantine was found to improve cognition only among patients with vascular dementia associated with SVD. On the contrary, donepezil's positive effect is lesser among those with SVD over those with cortical subtype of vascular dementia. Nimodipine was shown to have mild benefit upon cognition only among those with vascular dementia associated with SVD. An open study has suggested that rivastigmine has positive effects in vascular dementia associated with SVD. Results of a pilot study using rivastigmine among Chinese patients with vascular dementia associated with SVD will be presented.

## 痴呆患者的自知力损害

S10.3

張新卿、王姮

中 首 都 科 大 宣 武 院 神 內 科, 北 京

目的：對輕中度痴呆患者認知和行為障 二 方面的自知力損害情 進行初步研究。方法：輕中度痴呆患者66例，對照組20例，採用 痴呆病覺缺失問卷(Anosognosia Questionnaire-Dementia, AQ-D)對 受檢者及其知情者進行問卷調查。自知力損害得分以AQ-Dd表示。 結果：痴呆組患者自知力損害明顯。AQ-Dd得分与簡短精神狀態 量表(MMSE)、日常生活活 力量表(ADL)、臨床痴呆評定量表 (CDR)得分具有顯著相關性，其相關系數分別為： $r=-0.511$  ( $P<0.01$ )、  $r=0.174$  ( $P<0.05$ )、 $r=0.389$  ( $P<0.01$ )。但是自知力損害与性別、年齡、 教育年限和抑郁 顯著相關性。結論：痴呆患者自知力損害比較常 。疾病的嚴重程度与自知力損害密切相關， 痴呆的加重，自知 力損害程度也加重。不同 型的痴呆患者自知力損害 著變異。

## Provision of Package of Care Based on Needs Assessment

S11.1

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Caring a person with dementia requires a comprehensive model of care. Owing to the nature of disease, the care plan should be based on individual needs with short-term and long-term goals. Furthermore, the model of care should include the care of primary caregivers because majority of the primary caregivers providing "round the clock" care to the person with dementia would experience caregiving burden.

The comprehensive care package has been developed by a group of professional staff and support workers at Kin Chi Day Care Centre, St James Settlement since 2001. It has been revised through evidence-based practice and evaluation of the outcomes of intervention.

The presentation will illustrate the process of development of the package of care for persons with dementia and their family caregivers with evidence based. Open discussion will be expected to discuss the future development for dementia care in Hong Kong.

## Medical Care for Persons with Dementia in the Chinese Community of Sydney

S11.2

E.H.C. Tam

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The philosophy of the Australia's Aged Care System is to ensure the older Australians will receive support and care when they need it most, which in practice is relying on the informal support system (family/friends/volunteers) and the multi-faceted formal support system through the Commonwealth and State governments and charitable organisations, comprising medical (family doctors/medical specialists/geriatricians), hospital services, pharmaceutical benefits scheme. Aged Care Assessment Teams (ACAT), rehabilitation and extended care services, social day activities centres, home and community care packages (home help, personal care, meals-on-wheels, home nursing, community support groups etc), and respite/permanent residential care.

The care plans are increasingly focused on effective management

of dementia in people with culturally and linguistically diverse (CALD) backgrounds, particularly relevant to the Chinese community which is the largest ethnic group of people from Non-English Speaking Background (NESB) in Sydney.

The challenges include the clinician's barrier—diagnosis of dementia with competency by and be understood to the clinicians, the interpreter barrier, the patient/family/carer's barrier to understand and accept the diagnosis and to comply with the agreed medical treatment and care plan, and the grossly inadequate cultural and linguistic specific community support (for patients and carers) and residential services for the Chinese people with dementia in Sydney and nationwide.

### Effect of a One-Year Nursing Intervention on the Negative Emotions and Burden in Family Caregivers of Dementia Patients S11.3

S.M. Shang<sup>1</sup>, Q.S. Liu<sup>1</sup>, Z.W. Wang<sup>1</sup>, P. Yue<sup>1</sup>, Y. Fu<sup>2</sup>, X. Yu<sup>2</sup>, Y. Liu<sup>1</sup>, H. Zhang<sup>1</sup>

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**Objective:** To evaluate the effect of a 1-year nursing intervention on the negative emotions and burden suffered by the caregivers of homebound patients with dementia in order to provide guidance and evidence for the management of dementia patients and their caregivers in community.

**Methods:** Fifty-three participants were randomly assigned to control group and intervention group. The caregivers in intervention group received problem-based guidance of knowledge and skills, stress-coping management and effective utilization of social support by regular home visit, telephone follow-up and phone consultations. Caregivers' depression, anxiety, and burden were measured using the Self-rating Depression Scale (SDS), Self-rating Anxiety Scale (SAS) and Caregiver Burden Inventory (CBI) at 3-month intervals. The repeated measures of analysis of variance were used to analyze the data by SPSS12.0 statistical software. **Results:** In intervention group, caregivers' depression was significantly reduced after 3-month intervention ( $P < 0.05$ ) and remained stable till the end of the intervention; caregivers' anxiety was significantly reduced at 3 month and 9 month ( $P < 0.05$ ), and remained stable at 12 month; caregivers' burden was significantly reduced at 9 month ( $P < 0.05$ ), and remained stable at 12 month. By contrast, there was no change in the caregivers' depression, anxiety and burden in control group. **Conclusion:** Nursing intervention can help to reduce negative emotions and burden in family caregivers of homebound patients with dementia.

### A Glimpse of Palliative Care in the Older Persons—From the Eyes of a Geriatrician S12.1

N.S. Ng

Haven of Hope Hospital, Hong Kong SAR

Geriatricians serve the medical needs of the older persons from acute assessment and diagnosis/treatment to the management of chronic illnesses which are often irreversible and require a palliative rather than a curative approach. In later parts of the trajectory of progressive incurable diseases, relief of physical, emotional/psychological and spiritual sufferings becomes the prime focus, ending in a respectable death from receiving tailor-made end-of-life care.

Existing practices, attitudes and health care systems may influence the quality of palliative care provided to the older patients. A timely, team-oriented, longitudinal and collaborative approach may be a solution to improving current services. However, challenges to delivery of end-of-life care to the old need to be overcome in order to allow progress to be made.

In symptom assessment, it is important to bear in mind that many older patients are reluctant or unable to accurately report their symptoms. Pain assessment in the cognitively impaired or those with communication difficulties is an example. Elderly subjects are often given more medications than the young due to multiple concomitant illnesses. Polypharmacy and age-related pharmacokinetic/pharmacodynamic changes pose them to increased risk of adverse drug reactions. Non-pharmacologic therapy should always be considered as an alternative.

Medical goal-setting in the care of seniors with chronic illnesses may change with progress of the disease—from preserving independence and autonomy early in illness to symptom relief, addressing caregiver and placement needs later in advanced disease.

A 'good death' in the older people depends on availability, effectiveness of palliative care services which have to be flexible to address factors relevant to this age group such as multiple comorbidities, increasing frailty/protracted dying process and psychosocial vulnerability. Administrative and government policy support is essential to facilitate changes in the health care system.

### The Effects of a Combination of Caregivers Support Group and Cognitive Training Therapy in Dementia Patients from a Memory Clinic Population S12.2

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**Objectives:** To evaluate the impact of a combination of caregiver support group and cognitive training in dementia patients on behavioural and psychological symptoms and caregiver burden compared to a control group. **Methods:** Thirteen patients at home in the intervention group and 13 patients at home as controls were studied in the setting of an university hospital over a period of 1 year. Controls were matched for age, gender, dementia severity, living arrangement and medication. **Results:** There were no significant differences between the intervention and control groups neither after 3, 6, and 12 months' intervention. **Conclusions:** There is lack of a positive impact in alleviating caregiver burden or behavioural and psychological symptoms after intensive interventions; a multi-center design and larger sample sizes are necessary to be applied.

### Long-term Care and Palliative Care S12.3

W.W.C. Chu

Haven of Hope Nursing Home, Hong Kong SAR

Ageing population is a common phenomenon worldwide. There are increasing frail elderly persons with chronic illnesses and dependent states requiring long-term care support. To those who are in last phase of life a quality end-of-life care provision is therefore of paramount importance.

A good end-of-life care in older persons is a combination of various domains, notably of spiritual, psychosocial, and physical aspects. The exercise of autonomy, preservation of dignity, improvement in personal relationship, attainment in spiritual growth, and wellness in physical state are all considered to be highly desirable in a "Good Death". In recent decades death and dying has been becoming more institutionalized and over medically oriented. In Hong Kong, terminal elderly persons are often being transferred to hospital in their last phase of life. These older persons and their families have little choice on this matter. A good planning and implementation of a peaceful death would then pose a serious challenge to an acute hospital setting. This may produce additional stress not only to the dying persons and their loved ones, but also to the health care staff involved. Such practice of unnecessary hospital transfer may also result in an increased burden in the overall health care resources.

Haven of Hope Christian Service has pioneered the "End-of-Life Care Service" in nursing home in Hong Kong since 2000. The elderly residents and the families are given the information and choice on such care provision in the residential home. Regular support and counseling are provided to the residents, families and staff so that a soft approach to such aspect of care are conveyed. We have seen good rapport and satisfaction from residents and their families who have received the care provision. There is also enhancement in clinical skills, personhood, and team building among staff.

In the symposium we would share on the essential ingredients in providing a quality end-of-life care service in a residential home. As there are various domains of needs in the frail elders this would require a combination of care provision in a coordinated fashion. The education of death and dying is essential in healthcare training as well as in the general public. The person-centered approach and respect to life are emphasized.

C. Lam

*Haven of Hope Christian Service, Hong Kong SAR*

In Hong Kong, the prevalence of dementia in elderly Chinese aged 70 is 6.1% in previous study (HF Chiu et al, 1998). In view of the global ageing population and the increasing incidence of dementia, formal and informal carers for demented elderly are in high demand. The identification on dementia and the care of the carer is well addressed in the past few years.

Haven of Hope Nursing Home is a non-government organization that is serving 270 frail residents. Majority of the residents are suffering from moderate to severe stage of dementia. Fifty-four residents in advanced stage of dementia are looked after in the Intensive Dementia Care Unit.

In order to identify the attitude and the actual need of our staff in looking after dementia clients, a small study is conducted in the staffs who are working in the Advance Dementia Care Unit. Staffs who show interests in the scheduled "Professional Training Course for Dementia Client" are also invited to join the study before the course start. It is a study with open-ended question.

There is high response rate of the study. The result of the study shows education, training of staff's knowledge, skill and support in various areas from the employer are highly demanded. The result of the study is considered to form the direction of future staff training and development.

### Locating Missing Person Who Suffered from Senile Dementia in Cities Full of High-Rise Buildings

S13.1

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According to the news, there are people who suffer from senile dementia have gone missing or eloped from their homes. It takes a great deal of effort and resources to locate these patients in a reasonable time frame. A tracking system is introduced for locating these patients such that the amount of resources used can be drastically reduced. In principle, Global Positioning System (GPS) receivers can give a precise location fixed in a range of 10 m if the patient is in an outdoor location where satellite signals can be easily received. However, satellite signals can hardly be received properly in the over-populated areas in Hong Kong because of the surrounding tall and dense buildings. The situation is even hopeless if the patient is staying indoors, therefore locating services based on mobile phone network are employed in the tracking system with an accuracy of hundred meters depending on the cell size of the base station used. The tracking system consists of a device which makes use of four types of locating technologies, namely, GPS, mobile phone network, radio directional finding (RDF), and ultrasonic sensing. The device has a mobile phone module, a GPS receiver, a radio frequency (RF) beacon, and an ultrasonic beacon. The mobile phone module is used to remotely turn on the RF beacon and/or ultrasonic beacon such that the location of the patient can be precisely found by means of RDF techniques in a range of meters. It is because the locating services can give a rough estimate of the location of the mobile phone module even the patient is staying indoors. In addition, the mobile phone module can retrieve the position data from the associated GPS receiver such that a precise fix can be obtained if the patient is staying outdoors. This paper describes the tracking system in detail and the results obtained from field tests.

### Portable Multi-sensory Stimulation System

S13.2

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**Background:** Due to aging populations all over the world, more elderly are suffering from a disease called dementia which cannot be cured at the moment. Although there are providers of multi-sensory stimulation services in the market, all the existing services are archived by allowing patients to enter a specially designed room such as snoezelen room. We are a pioneer to develop a portable multi-sensory stimulation providing device. This allows therapists to take it to other places whenever and wherever they like. Aside from this, the effect of our design is not confined to a room. It can be used outdoor as well. **Methods:** This project has developed a portable, integrated multi-sensory stimulation apparatus which provides different stimuli including cognitive stimuli, visual stimuli, olfactory stimuli, tactile stimuli and auditory stimuli to users by making use of a memory game, optical fibres and a projector, an aroma diffuser, magic tactile boards and an audio delivery system respectively so as to prevent elderly from dementia, which may also be extended to help children with learning and behavioural disabilities and relieve stress. **Results:** A prototype of the portable multi-sensory stimulation has been built and tested which comprised a memory game, optical fibres, a projector, an aroma diffuser, a pair of magic tactile temperature boards and an audio delivery system. Further study will be needed to evaluate the performance of this device on person with dementia.

### Extensive Nuclear Localization of $\alpha$ -synuclein in Normal Rat Brain Neurons: an Immunohistochemical and Immunoelectron Microscopic Study Using a New Monoclonal Antibody

S13.3

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Alpha-synuclein, a 140 amino acid protein richly expressed in the brain, has been strongly implicated in the pathogenesis of neurodegenerative diseases, especially Parkinson's disease. Although the protein was initially nominated as synuclein for its localization in both presynaptic terminals and portions of nuclear envelope in the electric organ of the Pacific electric ray *Torpedo californica*, the nuclear location has not been consistently confirmed in mammal brain neurons in subsequent studies. In the present study, by using recombinant human  $\alpha$ -synuclein to immune Balb/c mice, we successfully obtained a hybridoma clone that produced monoclonal antibody specifically against  $\alpha$ -synuclein. Epitope mapping using phase polypeptide display showed that the antibody recognized the 115-121 amino acid residues of  $\alpha$ -synuclein, a specific sequence for this protein. Western blot analysis demonstrated that the antibody detected a 19kD protein in the whole cell homogenates of the rat or human brain tissues. This molecular size was identical to that reported for this molecule. Immunohistochemical staining of the normal rat brain using the antibody revealed that the  $\alpha$ -synuclein immunoreactivity was not only localized in the presynaptic terminals but also in the nuclei of many regions of brain neurons. The nuclear localization of  $\alpha$ -synuclein was reconfirmed by Western blot analysis using nuclear extract in which the same size of protein as 19kD was detected. Immunoelectron microscope study using colloidal gold as probes indicated that  $\alpha$ -synuclein was not only distributed in the portion of nuclear envelope, but also inside the nucleus. We have made

systemic mapping of the nuclear positive neurons in the rat brain. We found that the nuclear positive neurons were distributed in very extensive brain regions, including layer II-layer VI of cerebral cortex, olfactory bulb, hippocampus, thalamus, hypothalamus, striatum, cerebellum, midbrain and medulla oblongata. Although previous studies have suggested that  $\alpha$ -synuclein may translocate into neuronal nucleus upon insults, this is the first report that this molecule is localized in the nucleus of so extensive neurons in the normal brain. The extensive localization of  $\alpha$ -synuclein in the nucleus of neurons indicates a physiological role of this molecule in gene regulation, which deserves extensive investigation.

### APP17 對老年性痴呆模型小鼠 習記憶能力及海 神 細胞線粒體自由基水平 化的影

S13.4

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目的：觀察APP17 ( $\beta$ -amyloid precursor protein, APP, 319-335 段)對APP轉基因小(APP695V717I) 習、記憶能力及海 神 細胞線粒體自由基水平 化的影。方法：3月齡的APP695轉基因小鼠 機分為模型組和APP17 治療組，正常對照組採用月齡和性別相匹配的C57BL/6J小鼠。APP17 治療組給予皮下注射APP17，每只每次0.34 $\mu$ g，每周3次；模型組和正常對照組給予等量的生理鹽水；25周后形成模型。應用水迷宮試驗觀察小鼠 習、記憶功能的 化，應用羥胺法和硫代巴比妥酸(TBA)比色法分別檢測海 神 細胞線粒體抗氧化 活性及自由基水平。結果：(1)水迷宮結果顯示，模型組小鼠存在明顯的 習和記憶功能障，其第3 d、4 d、5 d游完全程的時 (93.22 $\pm$ 16.35、86.73 $\pm$ 20.26、77.13 $\pm$ 29.35)秒、和錯誤反應次數(6.63 $\pm$ 2.16、5.81 $\pm$ 2.13、5.33 $\pm$ 1.41)均較正常對照組(70.89 $\pm$ 20.19、61.25 $\pm$ 21.88、54.63 $\pm$ 16.92)和(5.01 $\pm$ 1.93、2.97 $\pm$ 0.96、2.31 $\pm$ 1.01)增多(P<0.05)；APP17 治療組小鼠的行為 障 明顯輕於模型組(P<0.05)，其上述的水迷宮檢測結果與正常對照組比較 顯著性差異。(2)與正常對照組小鼠海 神 細胞線粒體超氧化物歧化(SOD)活性(103.65 $\pm$ 21.92)和丙二醛(MDA)含量(5.69 $\pm$ 2.01)比較，模型組SOD活性(49.11 $\pm$ 8.73)明顯降低(P<0.01)，MDA含量(13.23 $\pm$ 3.37)顯著增加(P<0.01)；APP17 治療組檢測結果與正常對照組接近，海 神 細胞線粒體SOD活性(94.28 $\pm$ 15.81)高于模型組(P<0.01)，MDA含量(4.97 $\pm$ 1.13)低于模型組(P<0.01)。結論：(1) APP695轉基因小鼠存在 習和記憶功能障；而且其海 神 細胞線粒體氧化應激反應明顯加劇。(2) APP17 可能具有抑制氧化應激反應、提高腦組 抗氧化能力的作用，進而保 習和記憶功能。

### 衰老過程中蛋白質的共性生化改 及相關研究

S13.5

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越來越多的研究表明， 物和人 的衰老過程是先天(遺傳)因子和后天(環境)因素相互作用，生死拮抗的過程。

為了更加深刻地認識衰老過程的 質，本文提出，在衰老研究中看基因突 不如看蛋白質聚 的觀：指出基因突 往往致病，造成病理性退行性(如癩 和線粒體基因突 疾病等)，不 真正衰老表征；蛋白質聚 則 所不在， 移默化，可造成 臨床症狀的生理性老化衍(如脂褐素積聚，神 維纏結，血管硬化，皮膚起皺等)，最終量 引起質 變，導致所謂真正衰老改 。

我們提出，在衰老研究中看因果不如看過程的思維方式：看生理生化因果循環，越看越複雜，越看越眼花，千 萬緒，斬不斷理還亂；看蛋白質生化損 積聚的淨過程(如，形成AGES/ALEs的生化形成過程)，則 絡分明，結果明確， 物及人 與增齡相關的主要增損性生化反應及過程可一目了然。

我們認為自由基損傷生物大分子，自由基是外因， 于衰老衍 的 因子和加速因子；各種生化分子結構中的煙-羥-羧-羧功能 的衍，以致最終產生二氧化碳的過程，是生化大分子的共性氧化衍，是生命物質本身的 化，是衰老改 的(內因)內在物質基礎。之，由抵抗應激、新陳代謝、蛋白更新和機體穩態等 的基因組成的網絡扮演 高等 物衰老病死的先天性制約因子的主要角色，而自 進行的自由基氧化和非 糖基化等生化副反應導致的損傷改 則為生物體衰老的主要后天驅 因子。由這些生化副反應以及老年色素研究的最新成果所推舉而出的羧基毒化衰老理論及其近期的展突破了當前“ 生物大分子(主要 基因和蛋白質)看生命

秘”的思維局限，進而 生化反應的共性元素，“分子功能”的水平，或所謂“ 分子水平”，看人 生理性衰老的共同分子機制，值此，衰老過程的生化本質基本水落石出。

## FREE PAPER SESSION

### Stable Expression of Amyloid Protein Precursor Gene in SH-EP1 Cells Transfected with Nicotinic Acetylcholine Receptor $\alpha_4\beta_2$ Subtype Gene

FP1.1

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Alzheimer's disease (AD) is one of the most common neurodegenerative diseases that affects the elderly. Neuropathologically, AD brains are characterized by the accumulation of extracellular amyloid plaques, mainly formed by a small peptide called  $\beta$ -amyloid (A $\beta$ ). Nicotinic acetylcholine receptor (nAChR) is the classical receptor of a family of ligand-gated cation channels. Among various nAChRs subtypes confirmed,  $\alpha_4\beta_2$  subtype is the most affluent in central nervous system. Many researches indicated that nAChRs played roles in development of AD by influencing processing of amyloid protein precursor. To search for the subtype that involved in processing of amyloid protein precursor, we constructed a co-transfection cell model as tool. Human APP695 gene was subcloned into pcDNA3.1-neomycin vector, and transfected using liposome into SH-EP1 cells which have been stably transfected with  $\alpha_4$  and  $\beta_2$  nAChRs subunits. Cells were maintained in medium with 0.5 mg/ml G-418 to ensure stable expression of phenotype. By limiting dilution assay, we obtained the single clones of transfected cells. As the clones grew, cells were collected for reverse transcription-PCR (RT-PCR) to select positive clones. Western-blotting was conducted to confirm the expression of positive clones. The result of our study indicates that we constructed a co-transfection cell model of amyloid protein precursor gene,  $\alpha_4$  gene and  $\beta_2$  gene successfully.

### Cholesterol Regulates $\beta$ - and $\gamma$ -Secretase Activities for A $\beta$ Production in Alzheimer's Disease

FP1.2

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**Background and Objectives:** Alzheimer's disease (AD) is characterized by A $\beta$  overproduction in brain. A $\beta$  is derived from cleavage of  $\beta$ -amyloid precursor protein (APP). Sequential APP cleavage by  $\beta$ - $\gamma$ -secretases produces A $\beta$ , while cleavage of APP by  $\alpha$ - $\gamma$ -secretases does not yield A $\beta$ . About 5% AD is inherited with mutation(s) in genes encoding APP or  $\gamma$ -secretase. However, 95% AD are sporadic and the mechanism that large amounts of A $\beta$  are produced in these patients is unknown. Recent studies suggest that sporadic AD is related to altered cholesterol metabolism. Since  $\beta$ - and  $\gamma$ -secretases are located in cholesterol-rich domains of cell membrane, we hypothesize that level of cellular cholesterol affects  $\beta$ - and  $\gamma$ -secretase activities in APP processing for A $\beta$  production. **Methods:** Human brain samples, N2a cells, cholesterol and  $\beta$ - $\gamma$ -secretase assays, ApoE allele typing, and transcription factor (TF) arrays are used. **Results:** Our studies show: 1) Cholesterol level is 27.15% higher in AD than age-matched non-demented (ND) brain (P<0.01). 2)  $\beta$ - $\gamma$ -secretase activities are significantly higher in AD than ND brain. 3) Addition of cholesterol strongly stimulates  $\beta$ - and  $\gamma$ -secretase activities in brain homogenates of ND and AD. 4) Addition of 10-80  $\mu$ M cholesterol to culture media or to in vitro assays significantly increases  $\beta$ - and  $\gamma$ -secretase activities in N2a cells. 5) Cholesterol efflux reduces  $\beta$ - and  $\gamma$ -secretase activities and A $\beta$  production in N2a cells. 6) 46% AD patients had ApoE4 alleles while none of the ND had ApoE4 alleles. 7) Profiling of 54 TFs shows that activities of several TFs involving cholesterol/lipid metabolism were significantly changed in AD brain. **Conclusions:** These results suggest that cholesterol

metabolism is altered in AD brain and cholesterol is an important factor that regulates  $\beta$ - and  $\gamma$ -secretase activities for A $\beta$  production.

### Carer Support Services in Australia—the Challenges Faced by Chinese Carers in a Culturally Diverse Society FP1.3

A. Cheng

Australian Nursing Home Foundation—ANHF Aged Services, Australia

#### Population profile of culturally and linguistically diverse communities

A substantial proportion of Australian population aged over 60 are migrants from culturally and linguistically diverse (CALD), with a variety of cultural customs, traditions and values. Currently, some 12.4% of Australians with dementia—around one in eight—do not speak English at home.

#### Community services available for carers of people with dementia

Government assist carers via Commonwealth Carelink Centre, Commonwealth Carer Respite Centre, Carer Resource Centre and National Dementia Helpline to provide timely, quality information, carer education and support that is both culturally and linguistically sensitive. They provide information, support and advice through freecall number.

The Government recognises the valuable contribution made by carers and is committed to provide ongoing funding to support carers through in-home, out-of-home, short- and long-term respite, flexible residential respite, day respite centre, emergency respite, etc. Other supportive services such as counselling, home help, information and education, home nursing, home modification, physiotherapy, podiatry, speech therapy, occupational therapy, food service, transport, medical aids and equipments are available to support carers in their caring roles. Carer support groups running in different locality provide emotional support, information and advice to enable them to perform their role effectively and confidently.

#### Challenges faced by Chinese carers

Although there are a lot of services available for carers, most of the Chinese carers are still struggling in keeping their demented family members to remain in their own homes due to poor access, language and communication problems, lack of culturally and linguistically appropriate services. As language and communication are important factors in service delivery, so too are the variety of cultural customs, traditions and value practiced by people from CALD communities. This reminds all aged care services need to be responsive to the particular profiles of their non-English speaking populations. Examples will be given from ANHF Aged Service to tackle these difficulties.

### A Preliminary Report on the Efficacy of Functional Enhancement Program in Maintaining Functional Ability of Elders with Dementia FP1.4

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**Background and Objectives:** Progressive deterioration in everyday functioning is the hallmark of the onset of clinical dementia. Apart from increasing forgetfulness, loss of independence is frequently associated with a sense of despair and uselessness. This study aims to evaluate if a Functional Enhancement Program (FEP) would be effective in maintaining functional ability and improving mood state of Chinese older persons suffering from dementia. **Methods:** Participants with dementia were recruited from old age homes. They were randomized into active treatment (Tx) and control (C) groups for the FEP. The Tx group focused on the daily tasks considered most significant by the subjects. The control group training was related to a random selection of tasks considered suitable for the level of disability of the subjects. Functional Enhancement Program was conducted by occupational therapists with a group treatment with thrice weekly sessions for 6 weeks. Baseline assessments included Mini-Mental State Examination, Cornell depression scale for dementia (CSDD), Chinese Neuropsychiatric Inventory (CNPI) and Disability Assessment for Dementia (DAD). After the FEP, reassessment was conducted at the

following week. **Results:** Thirty-three subjects were recruited into the FEP (17 test versus 16 control groups). The mean MMSE score at entry was 16.5 (3.8). At the end of the FEP, there was no significant difference in MMSE and CSDD scores in both Tx and C groups (paired *t* test, *P*=n.s.). A decrease in CNPI depression score in the Tx group, but not in C group, was found (0.35[3.09] versus -0.06[1.65], *t*=0.63, *P*=n.s.). A significant improvement in the Basic ADL initiation score was found in the Tx group (paired *t*=2.9, *P*=0.01). Similar improvement was not found in the control group (paired *t*=1.0, *P*= n.s.). **Conclusions:** In this preliminary analysis, a trend for improvement in mood state and motivation to perform ADL was found in demented elders undergoing active functional training. Further observation with larger sample size and longer-term observation will bring more definitive information for the benefits of the FEP.

### Association of Prostaglandin-Endoperoxide Synthase 2 Polymorphisms and Alzheimer's Disease in Chinese FP1.5

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**Background and Objectives:** Alzheimer's disease (AD) is the most common form of dementia among the elderly. Cyclooxygenase-2 (COX-2, encoded by the gene prostaglandin-endoperoxide synthase 2, PTGS2) is a key enzyme in the conversion of arachidonic acid to prostaglandins. The prostaglandins produced by COX-2 are involved in inflammation and pain response in different tissues in the body. Enhanced COX-2 expression had been shown in regions of brains from patients with AD. We therefore investigated the association of polymorphisms on PTGS2 gene and the risk of AD in the Chinese population. **Methods:** 257 AD patients and 244 age-matched healthy Chinese subjects were recruited in this case-control study. Among the 38 SNPs from the HapMap database and data from SNP500Cancer database, IVS5-275T>G and Ex10+837T>C in addition to three tagging SNPs were chosen to comprehensively cover the genetic variations in the PTGS2 gene. **Results:** We found that promoter SNP (-2319) and SNP at the 3' region (Ex10+837T>C) of PTGS2 gene were associated with the risk of AD (*P*=0.01 and *P*=0.03, respectively). Carriers of T allele had a 1.5 fold increase in the risk of AD. **Conclusion:** This study suggested that PTGS2 gene was a predisposition gene and arachidonic acid metabolism might be involved in the pathogenesis of AD. The results presented here provided further evidence to support a role of inflammation in the development and progression of AD.

### Obesity and Cognitive Level Among the Baltimore Epidemiologic Catchment Area Cohort FP2.1

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**Objectives:** Since obesity is linked with insulin-resistance, it may be associated with dementia independent of cardiovascular factors. Our objective is to explore in a community-based cohort the association between obesity, defined by BMI (weight [kg]/height [m]<sup>2</sup>) using NHLBI criteria, and level of cognition, as assessed by MMSE score. **Methods:** We report analyses of cross-sectional data from the latest (fourth) wave of the Baltimore Epidemiologic Catchment Area (ECA) cohort, which comprises 1071 East Baltimore adults surveyed in 2004-2005. Bivariate and multivariate logistic regression models were controlled for age, gender, education, race/ethnicity, exercise participation, health status, as well as cardiovascular conditions and risk factors. **Results:** Of our total sample, 5.1% had low cognitive levels (MMSE<24), 31.6% were obese, and 26.8% were older than 65 years. Obesity (defined as BMI  $\geq$  30) was not associated with level of cognition (OR: 0.74, 95%CI: [0.38-1.46]). No association was found in additional analyses using models with stratified BMI status (normal, overweight, obese I and obese II) or with

the specific domains of executive function and immediate recall memory, as measured by the MMSE. **Conclusions:** Obesity does not appear to be independently associated with level of cognition. These results are in disagreement with existing research that has indicated both an adverse and protective association of obesity and level of cognition. Limitations of this study include its cross-sectional design and lack of clinical cognitive assessments. Future research should utilize more extensive cognitive measures to investigate a prospective relationship between obesity and the different domains of cognitive function.

#### 活体靶向淀粉 蛋白PET顯像用小分子探針研究

FP2.2

鄭明

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利用小分子探針作為A $\beta$ 聚集體的PET顯像劑是 上早期診斷AD研究的熱 。 [<sup>18</sup>F] FDDNP和[<sup>11</sup>C]PIB已進入臨床研究。由於PIB的優良性質和C-11半衰期很短，使用更 命的核素（如F-18）標記成為新的熱 。本文以2-氨基苯并 唑 化合物為原料，通過 性 件下水解，脫水環化，部分化合物去甲基化反應，合成了一系列6-取代BTA 化合物，測定比較了6種化合物與AD死者腦勻漿的親和力 弱，k<sub>i</sub>值均在1nm左右。同時以PIB為前體，[<sup>18</sup>F] FETOTs為中 體在 性 件下選 擇性合成了[<sup>18</sup>F] O-FET-PIB。体外放射性自顯影和模型大鼠（右腦注射A $\beta$ ）的microPET研究表明該 在左右腦分布有明顯差異，但組 分布 驗中未 著 別。

#### Isoform Difference of apolipoprotein E proteolysis by Cathepsin D: Implication for Alzheimer's Disease

FP2.3

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**Objectives:** Proteolysis of apolipoprotein E (ApoE) may be involved in the pathogenesis of Alzheimer's disease. Cathepsin D may be a candidate aspartic protease involved in ApoE proteolysis in human brain. In current study, we examined whether Cathepsin D can proteolysis ApoE and characterized the proteolysis of ApoE by Cathepsin D. **Methods:** The human recombinant ApoE3 and ApoE4 cleavage products by human liver Cathepsin D under the different conditions were analyzed by using Western blotting. **Results:** Three-hour incubation of human Cathepsin D with recombinant ApoE3 and ApoE4 resulted in partial cleavage of both ApoE3 and ApoE4 and the release of a C-terminal fragment. The degradation of ApoE3 and ApoE4 was completely inhibited by addition of the aspartic protease inhibitor pepstatin A. Cathepsin D cleaved recombinant ApoE3 and ApoE4 in a time and dose-dependent manner. Optimal cleavage was seen at pH 4.5. ApoE4 was more susceptible to proteolysis than ApoE3. **Conclusions:** Human liver Cathepsin D aspartic protease can cleave ApoE3 and ApoE4. The proteolysis of ApoE mediated by Cathepsin D displayed an isoform difference between ApoE3 and ApoE4. Therefore if the role of proteolysis of ApoE in AD is merited, the strategy to inhibit ApoE proteolysis by specific and selective aspartic inhibitors to prevent the production of ApoE fragments may provide novel therapeutic approaches to the treatment of AD.

#### A Population-based Study of the Prevalence of Behavioural and Psychological Symptoms of Dementia in Hong Kong

FP2.4

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**Background and Objectives:** Dementia has emerged as an important healthcare issue. It is estimated that as many as 4% of the local elderly population have dementia. Behavioural and psychological symptoms of dementia (BPSD) are integral components of dementia and are associated with poorer prognosis, increased carer burden, higher costs of care, and

premature institutionalization. However, there is a paucity of data on the prevalence of BPSD among the local community-dwelling older adults. This study aims at investigating the population-based prevalence of BPSD and their relationship with dementia severity in Hong Kong. **Methods:** In the first phase of the study, a random sample of 6100 community-dwelling individuals older than 60 years old across Hong Kong were assessed by trained interviewers using screening instruments including Mini-Mental State Examination (MMSE). Psychiatrists conducted thorough assessment on 931 subjects in phase two. Psychiatric diagnoses were established according to standardized criteria. Clinical Dementia Rating Scale (CDR) was administered to assess the severity of dementia whereas Neuropsychiatric Inventory (NPI) was used to assess the level of BPSD. In addition, carer stress was determined by NPI-Distress Scale (NPI-D). **Results:** The prevalence of BPSD among individuals with mild cognitive impairment and dementia in Hong Kong were 36.3% and 58.2% respectively. Among them, apathy (28%), depression (22.4%), and night-time behavioural disturbances (22.4%) were the most common neuropsychiatric symptoms in dementia subjects. The mean NPI total scores were 2.13, 4.21, 9.79 and 14.38 for subjects at CDR stages 0.5, 1, 2, and 3 respectively. Using factor analysis with varimax rotation, a three-factor structure was demonstrated, namely activity disturbances, psychotic symptoms, and motivation/mood disturbances. Meanwhile, the majority of carers experienced stress associated with BPSD as exemplified by the NPI-D scores. **Conclusions:** BPSD are common among community-dwelling older adults with mild cognitive impairment and dementia in Hong Kong. BPSD aggravate as disease progresses with the highest total NPI scores reported in those with moderate and severe dementia. In view of their high prevalence and potentially significant effects on dementia persons and their caregivers, early detection and management of BPSD should be fostered.

#### A Case Study Approach to Engaging Frail-aged Nursing Home Residents in Advance Care Planning

FP2.5

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**Background and Objectives:** Discussion concerning end of life seems unfavourable in the Chinese society. This study aims to test the feasibility of an advance care planning program entitled "Let Me Talk". The main task of this program is to engage the residents in a dialogue for making explicit about their life and health concerns, life views and end-of-life care preferences. **Methods:** Yin's case study method was used as the research strategy to analyse the factors that facilitate and impede the program implementation among the frail aged residents. Each individual was seen as a single case, the embedded units were quality-of-life concerns and end-of-life care preferences. Nursing home resident, aged 65 or above, mentally sound, had impairing health and partially dependent were recruited. Conversations in the "Let Me Talk" were documented for qualitative content analysis, and quality-of-life concerns and care preferences were measured by means of structured questionnaire at three time points over 12 months. This paper reports the findings of the first 6 months. **Results:** Thirty-one participants had participated in the "Let Me Talk" program. Twenty-three participants had explicitly articulated their care preferences, either wishing to extend their own autonomy over the future care or indicating their preference to let the doctor decide. Of these 23 elderly people, only seven were willing to let their family members know about their preference. Four participants remained indecisive about their future care. It is noteworthy that four participants refrained from any discussion about end-of-life care preference. **Conclusions:** Although advance care planning is innovative concept among the local frail aged persons, most participants were open in discussing end-of-life issues. They also treasured the chance to share their personal experiences and views throughout the program. This program is instrumental to help the elders communicate their end-of-life care preferences to family and care providers.

#### Clinical Features and Rate of Cognitive Decline in Chinese Alzheimer's Disease and Vascular Dementia Patients

FP2.6

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**Background and Objective:** To compare the clinical features and rate of cognitive decline in Alzheimer's disease (AD) and vascular dementia (VaD). **Methods:** Subjects with AD and VaD in Memory Clinic of Queen Mary Hospital from 1997 to 2006 were studied. Mini-Mental State Examination (MMSE), clinical dementia rating (CDR), geriatric depression score (GDS), Hachinski score, Barthel Index (BI) and Lawton score were measured on presentation. The rate of cognitive decline was estimated by calculating the annualized rate of change in MMSE scores. **Results:** There were 403 AD and 136 VaD. Mean age ( $\pm$ SD) were 78.8 $\pm$ 8.3 and 77.7 $\pm$ 7.9 years respectively ( $P=0.209$ ). There were more female in AD (71.7% vs 58.1%,  $P=0.003$ ). Time from symptom to clinic visit were 41.0 $\pm$ 28.3 months in AD and 33.4 $\pm$ 39.5 months in VaD ( $P=0.074$ ). The mean CDR ( $\pm$ SD) was 1.30 $\pm$ 0.70 in AD and 1.29 $\pm$ 0.74 in VaD ( $P=0.92$ ). AD scored a lower MMSE, GDS and Hachinski score than VaD (MMSE, 15.2 $\pm$ 5.2 vs 16.6 $\pm$ 5.4; GDS, 7.1 $\pm$ 5.7 vs 8.8 $\pm$ 7.3; Hachinski score, 1.1 $\pm$ 1.7 vs 6.1 $\pm$ 3.5; all  $P<0.01$ ). The functional scores were higher in AD (BI, 18.3 $\pm$ 3.4 vs 16.8 $\pm$ 4.6; Lawton score, 5.7 $\pm$ 2.4 vs 4.8 $\pm$ 3.2; all  $P<0.01$ ). The average annual rate of decline in MMSE was 0.9 $\pm$ 3.7 point in AD and 1.2 $\pm$ 3.2 point in VaD ( $P=0.485$ ). The rate of decline in AD with and without use of drug treatment were 0.75 $\pm$ 3.4 point and 1.0 $\pm$ 4.0 point respectively ( $P=0.511$ ). **Conclusion:** AD and VaD had similar disease stage on presentation. VaD were more physically impaired and had more depressive symptoms. Rate of cognitive decline was similar at approximately 1 point of MMSE per year.

## LUNCHEON WORKSHOP

### Management of Memory Problems in General Practice

LW1.1

H. Brodaty

Professor of Age Care Mental Health, Primary Dementia Collaborative Research Centre, University of New South Wales, Sydney, Australia

Memory problems are ubiquitous in older people and will become even more common with the ageing of the population. Surveys of community dwelling elders and of general practitioners (GPs) indicate that there are difficulties in the identification and management of dementia in primary care.

This presentation will include (i) A 7-step algorithm to help with diagnosis of memory loss occurring in older people presenting themselves to GPs, including how to differentiate normal ageing from early Alzheimer's disease (AD); (ii) Principles of management of dementia for GPs; (iii) Management of dementia by stage of disease; (iv) Focus on pharmacological management of AD; and (v) Latest treatments available.

### Management of Dementia Patients by Family Physicians in Private Sector—Experience from the Hong Kong Alzheimer's Disease Association and Evangel Hospital Collaboration Project

LW1.2

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<sup>2</sup> Honorary Secretary, Hong Kong Alzheimer's Disease Association

In 2005 the Hong Kong Alzheimer's Disease Association (HKADA) entered into an agreement with Evangel Hospital (EH) in that private family physicians of EH would provide medical care to cognitively impaired clients referred from the Early Detection Service of HKADA. From October 2005 to August 2006, 16 clients thus referred attended the Family Clinic of EH.

This presentation will include: (1) Background information of the collaboration model; (2) Results of cognitive assessment and investigations; (3) Diagnostic spectrum of cases; (4) Management and treatment of patients; and (5) Individual case presentations to illustrate learning points.

## Principles of Neuroimaging for Dementia

LW2.1

C.R. Jack

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**Background:** Various pathologies contribute to dementia in the elderly population. Although the most common cause of dementia is Alzheimer's disease (AD), other pathologies contribute to dementia in the elderly population as well. These include cerebrovascular disease, dementia with Lewy bodies (DLB), and frontotemporal dementia (FTD). The ideal biomarker for dementing disorders would be a direct in vivo measurement of the specific pathologic process. Most neurodegenerative dementias are associated with deposition of abnormal proteins— $\beta$ -amyloid and tau in AD, tau and ubiquitin in some forms of FTD, and alpha-synuclein in DLB. Cerebrovascular disease also seems to play a significant role in determining the development of dementia in individual subjects. Major advances have been made recently in labeling of amyloid plaques and/or plaques and neurofibrillary tangles with nuclear medicine-based probes. However magnetic resonance imaging (MRI) can also provide specific information as to the pathologic processes underlying dementia. **Methods:** The various imaging modalities that are sensitive to some aspect of pathology contributing to dementia will be reviewed. This includes positron emission tomography (PET) amyloid labeling compounds, structural MRI, magnetic resonance spectroscopy, FGD PET, diffusion tensor MRI, and functional MRI. **Results and Conclusions:** Each of these modalities contributes potentially unique information illuminating various aspects of the pathologies which underlie dementia in the elderly population.

### Case Discussion on Mild Cognitive Impairment/Dementia Syndrome

LW2.2

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Diagnosing various dementia syndromes, especially at its earliest manifestation, can be a difficult task. Various structural and functional neuroimaging techniques including magnetic resonance imaging, magnetic resonance spectroscopy, single-photon emission computed tomography, or positron-emission tomography, have proved to be an invaluable tool in the evaluation of cognitive disorders. In this workshop, different cases of mild cognitive impairment (MCI)/dementia syndromes along with its imaging findings will be presented and discussed. The objective of this workshop is to illustrate how neuroimaging can assist in diagnosing MCI/dementia syndromes.

## EVENING SYMPOSIUM

### Capacity Test and Finance Management

ES1

C.C.Y. Chiu

Chairperson, Guardianship Board, Hong Kong SAR

The Guardianship Board is an independent quasi-judicial tribunal and independent of other Government departments of the HKSAR, empowered to make orders appointing guardians for adults who are unable to make decisions about substantial proportion of matters of their personal circumstances: welfare, residence, medical or financial affairs because they have a mental incapacity (mentally incapacitated persons). It was established on 1 February 1999 under Part IVB of the Mental Health Ordinance (Cap 136). It is a multi-disciplinary Board consisting of the Chairperson and 56 volunteer members, including lawyers (Panel A), doctors, social workers, nurse specialist, occupational therapist and psychologists (Panel B), and persons having personal

experience of the mentally incapacitated (Panel C). It is supported by the Secretariat, which consists of the Chairperson, the Board Secretary, Assistant Board Secretary, and two other staff. The Chairperson is appointed by the Chief Executive of the HKSAR Government. Hong Kong SAR, a common law jurisdiction, is believed to be the first jurisdiction in the whole of Asia to have a guardianship system since 1999.

Like any courts of protective jurisdiction, the Guardianship Board is mindful of its duty to satisfy itself of the incapacity threshold of the concerned person before receiving him/her into guardianship. Thus, the law of capacity (mental competence) will be examined in the context of UK case *Re: C (1993)* together with the latest legislative developments in United Kingdom in March 2005 when the Mental Capacity Act was passed. Practical difficulties relating to assessment of financial capacity of a concerned person will be highlighted and the legal requirements Mental Health Ordinance of HKSAR will be addressed. The relevance of lawyers' practice to the law of capacity will be explained by drawing particular references to the UK cases (*Pesticcio v Huet and others [2003]*; *Williams v Williams [2003]*) and the law relating to testamentary capacity (*Banks v Goodfellow [1870]*; *re: Sabatini [1970]*).

The aim of the guardianship regime is to protect and promote the interests of mentally incapacitated persons. The development of the Board in the past 8 years shows that guardianship clients or subjects are predominantly elders with some form of mental incapacities. The numbers of applications on elderly (i.e. age on or above 60 years old) of recent years are 77.6% in 2004, 76.4% in 2005 and 73.3% in 2006.

Finances of the subject person are always a predominant concern to the Guardianship Board as it affects the long-term welfare planning. The financial powers of a legal guardian will be mentioned alongside with other enduring tools and court receivership/committeeship in local context and on comparative basis (UK and New South Wales, Australia will be examined).

Regarding protection, the Guardianship system is now accepted as a form of ready means with which the welfare of the vulnerable people with cognitive deficits is protected and promoted, particularly as against all kinds of abuses. The Board received six and eight applications on financial abuse in 2005 and 2006 respectively. This presentation will also centre upon the role of Guardianship Board in handling financial abuse cases of mentally incapacitated adult.

## Advance Directives and Treatment-limiting Decision-making in the End of Life ES2

**S.M.C. Pang**

*School of Nursing, The Hong Kong Polytechnic University, Hong Kong SAR*

To uphold the principle of respect for self-determination, many countries have legislated advance directives for medical care. Advance directive is a documentation of a person's will regarding his/her preference for limiting life-sustaining treatment at the end stage of life. The signed document would ensure that if or when such a medical situation were to occur, the medical doctor would follow the person's advance directive in making medical decisions about his/her care. However, the implementation of an advance directive is difficult because people may change decisions over time and in different life conditions. It is also difficult for people to imagine all the treatment options available in the future. Whether tube feeding is one of the life-sustaining treatments same as cardiopulmonary resuscitation and assisted mechanical ventilation remains controversial despite the issue has been debated over decades. Based on the findings of some local opinion surveys, this paper will analyze the attitude and knowledge of Hong Kong general public and health professionals towards advance directives and life-sustaining treatments and its implication on clinical practice. In view of the significant discrepancies between the health professionals and lay public regarding their views on the issue of treatment-limitation in end-of-life care, emotionally laden conflicts embedded with unresolved ethical dilemmas will inevitably occur when such decisions are to be made in the clinical context at the time that the patient is approaching life closure. To minimize such conflicts at later days, health professionals need to take a proactive stance to engage the public in conversations about advance care planning.

## Dementia for the Non-healthcare Professions ES3

**D.L.K. Dai**

*Chairman, Hong Kong Alzheimer's Disease Association, Hong Kong SAR*

Dementia is prevalent among the elders of Hong Kong. A recent survey revealed that 10% of persons aged 70 years and above suffered from the condition, and a significant proportion of affected elders did not know they had the condition. Dementia has heterogeneous causes, with Alzheimer's disease comprising about 70%, vascular cause 20%, and the remaining other non-Alzheimer's entities. Dementing illnesses mainly occur in elders, but young persons in their mid-ages can also be affected. The latter may be fronto-temporal dementia which affects the emotional control and speech of the person at an early stage. Medical treatment is available for Alzheimer's disease in the early and moderate stages. Diagnosis is possible even in the subclinical stage now with advanced imaging. However, dementia affects an individual beyond the medical and cognitive domains, and the family becomes over-burdened. With earlier recognition, more accurate diagnosis and rising expectations from patient and the family, legal and ethical considerations come into the management plans at different stages of the disease. These issues revolve around mental competence and autonomy in decision-making. The medical and legal professions are often called to examine a client's "mental soundness", which refers to "mental competence" on a legal sense and "mental capacity" on the medical side. These are often misunderstood by the professions. Mental competence is a legal definition and refers to a person's capacity to make decisions and perform certain acts, based on five established legal standards; and in extreme cases, the "competence" is settled in courts of law. There is an underlying presumption of capacity to exercise choices in a person until proven otherwise. Mental capacity on the other hand is a clinical status evaluated by a healthcare professional. Both capacities are situation-specific and each situation under question should be examined on its own right. The assessor must be aware of executive brain functions such as emotional control, planning, judgement; and communication which are affected at different stages in different diseases. Although challenges to a person's mental competence are often made on legal basis, evidence often depends on expert medical assessment. With the ageing population, increasing affluence and public transparency, the legal and medical professionals will be increasingly called to give evidence on "mental soundness". This will find application in consent to treatment, advance directives, withdrawal of life-sustaining treatments, and participation as a research subject; and on the legal side, challenge to a testamentary capacity for a will. Decision-making is affected to different degrees in a person from the mild to the severe stages of the illness in diverse issues. The time is ripe for a dialogue in these issues between the healthcare and non-healthcare professions engaged in care of the old and cognitively impaired.

## PRE-CONFERENCE WORKSHOP

### Cognitive Assessment—from Conventional to Innovative Pre-C1

**D.W.K. Man**

*Department of Rehabilitation Sciences, The Hong Kong Polytechnic University, Hong Kong SAR*

In this presentation, an outline of chronological development of cognitive assessments would be firstly presented and an analysis of the relative merits of different mode of assessments would be compared and contrast is provided. The assessment approach can be conceptualized from a conventional end (typical formal neuropsychological tests, behavioural assessment and situational assessment) to innovative end (more flexible informal test, computer-aided and artificial-intelligent assessment protocols).

Special highlight would be geared towards the application of cognitive assessment for diagnosis, as outcome measures and for interventions monitor for elderly people including those with dementia at different stages/according to contemporary classification systems.

The innovative dimension of cognitive assessment development and application would be tied to the rapid development of computer or information technology which may include: (a) Computer-aided assessment protocol for basic and functional cognitive skills; (b) Tele-cognitive assessment including e-questionnaire and e-tests; (c) Virtual-reality environment application; and (d) Use of artificial intelligence or rule-based reasoning.

Discussion would be centred on the need of theory-driven assessment in the full spectrum of conventional and innovative cognitive assessments, the debate of generalization issues as well as the inter-link between the assessment approaches with conventional and innovative interventions.

## Use of Cognitive Assessments in Dementia Research Pre-C2

**J.C.C. Chung**

*Department of Rehabilitation Sciences, The Hong Kong Polytechnic University, Hong Kong SAR*

Use of cognitive assessments as one of the outcome measures is not uncommon in dementia practice research. Frequently asked questions related to this issue include which cognitive assessments should be used, how to select among cognitive assessments, and when to conduct the assessments. This seminar will discuss the factors to be considered when choosing cognitive assessments and basic research design for outcome research in dementia care.

## Cognitive Assessment—from Hospital to Community Practice Pre-C3

**G.Y.Y. Lee**

*Occupational Therapy Department, Kwai Chung Hospital, Hong Kong SAR*

Community Psychogeriatric Teams have been established in the Hong Kong Hospital Authority since 1993. There are significant development from the hospital based on patient service, day patient service, out-patient service, memory clinics to community innovative services (collaborated between the Hong Kong Hospital Authority and non-government organizations or initiated by non-government organizations such as the Hong Kong Alzheimer's Disease Association). There is a great move of psychogeriatric care services towards community and outreaching care model in the past decade.

In the presentation, the spectrum of service provided by occupational therapists and the multi-disciplinary team will be discussed. There will be special highlight on the commonly adopted cognitive assessment tools employed in the elderly and dementia services in Hong Kong, based on the survey done by health care professionals in 2006 and also the recommendations made by clinical experts. Besides, some practical consideration in employing cognitive assessment tools in the hospital-based and community-based practice will also be discussed, including assessment using validated assessment tools or clinical observations.

Finally, appropriate validated Chinese cognitive assessment tools might be selected for different elderly clients in Hong Kong, with respect to their functioning at different stages of the dementia illness. Professionals as a team might further develop community-based innovative service to improve the cognitive rehabilitation service for the elderly/dementia clients in the future.

## POST-CONFERENCE WORKSHOP

### Brain Stimulation in Neuropsychiatry Post-C1

**P. Sachdev**

*School of Psychiatry, University of New South Wales and Neuropsychiatric Institute, Prince of Wales Hospital, Sydney, Australia*

**Objective:** To describe the novel brain stimulation techniques currently in use in the investigation and treatment of neuropsychiatric disorders regarding their efficacy and potential future applications. **Methods:** A selective review of the literature concerning transcranial magnetic stimulation (TMS), vagus nerve stimulation (VNS), deep brain stimulation

(DBS), and transcranial direct current stimulation (tDCS) was conducted using Medline, Current Contents, EMBASE and literature known to the author. **Results:** A summary of each procedure is provided giving a succinct overview of efficacy, current applications and possible future indications. In particular, TMS has quickly established itself as a useful investigational tool and is emerging as a possible antidepressant therapy. Similarly, VNS has been applied successfully in the management of intractable epilepsy and is undergoing evaluation in the management of patients with treatment-resistant depression. DBS has shown significant promise in the treatment of Parkinson's disease and may have use in the management of obsessive-compulsive disorder and treatment resistant depression. Transcranial direct current stimulation is an old technique witnessing a resurgence, but its investigation is still at an early stage. **Conclusions:** Novel brain stimulation techniques are currently being used to study brain function in health and disease, and hold great promise for neuropsychiatry in the future.

## Neuropsychiatry in Stroke Post-C2

**W.K. Tang**

*The Chinese University of Hong Kong, Hong Kong SAR*

### Prestroke and Poststroke Dementia (PRSD and PSDE)

The frequency of PRSD in the local stroke population was 12.3%, which is similar to the figures for Caucasian populations. The independent predictors of PRSD were cerebral atrophy, age, atrial fibrillation, and previous transient ischemic attack.

Poststroke dementia is common among Chinese stroke patients in Hong Kong, and its frequency (19.6%) is comparable to the figures that are found in Caucasian populations. The clinical determinants of PSDE, after the exclusion of patients with PRSD, are premorbid factors in terms of the level of cognitive function and level of education, and stroke-related factors that include the severity of stroke, leukoaraiosis, and bilateral lesions.

### Poststroke Depression (PSD)

The frequency of PSD was 16 to 17%. A female gender, a high Modified Life Event score, and subcortical and anterior cerebral artery lesions were independent risk factors for PSD, and a high Lubben Social Network score was a protective factor. Therefore, both psychosocial factors and the location of cerebrovascular lesions play an important role in the development of PSD. Poststroke depression in Chinese patients seems to have a favorable short-term outcome.

### Poststroke Emotional Incontinence (PSEI)

The frequency of PSEI, according to the Kim's criterion, is 6.3%. Univariate analysis found that PSEI was associated with age, previous TIA, National Institute of Health Stroke Scale total score, cortical infarcts, and frontal-cortical infarcts. Multivariate logistic regression suggested that past TIA and frontal cortical infarcts were independent risk factors for PSEI.

## Virtual Reality-based Memory Training for Persons with Mild Cognitive Impairment Post-C3

**D.W.K. Man**

*Department of Rehabilitation Sciences, The Hong Kong Polytechnic University, Hong Kong SAR*

**Background:** Application and evaluation of an advanced form of computer technology—virtual reality (VR) has been increasing for persons with cognitive impairments. The aim of this project was to develop and evaluate a non-immersive type, VR-based memory training programme in enhancing community living skills for persons with mild cognitive impairment (MCI). **Methods:** A pre- and post-test quasi-experimental design was adopted. Twenty-seven elderly subjects (mean age=80.3) were successfully recruited from local geriatric day centers and randomly assigned to either a VR or non-VR group. They were medically stable and at the stage of MCI as indicated by the score of 0.5 by the Clinical Dementia Rating Scale and free from physical, neurological and visual impairment. Outcome measures included the Multifactorial Memory Questionnaire, Fuld Object Memory Test, Hong Kong Lawton Instrumental Activities of Daily Living, session-based computer scoring to record the level of accomplishment, accuracy and

time required. Focus groups were also organized to gather feedback from subjects for their use of strategies in community living activities. A non-immersive, VR-based memory training programme was developed based on two selected scenarios: home and convenience shop. Similar training structure and content in the form of a training manual was constructed for non-VR group and delivered by therapists. **Results:** Significant improvements were found for the Fuld Object Memory Test and Multifactorial Memory Test by repeated measures of ANOVA and focus group feedback evaluation. **Conclusion:** Initial findings seem to suggest positive results from VR-based memory training and for application to community living skills. This innovative and tailor-made intervention program might meet different cognitive needs of the elderly living in the community.

#### Normal-abnormal Functioning of Inhibitory Control Post-C4

**T. Lee**

*The University of Hong Kong, Hong Kong SAR*

Human brain is known for its ability to inhibit goal irrelevant impulses in accordance with the intentions of the individual and the demands of the situation. In doing so the most advantageous choice of behavior essential to human survival could be selected. To understand the neural correlates of inhibitory control, as well as the effect of normal aging or neurological conditions on such regulatory function, a program of behavioral and functional imaging studies have been conducted. Findings suggest that a coordinated effort of brain regions that are closely interacting, but nevertheless anatomically dissociable, is essential to effective inhibitory control. For individuals presented with impulsive behavior, attenuation

of activity in the anterior cingulate and the additional recruitment of the right inferior parietal region were noted. Further theoretical and clinical implications of our findings will be discussed.

#### Conduction Dysphasia in Patients with Acute Cerebrovascular Accident Post-C5

**H.M. Ma, D.L.K. Dai**

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**Objective:** To determine the prevalence of conduction dysphasia in patients with acute cerebrovascular accident (CVA) and its associated factors. **Methods:** A nested case-controlled study was conducted in acute stroke unit (ASU) of a tertiary teaching hospital serving a 1.2 million population. We retrospectively examined the radiological report of computed tomography or magnetic resonance imaging (MRI) scan of brain on 100 consecutive patients admitted to the ASU in October and November 2006. Inclusion criteria included those admitted for the first episode of CVA with infarct over left superior posterior temporal gyrus shown on MRI brain. Patients admitted for recurrent CVA were excluded. Each patient was matched to two patients, one with lesion over right superior temporal gyrus and the other with lesion over left anterior superior temporal gyrus. These patients were assessed by experienced clinicians and speech therapists to demonstrate the clinical characteristics of conductive dysphasia. **Results:** The prevalence of conductive dysphasia in acute stroke patients is approximately 5%. (preliminary) **Conclusion:** A large-scale study is warranted to establish the prevalence of conductive dysphasia in patients with acute CVA. (preliminary)