

## 2<sup>nd</sup> Asian Society Against Dementia Congress and 3<sup>rd</sup> Annual meeting of Taiwan Dementia Society

Taiwan Dementia Society (TDS) and Asian Society Against Dementia (ASAD) jointly hosted the 2nd Conference of ASAD and the 3rd Annual Conference of TDS at Chung-Ho Memorial Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan from October 17th to 19th, 2008. The combined conference also co-hosted by other 11 professional societies, International Working Group on Harmonization of Dementia Drug Guidelines, Taiwan Neurological Society, Taiwan Alzheimer's Disease Association, and others. Three official institutions, National Science Council, Department of Health, Executive Yuan, and Kaohsiung City Government, also hosted the congress together. The Congress has come to its fruitful close, and the 3rd ASAD Congress will be held in Korea on Oct 11th to 13th, 2009.

### CURRENT STATUS OF DEMENTIA IN ASIAN COUNTRY

**CURRENT STATUS OF DEMENTIA IN JAPAN: SOME LEGAL ASPECTS.** AKIRA HOMMA (*Director, Department for Dementia Intervention, Tokyo Metropolitan Institute of Gerontology, President, Japan Society for Geriatric Psychiatry, President, Japan Society for Dementia Care, President, Asian Society Against Dementia*)

According to the recent projection on the number of persons with dementia from 2005 to 2035 by Awata and associates, more than 2 million persons with dementia will increase up to more than 4.5 million. Although the care management for them is covered by the long-term care insurance started in 2000, the medical treatment is done by the conventional national medical insurance. Due to the increase of the payment for the care cost along with the steeply increased eligible persons for the long-term care insurance, the government is encouraging the home care for them. However, the most major issue is that the infrastructures and the formal services to support them are apparently insufficient, especially for persons with dementia. The Ministry of Health, Labor and Welfare recently organized the taskforce committee to make the long-term care insurance system durable in the future. The second major issue is that low recognition and awareness of dementia even in nowadays. Such low recognition will easily result in the delay of the diagnosis and the treatment. In the urban areas of Japan, the referral rate of persons with very early stage of dementia is increasing. In my out-patient clinic, not a few patients visit by themselves with a complaint of memory loss. However, in rural areas, which comprise major part of Japan, many patients with miscellaneous BPSD finally visit the medical facilities with their families. Another major issue is the medical treatment of demented persons with surgical complications. Some other issues which have to be solved will be discussed in the context of supporting dignity or no discrimination.

**CURRENT STATUS OF DEMENTIA IN TAIWAN.** CHING-KUAN LIU (*Professor and chairman of Neurology, Kaohsiung Medical University, President of Taiwan Dementia Society, Vice Superintendent, Kaohsiung Medical University Chung-Ho Memorial Hospital*)

The aged population in Taiwan has increased rapidly, from 7.03% in 1993 to 10.4% in 2006 and the increasing rate is one of the leading countries worldwide. According to our previous study, we adjust with the current age structure. According to current age structure in Taiwan, the age-standardized PR (ASPR) was 5.8%. AD (53.7%, PR=2.0%, ASPR=3.5%) was the most common cause of dementia, followed by VaD (PR=0.9%, ASPR=1.1%), and mixed dementia. According to current age structure in Taiwan, the age-standardized IR (ASIR) was 1.80% per year. AD (ASIR=0.86%) was the most common cause of dementia, followed by VaD (ASIR=0.43%) and mixed dementia. After adjusting for sex, increasing age was significantly associated with total dementia and AD ( $p<0.01$ ). Illiteracy was associated with a marginally increased risk for total dementia  $aRR=1.59$   $p<0.1$  as was female sex for AD ( $aRR=1.92$ ,  $p<0.1$ ). The two-year mortality rate was high among the demented (48% in total dementia, 38% in AD, and 60% in VaD). Mild cognitive impairment (MCI) is a probable precursor of dementia for its significantly higher developing rate to AD compared with general aged population. The overall prevalence rate of MCI is 10.02%, and the higher prevalent rate is noted in illiterate subjects: 10.70% compared with the literate: 9.33%. It was estimated that there were 140,000 patients with dementia among the 23 million inhabitants of Taiwan in 2005, and the number of dementia patients will increase to 660,000 by 2050. Currently, there are 43,000 newly diagnosed demented patients every year and will increase to 200,000 every year by 2050. The Taiwan Geriatric and Gerontology Society is authorized by the government to support local hospitals to transform from a general hospital into geriatric facilities. Besides, the Taiwan Geriatric & Gerontology society is also collaborated with Taiwan Dementia Society and Taiwan Geriatric Psychiatry Society in training geriatricians

in neuropsychiatry disorders including dementia and cognitive impairment in order to act as the first-line doctors to denitrify dementia patients. TDS and TADA are also busy with organizing training program for their members of physician, nurses, therapeutics as well as caregivers.

**THE CURRENT STATUS OF DEMENTIA IN ASIA: PHILIPPINE SITUATION.** SIMEON M. MARASIGAN (*Professor, Department of Neurology and Psychiatry, Faculty of Medicine and Surgery, University of Santo Tomas, Chairman, Department of Neurology & Psychiatry, University of Santo Tomas Hospital*)

Recognition of dementia in the Philippines as a national concern is still in its infancy stage when compared to most advanced countries. But because of the growing population of the elderly people and the popularity of Alzheimer Disease many Filipinos are now aware of how serious and dreadful the disease is. Over the past decade, dementia research despite many limitations progressed remarkably. At the forefront of this development is the Philippine Neurological Association which included a dementia council in its active committees. Linking with the National Nutrition Survey, it estimated the overall prevalence rate of dementia at 11.5% (60-69 years old) and 15.6% (beyond 70). Dementia screening tools and neuropsychological assessment have been locally translated and validated. Hospital surveys and demographic data about AD and other dementias became available. Memory clinics and centers were established in big hospitals with the development of dementia neuroimaging protocols. The availability of treatment dramatically enhanced help-seeking behavior of patients with dementia. Establishment of dementia specific home care facilities and institutions though is very slow. This is probably because of strong family ties and filial piety. Advocacy groups and medical societies for dementia are increasing in number. The Dementia Society of the Philippines (DSP) is now 6 years-old. Its annual Philippine Conference in Alzheimer Disease brought to the Philippines respected dementia specialists and researchers. Through a workshop in 2004 with the allied specialist group, The DSP developed an educational module on early surveillance in dementia with recommendations in the pharmacologic and non-pharmacologic treatment. The module is now being used by the society in reaching out to general practitioners. On October 20-21, 2006, the DSP hosted the 4th Asia-Pacific Conference of the International working group on harmonization of dementia drug guidelines with the main goal of bridging clinical trials in Asia which is vital in the development of dementia drugs in the region. This congress also witnessed the birth of the Asian Society Against Dementia (ASAD).

**THE RAGAMA DEMENTIA RISK IDENTIFICATION STUDY: INTERIM ANALYSIS AT TWO YEARS.** ASITA DE SILVA (*The Ragama Health Study Group, University of Kelaniya, Sri Lanka, Clinical Pharmacologist & Director, Clinical Trials Unit, Department of Pharmacology, Faculty of Medicine, University of Kelaniya, Ragama, SRI LANKA*)

Background: Risk factors for cardiovascular disease are established modifiable risks for dementia. Sri Lanka has a national prevalence rate of 18% for hypertension and 36% for obesity. With a rapidly aging population where the percentage of those over 60 years is expected to reach 21% within the next ten years, Sri Lanka has a dementia prevalence rate similar to that reported from the West. In the absence of definitive treatment, strategies to delay onset or reduce risk for dementia would be greatly beneficial. Objective: To determine whether cardiovascular disease risk factors are associated with an increased risk for dementia and AD in Sri Lanka and to develop a cohort for long-term observational and interventional studies. Methods: This prospective cognitive study is being conducted as part of a large, community-based epidemiological survey being conducted in Ragama to establish diagnostic criteria for metabolic syndrome (Ragama Health Study). 2470 adults 45-65 years of age identified by a stratified random sampling technique underwent detailed lifestyle and significant event history, physical examination, cognitive assessment with MMSE, and biochemical analysis of blood. Of this, 496 subjects who had a MMSE score of  $\leq 21$  (maximum 30), were recruited for long-term follow up. As a sub-study, another cohort of 43 patients with mild-moderate AD identified during this survey was

prospectively assessed. Advice on physical activity and treatment for hypertension were indicated were given by the principal investigator. All patients were on specific drug treatment for AD. Results: Baseline data (cohort profile) for the 496 subjects (males 42.3%) are reported here [mean (range)]; age 55.3 (45-65) yrs, MMSE 18 (0-21), BMI 24.2 (15.5-35.6), systolic BP 138.2 (88-238) mmHg, fasting blood sugar 117.4 (65-473) mg/dl, serum cholesterol 216.5 (112-381) mg/dl, serum triglycerides 130.9 (36-428) mg/dl, and serum insulin 8.7 (0.6-61)  $\mu$ u/ml. Discussion: This cohort will be followed up prospectively with detailed cognitive assessments, blood analyses, and brain imaging annually. The sub-study revealed that regular physical activity and control of blood pressure have positive effects on cognitive function in AD patients. In the absence of disease modifying drug therapy, lifestyle interventions and control of vascular risk factors are important to delay cognitive decline in AD. The ultimate aim of this study is to reduce dementia burden by identifying modifiable risk factors in order to introduce appropriate interventions.

**CURRENT STATUS OF DEMENTIA IN INDONESIA.** PAULUS ANAM ONG  
(Department of Neurology, Hasan Sadikin Hospital /Padjajaran University Bandung Indonesia)

As one of the countries in Asia, Indonesia also faces the problem of a rapidly growing population. The estimate doubled number of elderly within 25 years from 13 million people (in 2000) to 25 million people (in 2025) will cause massive medical, social, and economic problems due to increase of dementia cases in the future. Despite the ravage it may cause, dementia is often under-recognized. Mild memory loss is not easily recognized due to culture related behavior, stigma of dementia and ignorance. The availability of service is another important factor of dementia care. Primary care physicians are not confident to make the diagnosis of dementia. The limited number and city concentrated of specialists in dementia make the referral system more difficult. Currently there are only four memory clinics in the entire country. The trend of change from extended family to nuclear family as the most often family in urban areas complicate the home care programs in Indonesia. Families caregivers are limited in number while professional caregivers are hard to find and unaffordable to most families. Temporary institutions for dementia patients are not available in Indonesia and many nursing homes do not accept elderly patients with dementia. A nationwide commitment is needed to overcome the complicated problems of dementia in Indonesia. Early detection and management of dementia must be put as one of the national healthcare priorities. More attention and funding must be allocated to provide training and referral system for the primary healthcare centers. Currently dementia awareness campaign, teams training for primary health care centers are ongoing. More memory clinics are expected to be set up in the coming years.

## EVIDENCE-BASED OT IN CARE OF PEOPLE WITH DEMENTIA

**OCCUPATION-ORIENTED COGNITION TRAINING FOR PERSON WITH MILD DEMENTIA.** HUNG-HSUN KO (Occupational therapist, The St. Joseph Home For Alzheimer's Disease and Related Dementia, The Catholic Foundation of Alzheimer's Disease and Related Dementia, Taipei, Taiwan)

Objective: Cognitive problem is the main symptom of dementia, it also results in great psychological and social impact of patients and family. Although at present we believe that the people have the brain plasticity across the life span, in addition to drug treatment, supplemented by cognitive training to improve the cognitive situation. However, past experience found that only cognitive training, patients often had low motivation. According to occupational therapy theory, occupation is a medium itself. Previous study also found that activity participation made more cognitive network. This study will present our finding through occupational-oriented cognitive training for mild dementia. Design: randomized, pretest-posttest, no-treatment controlled and single-blinded. Setting: In the first stage, the treatment group received cognitive training once a week for 10 times. In the second stage twice a week for another 10 times. The controls were provided with general consultation services. Participant: people with mild dementia living in community. Intervention: This study apply occupational-based cognitive training programs. Every program designed by experienced occupational therapist and based on participant's occupation. Results: We found that mild dementia patients and other patients with moderate to severe significantly different characteristics, activities must be compatible with the design process so that their characteristics and the attitude change the face of dementia, their families and the participation of members of the support groups is also an important factor. In addition, put cognitive elements into their activities, with the participation of a better motivation. Conclusion: Experience from this group found that mild dementia still retain a certain self-awareness and the perceived ability, they need more support and warm-up before the cognitive training. Of course, the attitude of facing dementia and support to the families of members of the Get better results. Although this study has not yet ended, but our finding can also provide the experiences promoting more local, more people to help patients with mild dementia.

**EVIDENCE-BASED COGNITIVE TRAINING PROGRAM FOR THE COMMUNITY WELL ELDERLY.** ATHENA YIJUNG TSAI<sup>1,2</sup>, CHEN-SHENG CHEN<sup>2</sup>, MING-JEN YANG<sup>2</sup>, CHUN-FU LAN<sup>1</sup> (1. National Yang-Ming University, Taiwan; 2. Kaohsiung Medical University, Taiwan; 1 Lecturer, School of Occupational Therapy, Kaohsiung Medical University; 1. MA, Department of Occupational Therapy, New York University; 1 PhD candidate, Institute of Public Health, National Yang-Ming University)

Health promotion or specific protection to prevent the incidence of disease deserves solid evidence support as in the clinical trials. In the previous version of Cochrane review protocol, cognition-based approaches of preventing or slowing progression of dementia were classified into : cognitive training (CT), memory training (MT), cognitive stimulation (CS) and bibliotherapy (BT) (Cameron MH, 2007). CT applies tasks requiring various elements of cognition such as memory, attention, problem-solving... etc and uses practice to improve cognition. MT practices tasks focusing on memory performance. CS involves group activities and discussion to enhance cognitive and social functions in general. In BT, participants receive reading materials which instruct them the strategies and knowledge of cognition improvement. To conduct a community-based evidence cognitive training program requires: 1) planning of the program, 2) recruiting participants, 3) evaluation and training, 4) reminding and further education. Experience of a community-based cognitive training program will be shared.

**WHICH OCCUPATIONAL THERAPY INTERVENTIONS OPTIMIZE DAILY LIVING FOR PEOPLE WITH DEMENTIA?** MARY EGAN, L LETTIS, C O'TOOLE , J BERENYI, M EDWARDS, K MOROS, C O'NEILL, S HOBSON, MITCHELL (Associate Professor, School of Rehabilitation Sciences, University of Ottawa, Ottawa, Ontario, Canada)

Objectives: Evidence-based practice has been defined by Sackett and colleagues as "the conscientious, judicious use of current best evidence in making decisions about the care of individual patients". The objective of this project was to identify and review the best evidence regarding the effectiveness of occupational therapy interventions to improve performance of or satisfaction with the accomplishment of functional activities among persons with dementia. Design: We searched the literature from 1990-2005 for quantitative studies of the effectiveness of interventions that could be carried out by an occupational therapist to improve performance of or satisfaction with daily activities among persons with dementia. Study designs accepted included randomized controlled trials, nonrandomized controlled trials, pretest post test studies, and multiple baseline repeated measures studies. Relevant studies were admitted to the review if they were published in English or French and at least 50% of subjects had dementia. Functional outcomes of interest included: mobility, transfers, bed mobility, travel, transportation, community mobility, wayfinding, grooming, feeding, dressing, toileting, washing, bathing, home maintenance, housework, meal preparation, money management, banking, medication use, telephone use, volunteer activities, paid work, grandparenting/child care, pet care, reading, watching television, crafts, socialization. Agitation, behavior disturbance, cognitive function, physical capacities (for example, muscle strength) and caregiver burden were not deemed functional outcomes and were not included. Setting: Interventions could be carried out in the community or in institutional settings. Results: Studies were identified and reviewed that examined methods to enhance the following five groups of functional activities: ambulation, communication and socialization, eating, activities of daily living and leisure. The results were as follows: Ambulation: walk-and-talk groups do not appear to have an impact on client ambulation; Communication and socialization: There was preliminary evidence to support the effectiveness of validation therapy and music therapy to improve communication and socialization in individuals with dementia. There was preliminary, high-quality evidence to support the effectiveness of cognitive stimulation interventions, learning therapy, Snoezelen programs, specific AD day programs and "The Breakfast Club" program to improve communication and socialization. The use of dolls or toys and reality-orientation therapy to improve communication and socialization in this population was not supported by the studies identified; Eating: There was low quality evidence to support the use of music to enhance eating in individuals with dementia, through increasing the amount of time spent at the table, the amount of food consumed, and decreasing agitation, irritability, depressed mood and fear-panic behaviours. There were several studies, of both high and low quality evidence, which supported the use of behavioural interventions (such as verbal prompts and positive reinforcement) to enhance eating. While the research does provide some support for the use of contextual interventions and animal-assisted therapy, there was not sufficient evidence to make a conclusive statement about the effectiveness of these interventions; Activities of daily living (basic and instrumental): There was consistent support in the literature (from both high and low quality studies) for the use of functional skills training programs and home-based occupational therapy interventions for improving performance of basic and instrumental activities of daily living. There was preliminary, high-quality evidence to support the effectiveness of family interventions, cognitive stimulation, and "The Breakfast Club" program to improve performance of activities of daily living; Leisure: There was limited evidence that resident-assisted Montessori-based programming may improve leisure engagement among persons with dementia. Conclusions: The results of this review revealed few well-controlled studies of interventions to enhance performance of and satisfaction with functional activities among persons with dementia. The available research supported the use of functional training programs, behavioral and family interventions. Further research using designs with good experimental control and consideration of different cultural contexts are recommended.

## EARLY DIAGNOSIS AND ASSESSMENT OF DEMENTIA

### LATEST UPDATES IN ALZHEIMER'S DISEASE AND MILD COGNITIVE IMPAIRMENT. RACHELLE S. DOODY (Professor, Department of Neurology, Baylor College of Medicine)

Objectives: to briefly review the standard treatment of AD as well as the experimental work relevant to AD and MCI. Design: Review of published and ongoing clinical studies and clinical trials. Setting: Academic research centers. Participants: patients with AD by standardized criteria. MCI will be discussed in terms of evolving definitions. Intervention: clinical trials will be mentioned. Measurements: cognitive, global, functional and neuropsychiatric measures. Results: MCI criteria continue to evolve, but most clinically identified cases will likely progress to AD, whereas community based cases are less likely to progress. The evidence base does not currently justify treatment of MCI with antidementia drugs. AD treatment is evolving with the addition of dimebon, bapineuzamab, beta and gamma secretase inhibitors, rage inhibitors, and nutraceuticals as potential therapeutic agents. Conclusion: AD is now well-established as a treatable disease, whereas the timing and desired treatments for MCI remain elusive.

### DIAGNOSIS OF ALZHEIMER'S DISEASE IN ITS PRE-DEMENTIA STAGE. SERGE GAUTHIER (McGill Center for Studies in Aging, Douglas Mental Health Institute, Montreal, Canada. Professor, Department of Departments of Psychiatry, Neurology & Neurosurgery, Medicine McGill University, Director, Alzheimer Disease and Related Disorders Unit, McGill Centre for Studies in Aging, Douglas Mental Health University Institute)

Objective: to diagnose Alzheimer's disease (AD) in its earliest possible stage in order to treat this condition more effectively. Design: definition of diagnostic criteria based on an expert meeting followed by validation from existing database and through prospective studies. Results: research diagnostic criteria were published (Lancet Neurology 2007, 6: 734-746) with emphasis on the need for (1) early and significant episodic memory impairment, (2) at least one abnormal biomarker among structural neuroimaging with MRI, molecular neuroimaging with PET, and CSF analysis for amyloid  $\beta$  and tau proteins. A progress report was published (Lancet Neurology 2008, 7: 668-670), and discussions took place during the International Conference on Alzheimer's Disease in Chicago, August 2008, and during the 1st Conference of Clinical Trials on Alzheimer's Disease in Montpellier, September 2008. Conclusions: it is premature to use the proposed research diagnostic criteria for pre-dementia AD in clinical practice until full validation has taken place for the most useful biomarkers, assessment of the risk of catastrophic reaction to the diagnosis in persons with full insight into their medical condition, and evidence-based treatments are available. On the other hand the availability of such criteria can lead to clinical trials in a subgroup of patients currently labeled with "Mild Cognitive impairment" with a potential regulatory label of "very early AD". The definition of the most appropriate efficacy outcomes in this population should be given high priority.

### COMPREHENSIVE GERIATRIC ASSESSMENT AND DEMENTIA. DING-CHENG (DERRICK) CHAN (Departments of Geriatrics and Gerontology, National Taiwan University Hospital)

Comprehensive geriatric assessment (CGA) is a "multidimensional and interdisciplinary diagnostic process to identify the needs and plans of care, and to improve outcomes of frail older people". Clearly-defined goals are necessary for the success of CGA. However, the goals are different in each case depending on location of program implementation, complexity of the medical problem, and intensity of the assessment. A core CGA team includes a geriatrician, a nurse, and a social worker. Physical and occupational therapists, pharmacists, dietitians, psychologists, psychiatrists, dentists are invited if necessary. Patients and their families are considered essential parts of the interdisciplinary CGA team. A standard CGA usually include the following 4 domains: Functional status is evaluated with Activities of Daily Living (ADLs), Instrumental Activities of Daily Living (IADLs), and mobility (eg: Timed Up and Go test). Mental health is assessed with tools to screen for delirium, dementia, and depression. Physical health evaluation usually encompasses detailed medical history and physical exams, medication review, screening for visual and hearing impairments, nutritional assessments, and screening for several geriatric syndromes such as fall and gait disturbances, incontinences, and frailty. Finally, socio-environmental domain usually addresses availability of support system, caregiver burden, advanced directives, economic wellbeing, environmental safety and other relevant issues. Individualized plan is created after interdisciplinary team meeting form healthcare professionals and evidences showed that CGA may reduce mortality, lengths of hospital stay, hospital readmission, nursing home admission, and improve functional performance. Several studies showed that CGA could be cost neutral if appropriate candidates are selected. Assessment of cognitive function is an essential part of CGA. Identification of cognitive impairments through CGA has been linked to outcomes of cancer and surgical patients. Memory problem is a common reason for initiating a CGA process in geriatric practices. However, the roles of CGA on demented patients are yet to be defined. One study reported the associations between Mini-Mental Status Exam (MMSE) scores and physical functioning, depression scores, comorbidities, nutritional status, number of geriatric syndromes, and number of medication uses among female demented patients after a CGA process. However, whether the plans

from CGA improve outcomes of demented elders are not certain. Traditionally, a memory clinic is a point of referral for patient with cognitive problems to get comprehensive assessments for early diagnosis and appropriate managements. While CGA addresses broad ranges of problems for frail elders, memory clinics focus on in depth evaluations and managements of dementia-related issues. Since most multidisciplinary memory clinics are staffed with geriatricians, adding CGA screening to standard evaluation process for patients with cognitive impairments would probably identify new problems and improve patient outcomes.

### EARLY DIAGNOSIS OF DEMENTIA: EXPERIENCE IN GERIATRIC CLINICS. CHIN-YING CHEN<sup>1,2</sup>, MHSC, KK LEUNG<sup>1,3</sup>, CY CHEN<sup>4</sup> (1. Department of Family Medicine, National Taiwan University Hospital; 2. Department of Geriatrics and Gerontology, National Taiwan University Hospital; 3. Department of Family Medicine, National Taiwan University; 4. Division of Gerontology, National Health Research Institute)

Although there is no proven benefit to screening all asymptomatic older individuals for dementia, the importance and clinical implication of early diagnosis of dementia could not be underestimated. It was because dementia is one of the common geriatric syndromes and dementia affects the motivation, ability and independency of the elderly. The geriatric clinic in this study is staffed with a geriatrician and a nurse. The patients were referred to a geriatric clinic either by their primary care physicians, their family members or by themselves due to geriatric syndromes or multiple co-morbidities. A battery of examination including: review of the cognitive complains, Mini-Mental State Examination (MMSE), Clocking Drawing Test (CDT), and Instrumental Activity of Daily Living (IADL) were used for the detection of dementia. A series of laboratory examination were done to exclude correctable causes of dementia. Dementia was suspected for a MMSE score less than 24 in a patient with more than six years of education and for a MMSE score of less than 20 in those with less than six years of education. Those who were suspected with dementia were referred to a neurologist for brain image study, definite diagnosis and certification of dementia. The result of our study revealed that a score of six in an 8-item scale including three item recall, attention and calculation had a sensitivity of 94.9% and a specificity of 59.1% in the detection of dementia. The 8-item scale was better than any of the followings such as: a score of two in three item recall (51.3%/87.3%), a score of one in three item recall (83.3%/53.6%), CDT by Watson method (39.0%/96.9%), CDT by Manos method (46.9%/96.9%), Mini-Cog with CDT by Watson (53.7%/95.5%), Mini-Cog with CDT by Manos (56.1 %/96.9%), a score of less than three in attention/calculation test (74.7%/77.3%), impairment of transportation or medication in IADL (67.2%/90.6%), and any impairment in IADL (77.2%/67.9%). Cognitive impairment noted by family members, the patient and family members, and the patient alone have positive predictive values of 69.9%, 49.9%, and 38.2% respectively in the identification of people with dementia. Our findings revealed that cognitive impairment noted by family members and a score of less than 6 in the 8-item scale can be used as a simple tool for the screening of early dementia.

## NEUROIMAGING IN DEMENTIA

### DIFFUSION TENSOR IMAGE STUDY IN NORMAL AGING POPULATION. JUNG-LUNG HSU (Department of Neurology, Shin Kong WHS Memorial Hospital, Taipei, Taiwan, Institute of Biomedical Engineering, National Taiwan University, Taipei, Taiwan)

The changes of cerebral white matter in relation to aging have been explored by diffusion tensor imaging (DTI) methods, showing specific changes both globally and regionally. A summary of these studies shows that age-related changes of FA or MD are localized to several regions. FA decreases with age and significant changes have been demonstrated in the anterior corpus callosum, both the anterior and the posterior limb of internal capsule, the posterior periventricular regions, and the deep frontal regions. Also, the FA increases in the bilateral putamen and the cingulate gyrus. On the other hand, the MD increases in the anterior and posterior periventricular regions and the anterior corpus callosum. However, the relationship between aging and cerebral white matter is complex and may not necessarily be linear as assumed in most previous studies. In this DTI study, we applied higher order regression models to assess potentially more complex nonlinear changes of white matter diffusion properties with aging. A total of 346 subjects (25 to 81 years old) were included in this analysis, and the results showed that the average global mean diffusivity (MD) as a function of age was best fitted by a quadratic order model, whereas the mean global fractional anisotropy (FA) was described optimally by a linearly decreasing function. The MD also had a larger adjusted R-square than the FA, suggesting that the MD could be a better biomarker in the aging study. The regional analysis showed that FA had a significant age-related linear decrease in the anterior corpus callosum, the bilateral internal capsule and the periventricular regions. On the other hand, the decrease of FA in the body of corpus callosum was found to be quadratic. The MD and eigenvalues were positively related to aging in several regions including the anterior corpus callosum, the bilateral frontal and periventricular regions, the bilateral thalamus, and the cerebellum. More than half of the regions were best fitted by quadratic or higher order associations. The difference between axial and transverse eigenvalues was distributed in the bilateral frontal and temporal subcortical regions, the corpus callosum, and the thalamus, suggesting that age-related white matter changes in these late-myelinating regions could be related to the loss of perpendicular diffusivity.

**NEUROIMAGING STUDY OF WHITE MATTER CHANGE IN DEMENTIA.** YA-FANG CHEN<sup>1</sup>, TA-FU CHEN<sup>2</sup>, TING-WEN TSANG<sup>2</sup>, MAU-SUN HUA<sup>3</sup>, HON-MAN LIU<sup>1</sup>, MING-JANG CHIU<sup>2,3</sup> (1. Department of Medical imaging, 2. Department of Neurology, National Taiwan University Hospital, College of Medicine, 3. Department of Psychology, National Taiwan University, Taiwan)

**Objectives:** To explore the white matter change using volumetry of white matter hyperintensities (WMH) and diffusion tensor imaging (DTI) in cases of Alzheimer's disease (AD), amnesic mild cognitive impairment (MCI) and healthy age-matched controls, and to investigate the relationship between white matter changes and cognitive functions. **Design:** Cross-sectional, case control study. **Setting:** National Taiwan University Hospital. **Participants:** 10 patients with amnesic MCI (2 female, 8 male, 70±9 years), 10 patients with AD (6 female, 4 male, 75±8 years), and 14 comparison subjects (6 female, 8 male, 67±7 years) participated in the study. Patients with MCI were diagnosed following Mayo clinic's criteria, and patients with AD fulfilled the NINCDS-ADRDA criteria for probable AD with clinical dementia rating (CDR) scores of 0.5 or 1. Comparison subjects were volunteers with normal cognitive function. All the subjects underwent a complete neuropsychological test battery. **Measurements:** Executive functions were examined with verbal fluency (VF) task, Wisconsin card sorting test (WCST)- modified version, trail making test (TMT), part A and B, and frontal behavioral inventory (FBI). Memory functions were examined with logical memory test including immediate recall, delayed recall and recognition MRI was acquired with a 1.5-Tesla GE Excite MRI system. Axial FLAIR (TR/TE/TI= 9000ms/80ms/2250ms, NEX= 1, 24 slices with 5-mm thickness) was used for volumetry of WMH. We used a Matlab-based ROI tools to measure the volume of WMH in different regions of the brain (frontal, parietal-occipital, temporal lobes). For DTI acquisition, we used single shot spin echo EPI acquisition with TR/TE= 6000ms/90ms, 25 uniformly distributed gradient directions, a b-value of 1000 s/mm<sup>2</sup>, and a NEX of 2. Twenty-four contiguous axial slices were acquired with 5-mm slice thickness parallel to the AC-PC connection. Post-processing of the DTI data was done on a GE work station (FuncTool, AW4.2). After automatic correction of the EPI distortion, the mean diffusivity (MD) and fractional anisotropy (FA) maps were computed and displayed along with a b=0 reference map. We measured the MD and FA at 12 different locations of white matter using ROI-based analysis on two slices which included the temporal horns on one slice, and the genu and splenium of the corpus callosum on the other slice. The 12 selected regions included temporal lobe white matter adjacent to the temporal horns on either side; genu and splenium of the corpus callosum, anterior medial subcortical white matter, anterior (frontal) periventricular white matter, posterior medial subcortical white matter and posterior (parietal) periventricular white matter on the same slice of the genu and splenium of the corpus callosum. **Results:** There were no significant differences among groups for gender, age and education years. We found significant group effect of general intelligence (WAIS-III) for both VIQ and PIQ controlling age and education. Group effect was significant for all executive function tests as well as memory tests controlling age and education. The volumetry of WMH showed more WMH in left frontal lobe in AD subjects. The DTI measurements showed significant difference with AD patients in genu of corpus callosum, left anterior and right anterior PV areas. The association between WMH/DTI and cognitive functions was examined by performing partial correlation controlling gender, age and education. For executive function, the volume of WMH in each different region of brain showed significant correlation with perseverative errors of WCST. The volume of total, temporal and parietal WMH was positively correlated with the time used TMT-B. MD of the anterior PV areas was positively associated with perseverative errors (right:  $r = 0.607$ ,  $p < 0.01$ ; left:  $r = 0.504$ ,  $p < 0.05$ ), and TMT-B (right:  $r = 0.459$ ,  $p < 0.05$ ); but was negatively associated with numbers of completed category of WCST (left:  $r = -0.447$ ,  $p < 0.05$ ). On the same ground, MD of the posterior PV areas was positively associated with perseverative errors (right:  $r = 0.570$ ,  $p < 0.01$ ; left:  $r = 0.696$ ,  $p < 0.001$ ) and the time used in TMT-B (right:  $r = 0.445$ ,  $p < 0.05$ ; left:  $r = 0.528$ ,  $p < 0.01$ ). Along the same line, FA of the frontal PV areas was correlated positively with numbers of completed categories of WCST (right:  $r = 0.635$ ,  $p < 0.01$ ; left:  $r = 0.623$ ,  $p < 0.01$ ), and VF (left:  $r = 0.458$ ,  $p < 0.05$ ); but was correlated negatively with the perseverative errors (right:  $r = -0.591$ ,  $p < 0.01$ ; left:  $r = -0.475$ ,  $p < 0.05$ ). FA of the left anterior medial area was correlated negatively with the time used in TMT-B ( $r = -0.427$ ,  $p < 0.05$ ). FA of the left posterior PV area was correlated negatively with perseverative errors ( $r = -0.504$ ,  $p < 0.05$ ). For memory function, volume of WMH showed no correlation; MD of splenium was negatively correlated with immediate recall ( $r = -0.384$ ,  $p < 0.05$ ); FA of the frontal PV areas was correlated positively with immediate recall (right:  $r = 0.428$ ,  $p < 0.05$ ; left:  $r = 0.410$ ,  $p < 0.05$ ) and delayed recall (right:  $r = 0.436$ ,  $p < 0.05$ ; left:  $r = 0.435$ ,  $p < 0.05$ ). **Conclusion:** We demonstrated in subjects with MCI and early AD (1) the executive and memory dysfunction, (2) differential performance of executive and memory tasks, and (3) frontal and parietal PV white matter change accounting for executive dysfunction. The mechanism of impaired executive functions is possibly by affecting the lateral cholinergic bundle from the degenerative AD process. The white matter change is correlated with the memory dysfunctions to a less degree.

**CHOLINERGIC DYSFUNCTION AND AMYLOID DEPOSITION IN ALZHEIMER'S DISEASE AND RELATED DISORDERS STUDIED WITH PET.** HITOSHI SHINOTOH (Asahi Hospital for Neurological Diseases and Rehabilitation, Molecular Imaging Center, National Institute of Radiological Sciences, Chiba, Japan)

Cholinergic dysfunction in the brain has been thought to play a pivotal role in dementias (cholinergic hypothesis). We developed a compound, N-[11C]methylpiperidin-4-yl acetate ([11C]MP4A), for measurement of brain acetylcholinesterase (AChE) activity by positron emission tomography (PET)(1). Using [11C]MP4A PET, we measured brain AChE activity in patients with Alzheimer's disease (AD) and related disorders and found

different degree and distribution of cholinergic deficiency in these disorders. We found a significant and extensive reduction of AChE activity in the cerebral cortex in 37 patients with AD, and the reduction of AChE activity was significantly correlated with severity of AD as assessed with Mini-mental state examination score(2). When the AD patients were subdivided into early-onset AD group and late-onset AD group, the reduction of AChE activity was more pronounced in early-onset AD (-23% compared with the normal mean) than late-onset AD (-13%)2. In 18 patients with Parkinson's disease, we found a significant reduction (-19%) of AChE activity, especially in patients with visual hallucination, while patients with progressive supranuclear palsy had only modest reduction (-10%) of AChE activity in the cerebral cortex but profound reduction (-38%) of AChE activity in the thalamus3,4. The extensive and severe reduction (-36%) of AChE activity was found in patients with dementia with Lewy bodies (DLB), and might explain the good response to the treatment with cholinesterase inhibitors in this disorder. Two patients with frontotemporal dementia with parkinsonism linked chromosome-17 showed also severe reduction of AChE activity in the cerebral cortex and thalamus5. The overabundance of extracellular amyloid-beta (Aβ) peptides in the human brain is thought to be as the initial and central event in the pathogenesis of AD (amyloid cascade hypothesis). The recent development of amyloid imaging ligands has made it possible to image amyloid deposition in vivo in humans. N-methyl-[11C]2-(4'-methylaminophenyl)-6-hydroxybenzothiazole, which was given a code as [11C] Pittsburgh compound B (PIB), is a most potent amyloid imaging ligand6. [11C]PIB PET studies have shown that almost all AD patients have high PIB binding in the cerebral cortex, two-thirds of patients with mild cognitive impairment have high PIB binding in the cerebral cortex similar to AD6. Most (about 80%) of patients with Lewy bodies have high PIB binding in the cerebral cortex7. One fifth of healthy elderly people have high PIB binding in the cerebral cortex8. Patients with amyloid angiopathy also have high PIB accumulation in the cerebral cortex, especially in the occipital cortex9. Longitudinal studies on healthy controls, MCI patients, and AD patients are underway in several institutions, and are expected to reveal the natural course of amyloid deposition in elderly people and AD. On the other hand, clinical trials of many anti-amyloid therapeutic drugs are underway10. The development of amyloid imaging techniques and anti-amyloid therapy may change the clinical practice of AD dramatically within a few years.

**IMAGING WATER DIFFUSION IN DEMENTED BRAIN: AN INTEGRATED APPROACH.** JUUN-JIE WANG (Assistant Professor, Department of Medical Imaging & Radiological Sciences, Chang Gung University, Taiwan)

**Objectives:** To develop a multi-parametric approach which integrated the various information contents related to brain connectivity and diffusivity to functionally evaluate the disease status of patients with Alzheimer's Disease using MRI. **Method and Design:** Pathologic changes in the cortical gray matter of the Alzheimer's Disease brain are characterized by the accumulation of β-amyloid plaques and neurofibrillary tangles along with neuronal and synaptic loss that produce brain atrophy. However, the study of Alzheimer's Disease is potentially challenging because of several reasons. First of all there existed no known biomarkers. The disease usually has an insidious onset, which can be a combination of genetic and environmental factors. It is difficult to differentiate from other types of dementia. The major radiographic finding from conventional Magnetic Resonance Imaging is global atrophy on patients at an advanced stage (1). The Magnetic Resonance Imaging techniques currently available for the diagnostic assessment of Alzheimer's Disease often used volumetric measurement. The medial temporal lobes and associated neocortical areas are severely affected. A high resolution, T1 weighted, magnetization prepared three-dimensional sequence allows manual trace of the brain structure on all contiguous sections where the structure of interest is evident. Volumes are usually calculated by computing the number of voxels within the traced images. Several studies have reported volume losses in mesiotemporal structures, which are indicative of atrophy in patients with Alzheimer's Disease, when compared with elderly control subjects (2,3). Apparently the measured volume varies from subject to subject, and even from neuro-radiologist to neuro-radiologist. Another main limitation of conventional Magnetic Resonance Imaging is that these findings can occur in other neurologic diseases, and may not be a specific marker for Alzheimer's Disease. Voxel-based morphometry (4), although not applicable for quantitative volume analyses such as boundary drawing methods, is a bias-free and not very time-consuming method, which is useful for ascertaining atrophic changes throughout the brain. This technique involves a voxel by voxel size comparison of the local concentration of any tissue structure between two groups of subjects. Voxel-based morphometry is accomplished by performing statistical tests between the two groups. The procedure involves spatially normalizing high-resolution images from all subjects in the study into the same stereotactic space, thus removing spatial and volume differences. The desired tissue of interest, usually gray matter, is then segmented from these images, and a smoothing algorithm is applied to the segmented tissue. Finally, numerous voxel size parametric statistical tests are performed to compare the smoothed images from the two groups. The result from Voxel-based morphometry analysis can be reported in subjects with Alzheimer's Disease, when compared with the age-matched healthy subjects (5). Diffusion tensor imaging is another magnetic resonance imaging technique that has been used to compare the integrity of white matter fibre tracts in patients with probable Alzheimer's disease. Previous pathological studies of patients with Alzheimer's disease have shown that white matter abnormalities, such as loss of oligodendrocytes and axons, together with reactive astrogliosis are often seen in the parietal lobe white matter and central white matter (5). Relative to normal controls, patients with probable Alzheimer's disease showed a highly significant reduction in the integrity of the association white matter fibre tracts, such as the splenium of the corpus callosum, superior longitudinal fasciculus, and cingulum (6, 7). By contrast, pyramidal tract integrity seemed unchanged. This novel finding is consistent with the clinical presentation of probable Alzheimer's

disease, in which global cognitive decline is a feature more prominent than motor disturbance. Functional Magnetic Resonance Imaging can often be used as a marker of the disease progression or as a potential surrogate marker of the effectiveness of new therapies. A complimentary approach to functional assessment is study of functional magnetic resonance imaging during the resting state. In the resting state functional magnetic resonance imaging, the patient does not have to perform a cognitive task because it does not rely on a comparison of task and baseline conditions. Patients with Alzheimer's Disease were found to exhibit decreased activity within a default-mode network during the resting-state, which included the posterior cingulate cortex and inferior parietal lobe. Other functional magnetic resonance imaging studies during the resting-state have suggested that the patients with Alzheimer's Disease showed mild decreased trends in the functional connectivity between the posterior cingulate cortex and hippocampus (8, 9). Compared with conventional functional magnetic resonance imaging, which required appropriate performance of cognitive tasks, the main advantage in measuring at the resting state as an investigative tool for the study of Alzheimer's Disease is that it will not be biased by the ability of the patients to perform adequately the paradigm (10). Conclusion: Because of the various information contents from the magnetic resonance imaging techniques, an integrated approach is necessary. In this presentation, we will propose an imaging processing platform for the comprehensive assessment of Alzheimer's Disease, which will incorporate different Magnetic Resonance Imaging techniques and could be easily extended to other radiologic imaging modalities. The purpose is to establish an integrated approach to the measurement of the microenvironment changes in the brain regions involved in the disease progress in patients of Alzheimer's Disease.

#### NEUROIMAGING AND BEHAVIORAL ABNORMALITIES IN MULTIPLESCLEROSIS: THE IMPORTANCE OF FRONTAL-SUBCORTICAL CIRCUITS. ANTHONY FEINSTEIN (Professor, Department of Psychiatry, University of Toronto, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada)

Objectives: To understand how magnetic resonance imaging can help define the neural circuits involved in abnormal mood and affect in patients with multiple sclerosis (MS). Design: Case control. Setting: Tertiary referral neurology clinic. Participants: All subjects had a confirmed diagnosis of multiple sclerosis according to the criteria of Poser or McDonald. Two disorders were chosen for study. The first was a group of 20 MS patients with major depression as defined by the DSM-IV. The second group comprised 13 MS patients with pseudobulbar affect (PBA) also called pathological laughing and crying. A tight definition of PBA was used which may be summarized as involuntary crying in the absence of sadness, or involuntary laughter in the absence of happiness, or a mixed state of involuntary crying and laughter in the absence of subjective mood change. Control subjects: Twenty MS patients with major depression were matched to 20 MS patients without major depression on the following variables: age, gender, duration of MS, disease course (relapsing-remitting, primary progressive, secondary progressive), degree of physical disability as measured by the Expanded Disability Status Scale (EDSS), cognition (as measured by a Neuropsychological Screening Battery for MS) and social stress (as measured by the Social Stress and Support Interview). For the second study 13 patients with MS and PBA were matched to 13 MS patients without PBA on the following variables: age, gender, disease course and duration and EDSS. Measurements: In both studies all subjects underwent brain imaging on a 1.5T MRI scanner. Thereafter, all images were analyzed in a four step procedure using in-house software. Step 1: head from brain removal. Step 2: fully automated brain segmentation that divided the brain into white and grey matter and sulcal and ventricular csf. In addition, the volume of all lesions (hyper and hypointense) were measured using semi-automated software. Step 3: The brains were parcellated into 26 anatomically distinct regions (13 regions in each hemisphere) using SABRE (Semi-Automated Brain Regional Extraction). Step 4: Segmented brain compartments and the lesion map were co-registered with the 26 discrete brain regions demarcated by SABRE. In this way total grey and white matter, csf and hyper and hypointense lesion volumes were quantified for each brain region. The two groups of subjects, depressed versus non-depressed and PBA versus non-PBA were compared across all imaging variables. Results: In the depression study significant between group differences emerged. Depressed subjects had a higher hyperintense lesion load in the left (dominant) medial inferior frontal and left anterior temporal regions. They also had significantly more atrophy (increased csf volume) in the left anterior temporal region. A logistic regression revealed that these three variables could account for 40% of the depression variance. In the second study, subjects with PBA had a significantly higher total hyperintense lesion volume plus a higher hyperintense lesion volume in the following discrete regions: bilateral medial inferior frontal, bilateral inferior parietal and right medial superior frontal. In addition, PBA subjects had a significantly higher total hypointense lesion volume in the brain stem. Controlling for overall total hyperintense lesion volume, a logistic regression analysis revealed that the brain lesions could account for 75% of the PBA variance. Discussion: Major Depression is common in patients with MS and has a lifetime prevalence approaching 50%. Until recently it was thought that depression arose as a reaction to disabling, incurable disease. However, the results of this study and others show that there is a firm link between the presence of depression and brain pathology. The relevance of these data is that they highlight the functional importance of certain key discrete frontal-subcortical neural circuits, namely the dorsolateral, orbitofrontal and anterior cingulate circuits, in the regulation of mood and behavior. From this it may be concluded that for some patients with MS major depression is an integral part of the neurological process. However, it is also important to note that brain pathology could account for no more than 40% of the depression variance. This may reflect the limitations of the MRI technology and data analysis together with the recognition that for many patients psychosocial factors are also important in the pathogenesis of major mood disturbance.

Pseudobulbar affect is less common than major depression in MS and will affect approximately one in ten patients over the course of their lifetimes. The topic has been poorly researched since Kinnear Wilson's classic 1924 paper. The present findings highlight the importance of bilateral brain pathology in the etiology of the syndrome (a difference compared with major depression) and illustrates that a widespread neural network is responsible for generating and modulating affect, be it laughing or crying. PBA may be viewed as a disconnection syndrome in which the bulbar nuclei are released from the top down control of certain cortical (frontal, parietal), subcortical (amygdala, hippocampal) and cerebellar influences. The fact that brain lesions could account for 75% of the PBA variance, as opposed to the 40% figure in major depression illustrates that Pseudobulbar affect is essentially a 'hard wired' brain problem in which psychosocial factors, although important as potential precipitating influences, have minimal etiological significance. Also of note is that major depression and Pseudobulbar affect share certain brain regions which is not surprising given the overlap in their clinical presentations (depressed patients cry).

## COGNITIVE NEUROLOGY IN DEMENTIA

#### HOW TO ENHANCE COGNITIVE FUNCTIONS IN AGED POPULATION AND DEMENTIA. MASARU MIMURA (Associate Professor, Department of Neuropsychiatry, Showa University School of Medicine, Tokyo)

Backgrounds: Cognitive deficits caused by dementing illnesses are chronic and progressive problems, debilitating patients and caregivers as well. Although it is hard to tackle, a number of approaches from various standpoints have been proposed to enhance cognitive functions in dementia and cognitively-impaired aged individuals. It is of importance to note that such interventions should be multi-domain and multi-disciplinary, combining both biological and non-biological approaches. Recent studies have suggested that a combination of pharmacotherapy and cognitive training may benefit individuals with Alzheimer's disease (AD). Cognitive training appears to be particularly effective for people with mild memory impairment who are on pharmacological treatment including donepezil. However, the mechanisms of pharmacological treatment per se are not fully understood. Objectives: Donepezil is well known to increase cortical acetylcholine, acting as reversible acetylcholinesterase inhibitor. Here, we propose another hypothesis with a set of data that donepezil would act as cognitive enhancer by increasing serum insulin-like growth factor-I (IGF-I) level, in addition to inhibiting acetylcholinesterase. IGF-I, that was once called somatomedin C, is a polypeptide protein hormone similar in molecular structure to insulin. It plays an important role in childhood growth and continues to have anabolic effects in adults. IGF-I has recently been known to have anti-aging effect. IGF-I deficiency is involved in cognitive deficits seen with aging and in neurodegenerative diseases such as AD. We previously demonstrated that donepezil increases serum IGF-I level. We further aimed at investigating whether decreased serum levels of IGF-I in AD individuals predict response to treatment by donepezil. Design: Baseline (pre-treatment) IGF-I level of AD patients was measured and compared to age-matched healthy control participants. The serum IGF-I levels of AD patients were again measured following 16 weeks of treatment with donepezil. Setting: The study was performed at the memory disorders clinic in Showa University Hospital. The study was approved by the Ethics Committee at Showa University School of Medicine. Participants: The study involved 106 elderly subjects: 50 patients with AD and 56 age-matched controls without dementia. Intervention: Participants with AD were given donepezil orally 3 mg/day for 4 weeks and 5 mg/day for additional 12 weeks. AD patients were divided into responders and non-responders based on the changes in Mini-Mental State Examination (MMSE) scores before and 16 weeks after treatment with donepezil. Serum levels of IGF-I and atherogenic lipoproteins were determined (as pre-treatment baseline and after 16 weeks of treatment with donepezil). Measurements: The patients with AD and control participants were assessed on IGF-I levels and the MMSE scores. Results: Before treatment with donepezil, there was a significant inverse correlation between serum IGF-I levels and the MMSE scores. Serum IGF-I levels and the MMSE scores were significantly lower in AD patients than in non-demented controls and were the lowest in non-responders to donepezil. On multiple logistic regression, non-responders to donepezil showed decreased serum IGF-I levels < 110 ng/ml and MMSE scores < 15 points before treatment. Conclusion: These findings suggest that decreased levels of serum IGF-I combined with MMSE scores before treatment could predict non-responders to donepezil among AD patients, which may be a simple and practical method for selecting patients expected to show a response to treatment. Additional experimental studies have demonstrated that interventions such as blue-light therapy, nutritional supplements including capsaicin and isoflavone, and raspberry aroma increase serum and/or cerebral IGF-I levels, thereby enhancing cognitive functions. We speculate that increasing IGF-I levels plays a crucial role in enhancing cognitive functions in AD and aged individuals.

#### SPATIAL FUNCTIONS IN PATIENTS WITH EARLY ALZHEIMER'S DISEASE. MING-CHYI PAI (Associate Professor, Department of Neurology, Institute of Gerontology, and Institute of Behavioral Medicine, National Cheng Kung University (NCKU) Chairman, Division of Behavioral Neurology, Department of Neurology, NCKU Medical Center, Tainan City, Taiwan)

It is true that many patients with Alzheimer's disease (AD) may have navigational impairment in the early stage of the disease. Although a few patients still keep the ability to navigate in their familiar environments for a long time, navigational impairment can be

among the incipient symptoms for some of the others. From our recent study by using a questionnaire (Questionnaire for Everyday Navigational Ability, QuENA), we found that at least 44% of the 329 AD patients who had visited our clinic currently had ever been lost. Additional 35% of the same group, although never reported having been lost, would make their family members worried about their potential to be lost. The mechanisms for the navigational impairment in AD patients are complex, in part due to the heterogeneous pathological changes of AD and the personal history of each patient. The Aguirre's classification of navigational disorders based on the symptom and the corresponding regional cerebral lesion provides a platform to dissect the possible causes for navigational impairment in AD. Here, I will present the results of the works from our laboratory most recently. Cognitive map representation: It is plausible to attribute way finding difficulty to cognitive map failure, since the hippocampus has long been thought as the bank of cognitive map where are damaged early in the course of AD. However, from clinical observation and experimental data, this speculation is perhaps not true. Most of the AD patients (89%), for example, have their first time getting lost in their familiar environments. This implies that the patients could arrive at a point near to their home and it is hence unlikely that a failed cognitive map would play a critical role. This is further supported by the result of our recent study, in which we used virtual reality (CG-Arena developed by Jacobs WJ) and two landmarks with which each participant had been familiar attached onto the sidewalls of the arena. The very early AD patients kept spatial representation of their home as good as the controls did. Moreover, the inclined angles between these two landmarks and their home provided by the two groups also showed no difference. Landmark or scene recognition: On the other hand, we also found that very mild AD patients (CDR 0.5) can verbally recognize familiar landmarks as good as the controls, but their electrophysiological responses are quite different. Recently, we have been working on the ability of these patients to recognize pictures of panorama street views taken from places near to each participant's home by manipulating their illumination and clearness. The preliminary results will be presented. Egocentric representation: Most of the AD patients who had been lost were lost on the way back home. One of the possibilities is that the sequential representation of the landmarks toward home is not the same as the reverse of it starting from home. This issue will be studied very soon. Sense of direction: A landmark after having been successfully recognized by the navigator must provide its directional information connecting to the next landmark or to the destination. In one of our ongoing studies by using virtual city, patients with very mild AD, regardless of the presence of getting lost experience or not, behaved as good as controls when mental rotation was tested based on the assumption that both of their cognitive maps and landmark recognition were intact. Problem solving ability: When patients realize they are lost, the ability to solve the situation will influence the outcome whether they need others to escort home or not. If we here focus on visual perceptual function, then the problem solving ability or executive function is beyond the scope of our interest. Conclusions: Visual perception of the street views or scenes might be the critical, if not the most important, deficit for AD patients accounting for the getting lost events. Restriction of the ambulation of the patients can eliminate the dangerous behavior, but this action also deprives the independent life and autonomy from them. This potential risk cannot be completely avoided unless why AD patients would be lost is completely understood.

**MUSIC THERAPY AND NEUROPSYCHOLOGY: A PROPOSAL TO MUSIC THERAPY BASED ON THE COGNITIVE PROCESSING OF MUSIC.** MASAYUKI SATOH (*Director of Medical department, Mie St. Cross Hospital, Mie, Japan*)

In the last decade, a considerable number of studies have been made on the cognitive processing of music. A patient with pure amusia due to the infarction of anterior portion of bilateral temporal lobes revealed the disturbance of the discrimination of chords. Using positron emission tomography, these regions were activated when musically naïve normal subjects listened to the harmony compared to the melody of identical music. So, we concluded that anterior temporal portion might participate in the recognition of chords. Several articles reported that the musician's brain was different from nonmusicians' functionally and anatomically. This difference was considered to be caused by the musical training for a long time. Recent studies clarified that the reorganization might occur by musical training for a few months. Melodic intonation therapy (MIT) is a method aimed to improve speech output of aphasic patients, using short melodic phrase with a word. The literatures of mental processing of music suggested that right hemisphere might participate in the expression of music, namely singing and playing instrumentals. So, it was supposed that MIT utilized the compensational function of right hemisphere for damaged left hemisphere. We also reported that mental singing improved the gait disturbance of patients with Parkinson's disease. Music therapy is changing from a social science model based on the individual experiences to a neuroscience-guided model, based on brain function and cognitive processing of the perception and expression of music.

**SLEEP, COGNITION AND DEMENTIA.** CHAUR-JONG HU (*Chief, Assistant Professor, Department of Neurology, Shuang-Ho Hospital, Taipei Medical University, Taiwan*)

Sleep disturbance and circadian rhythm disarrangement are both common manifestations of behavioral psychiatry symptoms of dementia (BPSD). BPSD also commonly occurs in patients with mild cognitive impairment (MCI). In Alzheimer's disease (AD) animals, sleep disturbance was found and is associated with the brainstem cholinergic neurons degeneration. These implicate that sleep disturbance is an important manifestations of AD. Sleep disturbance could be an indicator for poor outcome of dementia and it usually causes a heavy burden for care-givers of dementia. Among a sleep, there usually are one or few cycles containing rapid eye movement (REM) sleep and non-

REM sleep in each cycle. Polysomnography (PSG) has become the most powerful tool for research of sleep. REM sleep is linked to dreaming and it is with characteristic physiological presentations, including rapid eye movement, generalized hypotonia and alteration of autonomic nervous tone. The recent researches have raised the association between REM sleep and some specific forms of memory, especially in sleep deprivation studies. The compelling evidence support that memory consolidation processes during sleep. Especially, rapid eye movement (REM) stage is crucial for some visual-spatial memory and specific task-learning. There are specific neurotransmitters responsible for the initiation and maintenance for different stages of sleep. The initiation of REM sleep is mainly acetylcholine-dependent. Interestingly, acetylcholine is insufficient in AD brains. Cholinesterase inhibitors which can increase intracerebral acetylcholine levels, have become the standard therapy of AD for improving cognitive function. Therefore, theoretically, REM sleep should be decreased in AD or MCI patients. However, the changes of sleep architectures among AD or MCI patients are still unconcluded. In this talk, we will discuss the interactions between sleep, memory consolidation and dementia. We also will present preliminary results which revealed low sleep efficiency in cognitive impairment patients and, during REM sleep, over-expression of iNOS, a molecule related to memory consolidation but no significant changes in PER-1, a molecule associated with control of circadian rhythm in mRNA levels. We conclude that the molecular mechanisms of the interactions might be important for dementia study and they need further investigation.

**DELUSION AND CONFABULATIONS IN ALZHEIMER'S DISEASE: NEUROPSYCHOLOGICAL AND NEUROIMAGING STUDIES.** KENICHI MEGURO (*Professor, Department of Geriatric Behavioral Neurology Tohoku University Graduate School of Medicine, Sendai, Japan, Head of Office Against Dementia, The Osaka-Tajiri SKIP Center, Osaka, Japan*)

Although confabulations and delusions are observed in Alzheimer's disease (AD), the relationship between the two has not been fully investigated. We studied 50 AD patients and 10 healthy participants. After dividing the patients into delusion and non-delusion groups, we assessed confabulations and cognitive function. We found that no confabulations appeared in the healthy participants, and only AD patients showed confabulations. The delusion group produced more confabulations on episodic subjects than on semantic subjects. There was a correlation between cognitive impairment and confabulations in semantic memory. These findings suggest that different mechanisms are involved in confabulations between semantic and episodic memories. Following the neuropsychological study, 41 AD patients and 12 healthy controls were studied with MRI and SPECT. Cerebral atrophy was assessed by voxel-based-morphometry and the correlations with confabulations were analyzed by SPM2. For the relations with delusion, the patients were divided into the delusion and non-delusion groups and SPECT was performed to evaluate cerebral blood flow and the group difference was analyzed by SnPM3. The semantic confabulation scores correlated with atrophy in the anterior cingulate, bilateral medial temporal lobes and right middle temporal gyrus. The delusion group had lower prefrontal cerebral blood flow than the non-delusion group. Different mechanisms are involved in confabulations between semantic and episodic memories in AD. Episodic confabulation is affected by delusion related to frontal dysfunction and semantic confabulation is associated with cognitive dysfunction.

**EVENT-RELATED POTENTIALS, CORTICAL FUNCTIONS AND DEMENTIA.** CHIOU-LIAN LAI (*Associated professor of Neurology, Director, Neurophysiological Laboratory, Department of Neurology, Kaohsiung Medical University Hospital, Department of Neurology, Faculty of Medicine, College of Medicine, Kaohsiung Medical University*)

Neuroelectric measurements can provide direct imaging of central nervous system function. Indeed, long-latency evoked potentials related to aspects of cognitive processing are referred to as cognitive EPs or endogenous event-related potentials (ERPs). This review will discuss how ERP recordings in patients with cognitive dysfunction can enrich our understanding of association among cognition, neuropsychological assessment and ERPs and how the brain produces ERPs. P300 is a positive shift that occur approximately 300msec after the onset of stimulus, particular when a subject detects an informative task-relevant stimulus. It is often elicited using the "oddball" paradigm, wherein two stimuli are presented in a random order, with one occurring more frequently than the other. Although it is accepted that P300 reflects information processing such as attention, stimulus evaluation, judgment, and decision-making, its cognitive significance of P300 remain unclear. Contingent negative variation (CNV) is a slow negative shift of brain electrical potential occurring between paired stimuli when the first stimulus is warning and the second signal requires the subject to perform a motor response. CNV has been claimed to be associated with various behavioral functions such as cognition, attention, expectation, estimation, and voluntary motor control. There are essentially no data regarding the use of the CNV in a clinical situation where one would need to classify a CNV as normal or abnormal. Current therapy is effective in treating the early manifestations of dementia and provides an opportunity for managing the disease while the patient's cognitive function is relatively preserved. Therefore, the boundary between normal aging and incipient Alzheimer's disease (AD) is of particular importance for both theoretical and practical reasons, in order to develop reliable, non-invasive methods for accurate and early diagnosis of AD. In the future, the combination of neuropsychological tests and ERP measurements is useful in improving reliability and increasing sensitivity to early cognitive decline or disease progression in AD.

## BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS OF DEMENTIA

### CURRENT USAGE OF ANTIPSYCHOTICS TO TREAT BPSD IN JAPAN.

AKIRA HOMMA (Director, Department for Dementia Intervention, Tokyo Metropolitan Institute of Gerontology, President, Japan Society for Geriatric Psychiatry, President, Japan Society for Dementia Care President, Asian Society Against Dementia)

During the last decade, the newer atypical antipsychotics have largely replaced the conventional antipsychotics and have been considered preferred treatments for a variety of behavioral and psychological symptoms of dementia (BPSD) including agitation, depression and psychosis during their illness course. Although there are multi-etiologicals for BPSD, and it is well known that somato-psycho-social factors may contribute to the emergence of BPSD, antipsychotic medications are commonly used to treat BPSD. In 2005, FDA released black box warnings, which basically stated that older patients with dementia-related psychosis who were exposed to the atypical antipsychotics were at an increased risk of death compared with placebo. This was based on the analyses of 17 placebo-controlled trials which were fairly brief, and the relative risk of death in these patients was 1.6-1.7 times that seen in placebo. The overall numbers are very small, and the percentages are also quite low. The rate of death in the drug-treated patients was about 4.5% vs 2.6% in the placebo, indicating the magnitude of risk was about 2% increase vs placebo. Also there were a number of different causes of death, but they fell into either cardio- or cerebrovascular kinds of causes or infectious causes, namely, upper respiratory infections. The release reminded us that none of antipsychotics is, at the present time, FDA and other official agencies-approved for the treatment of psychosis and agitation in AD and related dementing disorders and importance of considering non-pharmacologic approaches to BPSD. This was a reason why we conducted a questionnaire survey for members of Japanese Psychogeriatric Society and Japanese Association of Psychiatric Hospitals. The survey aimed to examine the usage of antipsychotics to treat BPSD according to the category of Behave-AD and the recognition of the above FDA's warning. A thousand and forty nine valid responses were obtained out of 3,544 members. An average number of patients in out-patient clinics were 36.9 per month. Alzheimer's disease was the most frequent diagnosis. Risperidone was the most frequently, that is, 88.3%, prescribed to treat BPSD. The first choice drug to treat BPSD was atypical antipsychotics through the eleven categories of Behave-AD. An outline of the results of the survey will be presented.

### PRIMARY PROGRESSIVE APHASIA. CHUANG-KUO WU (Assistant Professor, CognitiveNeurology & Alzheimer's Disease Center (CNADC), Northwestern University Feinberg School of Medicine)

While memory loss accounts for the initial manifestation of Alzheimer's disease (AD), language impairment is the most salient aspect of earliest presentation of primary progressive aphasia. This study will review medical literature regarding primary progressive aphasia. Over the past three decades, PPA has been investigated and debated as a separate neurodegenerative disorder. In fact, Dr. Pick already described such a case in his original articles. Because of outstanding lobar atrophy in the frontal lobe of left hemisphere, nowadays, PPA has been classified as one of two subtypes of frontotemporal lobar degeneration (FTLD). According to Mesulam's clinical criteria of PPA, these patients should have progressively impaired language function without other cognitive dysfunction (i.e., primary) for the initial two years. Neuropsychological assessments cannot be administered easily for these patients. According to their caregivers, PPA patients can preserve their activities of daily living in the beginning stage of disease course. When language impairment progresses and other cognitive domains are affected, they become demented. The neuro-imaging studies of PPA patients demonstrate a selective atrophy of the prefrontal perisylvian region of the dominant hemisphere (usually left side). The pathological examination reveals a variety of underlying pathologies. Among them, Alzheimer pathology can be documented in about 30% of subjects examined in a recent autopsy series. Classic Pick's disease, Tau protein predominant pathology, cortico-basal degeneration pathology, FTLD-ubiquitin inclusions and even Creutzfeldt-Jakob disease all had been reported. Moreover, three clinical subtypes are recently acknowledged: agrammatic, logopenic and semantic variants. At the Northwestern Alzheimer's disease center, our recent autopsy series suggested agrammatic PPA subjects most likely had tauopathy whereas majority of logopenic PPA cases had Alzheimer pathology. Future molecular and genetic studies shall provide more insights of this unique neurodegenerative disorder so that we can develop effective treatment strategies.

### EATING PROBLEMS OF DEMENTIA PATIENTS. MANABU IKEDA<sup>1,2</sup>, SHUNICHIRO SHINAGAWA<sup>3</sup> (1. Professor, Department of Psychiatry and Neuropathobiology, Faculty of Medical and Pharmaceutical Sciences, Kumamoto University, 2. Division of Clinical Research, Kikuchi National Hospital, 3. Department of Psychiatry, Jikei University School of Medicine)

Background: Despite numerous reports of altered eating behaviors in dementia, there have been few systematic studies. Especially, those of abnormal eating behaviors in frontotemporal lobar degeneration (FTLD) and dementia with Lewy bodies (DLB) are scarce. It also remains unclear whether these altered eating behaviors are due to disease specific factors, ethnic-cultural factors or both. Objectives: 1) To investigate the frequency and severity of change in eating behaviors in FTLD and Alzheimer's disease (AD) patients, and to compare the profile of abnormal eating behaviours in Japanese and Western

patients. 2) To clarify the frequency, characteristics of eating problems in Japanese DLB patients. Methods: 1) Three groups of patients were involved in this study: frontotemporal dementia (FTD) (Japan:N=18, U.K.:N=23), semantic dementia (SD) (Japan:N=11, U.K.:N=25), and AD (Japan:N=43, U.K.:N=43). A questionnaire was administered that consisted of 36 question items investigating the following five domains: swallowing problems, appetite change, food preference, eating habits, and other oral behaviors. 2) Study participants were 29 consecutive Japanese DLB patients and 33 patients with AD, matched for age and MMSE score, CDR score and education. In order to assess characteristics of eating / swallowing problems in DLB patients, we used above-mentioned comprehensive questionnaire which had originally been designed to assess eating problems in FTLD/ AD patients, and had revised for DLB patients. Revision of the questionnaire was conducted by adding 4 new question needed for DLB and deleting 7 question needed for FTLD. Results: 1) In U.K. patients, the score in all five domains, except swallowing problems, were higher in FTD than in AD, scores for change in appetite, food preference, eating habits were also higher in SD than in AD. In Japanese patients, FTD had higher score than AD in all five domains except swallowing problems, and higher score than SD for appetite change and other oral behaviors. Japanese SD patients had higher score than AD in domains of food preference and eating habits. Weight gain of more than 7.5 kg was found in 30% of the FTLD cases in U.K., while less than 10% of those in Japan. 2) DLB patients scored significantly higher in items of "difficulty in swallowing foods", "difficulty in swallowing liquids", "coughs or chokes when swallowing", "takes a long time to swallow", "suffering from sputum", "loss of appetite", "needs watching or help", and "constipation" than AD patients. Conclusions: Increased appetite, alteration of food preference and eating habits were common in patients with FTLD in UK. In AD, by contrast, changes in eating habits were less common. The findings in Japan were similar to those findings in U.K.. Changes in eating behaviors in FTLD groups appear to be universal, although ethnic-cultural factors might affect these results to some extent. Eating and swallowing problems were more frequent in patients with DLB than patients with AD. Although DLB patients show many eating problems, causes of each problem are various, not only depending on the severity of dementia or Parkinsonism. We have to be cautious about eating problems in order to prevent accidents in managing FTLD and DLB patients.

### BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS OF ELDERLY CHINESE PATIENTS WITH DEMENTIA. JEN PING HWANG, SHIH-JEN TSAI, CHENG-HUNG YANG (Division of Psychiatry, School of Medicine, National Yang-Ming University, Taipei, Taiwan. Section of Geriatric Psychiatry, Taipei Veterans General Hospital, Taipei, Taiwan)

Behavioral and psychological symptoms of dementia (BPSD) is not uncommon in clinical psychiatry, and it is the major source of caregiver and family burnout, may provoke elderly abuse, can cause premature institutionalization, increase cost of care, and result in poor quality of life. Our research team conducted a series of studies to describe the frequency, types and characteristics of BPSD, focus on psychotic symptoms and behavioral disturbances of 167 psychiatric inpatients with dementia consecutively admitted to our geropsychiatric ward of Taipei Veterans General Hospital from 1989 to 1997. The BPSD were obtained from a semistructured interview according to BEHAVE-AD and it also recorded by observing inpatients in the ward. The results showed the frequency of psychotic symptoms in our inpatients with dementia was 71.8%, an the most common psychotic symptom was delusion (59%), the frequency of behavioral disturbances in our inpatients with dementia was 70.7%, and the getting lost, repetitive phenomena, sleep disturbance and aggression were very common behavioral disturbances in our inpatients with AD. The conclusions of our studies showed the frequency of BPSD was much higher than those of neurologist's studies in Taiwan. We also found some BPSD may be the early symptoms of dementia when the patient's cognitive impairment was not apparent or relatively mild and the strong association between different symptoms of BPSD.

### GROUPING FOR BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS OF DEMENTIA. JONG-LING FUH (Professor of Neurology, National Yang-Ming University School of Medicine, Staff Neurologist, The Neurological Institute, Taipei Veterans General Hospital, Taipei, Taiwan)

Objectives: The behavioral and psychological symptoms of dementia (BPSD) refer to a heterogeneous range of psychological reactions, psychiatric symptoms, and behaviors occurring in people with dementia. Factor analysis techniques have been used to explore behavioral dimensions that may comprise BPSD. Design: The published studies using factor analytic techniques to identify the sub syndromes contained within the Neuropsychiatric Inventory (NPI) were reviewed. Results: Ten articles were found from PubMed survey. Three to five sub-syndromes were found in these studies and different terms were used to label them. Despite some differences among these studies, the associations of the following symptoms were very consistent: (1) depression and anxiety, (2) delusions and symptoms of hallucination, (3) agitation and irritability, (4) disinhibition and euphoria. Conclusion: BPSD could be divided into several groups of symptoms. The four common sub-syndromes may reflect four distinctive pathophysiological disorders. It warrants further study to prove it.

**SLEEP QUALITY OF THE FAMILY CAREGIVERS OF THE PATIENTS WITH ALZHEIMER'S DISEASE AND THE RELATIONSHIP TO SLEEP PROBLEMS OF THE PATIENTS.** PAICU WT TSENG<sup>1</sup>, MEI CHANG<sup>2,4</sup>, MING-JANG CHIU<sup>3</sup> (1. Department of Psychiatry, Mennonite Christian Hospital, Hualien, Taiwan; 2. School of Nursing, 3. Department of Neurology, College of Medicine and Hospital, National Taiwan University, Taipei, Taiwan. \* Correspondence authors)

Objective: To understand the sleep problems of the family caregivers of the patients with Alzheimer's disease (AD) and to describe the relationship between sleep quality of the family caregivers and sleep problems of the AD patients. Design: A cross-sectional observational study was carried out by interviewing family caregivers of AD patients with structured questionnaires. Participants: We recruited the sample populations from 5 district health centers in Taipei city and a neurological clinic of a University Hospital. In total 88 pairs of AD patients and their family caregivers were enrolled. We excluded those pairs with shift or hired caregivers. Measurements: Sleep quality of the family caregivers were measured by the Chinese version of Pittsburgh Sleep Quality Index (CPSQI). All family caregivers rated the sleep problems of the AD patients using the Sleep Disorders Inventory (SDI). Depressive symptoms of the family caregivers were evaluated by the Iowa short-form Center for Epidemiologic Studies Depression scale (CES-D). Dementia severity of the AD patients was assessed by the Clinical Dementia Rating scale (CDR). Results: Sixty-eight percents of the family caregivers had poor sleep quality (CPSQI > 5) with a mean score of 7.9 ± 4.0. Seventy-four percents of the patients with AD had sleep disturbance but the mean SDI score was 1.9 ± 1.6 with a mean distress score of 0.61 ± 0.8 representing a mild distress. There were 18% of the family caregivers who reported depression (CES-D > 10). The sleep quality of the family caregivers was significantly correlated with their own depressive symptoms ( $r = .52, p < .001$ ) and SDI score of the AD patients ( $r = .28, p < .01$ ). The hierarchical multiple regression analysis revealed that high depression score, low education year of the family caregivers (33 %) and sleep disturbance of the AD patients predicted poor sleep quality in the family caregivers (in total 36%). Conclusion: We found that the majority of the family caregivers of the AD patients had poor sleep quality which was associated with depression of the family caregivers and sleep disturbance of the AD patients. In addition, the family caregivers with low education were vulnerable to poor sleep quality.

## MANAGEMENT OF DEMENTIA IN PRIMARY PRACTICE

**PHARMACOLOGICAL TREATMENT FOR ELDERLY DEMENTED PATIENTS.** DUNCAN RONALD FORSYTH (Consultant Geriatrician, Addenbrooke's Hospital, Cambridge, England Chair of England Council)

The ageing of any society will inevitably lead to increasing numbers of dementia sufferers. Despite amazing advances in public health, surgery and medical therapies there remains no cure or preventative therapy for chronic progressive neurodegenerative diseases. So, prolonged life expectancy brings with it a sword of Damocles – dementia! In this talk I shall discuss the detection of dementia for without a diagnosis treatment will not be considered. A clinical differentiation of the type of dementia will determine secondary preventative measures, e.g. modifying vascular risk factors and help to advise sufferer and family members on the likely trajectory of the dementia. Comorbidities will influence the likely risk benefit analysis of anti-dementia therapies (acetylcholinesterase inhibitors). Reference will be made to the impact of UK national guidance on antedementia therapies (NICE – National Institute for Clinical excellence) and how the English National Dementia Strategy is set to improve the overall care for people with dementia and their carers. Finally new and potential therapeutic strategies will be discussed.

**COGNITIVE TRAINING IN MILD COGNITIVE IMPAIRMENT.** KER-NENG LIN<sup>1,3</sup>, PEI-NING WANG<sup>1,2</sup>, HSIU-CHIH LIU<sup>1,2</sup> (1. Department of Neurology, Taipei Veterans General Hospital, Taiwan; 2. Department of Neurology, National Yang-Ming University School of Medicine, Taiwan; 3. Department of Psychology, Soochow University, Taiwan)

Objectives: To see if memory training can slow down Mild Cognitive Impairment (MCI) elders' cognitive deterioration and can postpone the onset of dementia. Methods: Sixty voluntary MCI elders were randomly divided into Memory Training group (MT) and Waiting List group (WL). In MT group, 30 subjects were divided into three classes with 10 subjects in each and received a two and a half hours' session of memory training each week for 12 weeks. The memory training skills were introduced and demonstrated to MT subjects by the leader, a clinical psychologist, including self - introduction, diary keeping, external aids for memory, practice for concentration - digit span memory, establishing personal phone book, identifying the differences, categorization - picture sorting / memory, elaboration of information, words pairs learning, and errorless learning of face - name associations. A session was usually started with self - introduction and previous homework discussion; followed by practice of previous skills and by introduction and practice of a new skill; ended with a homework assignment. All the 60 subjects received three cognitive and emotional assessments at baseline, 3 months (within 2 weeks after training ended for MT group), and 6 months. Results: The results suggest that MT group did not show better cognitive performance than WL group at the 2nd or 3rd assessment. However, as compared with baseline, more MT subjects showed maintaining or slight improving cognitive abilities than WL subjects in 2nd and 3rd assessments (Chi-square test,  $p < 0.05$ ). More MT

subjects with lower score on anxiety and depression scales than WL subjects suggested that MT subjects had lower level of anxiety and depression. Conclusion: Though memory training did not help MT subjects to have better cognitive performance than WL subjects, lower levels of anxiety and depression were seen in MT subjects. The frequency and duration of memory training may explain the limited efficacy of the training. Based on the positive responses of the MT participants (i.e., high attendance rate), we highly recommend the implement of these memory training exercises in daily activities of elders in the community. Using of memory training to slow down the onset of dementia fulfills the notion of medical economics, however, further investigation of its efficacy in improving cognitive abilities is strongly recommended.

**NUTRITIONAL ISSUES OF DEMENTIA CARE IN OLDER PATIENTS.** CHUEH-LIEN YANG (Chief, Clinical Dietetics Section, Department of Food and Nutrition, Taipei Veterans General Hospital Standing Director, Taipei Dietitians Association)

Dementia is a growing public health concern with potentially devastating effects, especially among the elderly population. There are many nutritional issues faced by demented patients and their caregivers. These issues include trying to ensure an optimal diet to slow the progression of the disease and encouraging demented patients to ingest enough calories to prevent weight loss. Dementia is a multi-factor pathological condition, and nutrition is one of the most important factors which may play a role on its onset and progression. Clinical and epidemiological evidence suggests that lifestyle factors, especially nutrition, may be crucial in controlling dementia. Deficiency in essential nutrients, such as certain B complex vitamins, can result in hyperhomocysteinemia, a well-known risk factor for atherosclerosis and associate with cognitive impairment in old age. A deficiency of antioxidants such as vitamins C and E, beta-carotene may also result in cognitive impairment. Some unhealthy behaviors may cause nutrition-related disorders such as hypercholesterolemia, hypertension, diabetes, and metabolic syndrome are also link to dementia. Diet plays an important role in the prevention of dementia, especially in the multi-infarct, alcoholic, vitamin B-12 and folate deficiencies related dementia, through effects on the risk factors. Control of risk factors may also prevent further progression. Diet with protein-rich foods (especially fish), non-starchy vegetables, low glycemic fruits, natural fats, low simple sugar (including fructose corn syrup food), processed foods; and moderate wine intake will be beneficial in normalizing insulin and blood sugar, providing a variety of antioxidant nutrients and improving brain function. For those demented patients, nutrition is also the dimension which may not be ignored. The impact of dementia on nutrition and eating/feeding will change throughout the course of the disease. In the early stage, they may forget to eat, feel depressed with poor intake, or become distracted and leave the table without eating. In the middle stage, the patients may be unable to sit long enough to eat, yet these at this stage may require more calories due to wandering and motor restlessness. In the late stage, they do not have intact oral motor skills for chewing and swallowing, thus become subject to malnourishment. Weight loss is a frequent phenomenon in demented patients. This can lead to general deterioration in the patient's health, increasing risk of fractures following falls and pressure ulcers, reducing resistance to infections, and raising mortality. The etiology of weight loss in demented patients may be multifactorial and the potential factors include cognitive decline resulting in an inability to prepare and eat foods, brain degeneration eliciting impairment of olfaction and taste, dementia related behavior problems such as restlessness and wandering, elevated energy expenditure, and the presence of comorbid medical illness. Many individuals with dementia have problems that put them at risk of poor nutritional intake, which may cause unintentional weight loss and increase mortality. As a result, how to develop an individualized plan of care to effectively manage the behaviors and strategies to ensure optimal nutrition and hydration can be a challenging experience. Best practices involving screening, assessment, planning, implementation and evaluation of food and nutrition programs; multidisciplinary working and caregiver education are also essential in combating malnutrition among older demented patients.

**FRAILITY IN OLDER PEOPLE AND ITS RELATIONSHIP WITH DEMENTIA.** LIANG-KUNG CHEN (Chief, Division of Geriatric Medicine, Department of Family Medicine, Assistant Professor in Family Medicine, National Yang-Ming University)

Frailty, one of the most fascinating topics in Gerontology, has gained extensive attentions in many different professional backgrounds, e.g. epidemiology, basic research to clinical practice. Despite all laboratory and clinical effort, the pathogenesis and pathophysiology of frailty remain mysterious. Currently, frailty is considered to be a progressive physiologic decline in multiple body systems, which is marked by loss of function, loss of physiologic reserve, and increased vulnerability to disease and death. Moreover, frailty increases susceptibility to acute illness, falls, disability, institutionalization, and death. The phenotypes of frailty include weight loss, weariness, low exercise tolerance, low level of physical activities, and slow walking speed. However, the inclusion or exclusion of cognitive impairment in the diagnostic criteria of frailty may be controversial. Frailty describes a state of older people, and it is strongly associated with poor clinical outcomes, like hospital admission, institutionalization, and deaths. However, all the abovementioned characteristics are also highly related to dementia. Although cognitive impairment is not included in the Fried's primary working definition of frailty, it is commonly included in the frailty index developed by geriatricians. Dementia and frailty may share common clinical presentations, however, whether frail demented older people may be at a higher chance of developing various adverse clinical outcomes remain to be determined. In conclusion, frailty and cognitive impairment are two common comorbid conditions in older people. Whether there exist a causal relationship is uncertain, but further investigation is needed to explore the mysterious association and the pathophysiology of frailty.



**DEMENTIA CAREGIVING: THE ROLE OF THE PRIMARY CARE PHYSICIAN.**  
FENG-HWA LU (*Associate Professor of Family Medicine, Division of Family Medicine, Department of Medicine, College of Medicine, National Cheng Kung University*)

Dementia is a syndrome characterized by a decline in cognition, behavioral disturbance, and interference with activity of daily function. Persons with dementia also suffer from multiple chronic medical problems and receive multiple drugs, so they need a comprehensive diagnosis and management to improve their outcome. The primary care physician is often the first doctor to observe patients with possible dementia and to make the diagnosis during caring patients' chronic diseases. Also, primary care physicians, especially family physicians provide care with characteristics of comprehension, continuity, coordination, accessibility and coordination, they are the most suitable physicians to take care patients with dementia. The role of primary care physician is to work with patients and families, and to emphasize some issues including 1) early diagnosis of dementia; 2) education about dementia; 3) psychological support for caregivers; and 4) assistance enhancing caregiver social support networks. Less than 50% of dementia patients are diagnosed by primary care physicians, since there are five main barriers for physicians to diagnose dementia in the primary care setting, including 1) failure to recognize and respond to symptoms of dementia; 2) perceived lack of need to determine a specific diagnosis; 3) limited time; 4) inadequate reimbursement; and 5) negative attitudes to the importance of assessment and diagnosis. How to resolve these barriers and to encourage physicians to diagnose and manage patients with dementia are very important. Continuing medical education can be used to improve physicians' knowledge of and confidence in dealing with dementia, then to increase the quality of care to dementia patients.

## SCREENING VERY MILD DEMENTIA IN ASIAN COUNTRY

**APPLICATION OF AD-8 TO SCREEN VERY MILD DEMENTIA IN TAIWAN.**  
YUAN-HAN YANG (*Assistant Professor, College of Medicine, Kaohsiung Medical University Medical. Staff Neurologist, Department of Neurological, Kaohsiung Medical University Hospital, Taiwan. Secretary General, Taiwan Dementia Society*)

Dementing illnesses such as Alzheimer's disease are significant health problems in the aging population. More than 140 thousands Taiwanese have dementia but few are correctly diagnosed at the earliest stages of the disease. This is due, in part, to the lack of easy-to-administer sensitive clinical tools to measure early cognitive decline. Published criteria for AD diagnosis require standard assessment of patients. Comparison of individual performance on cognitive test measures with normative values, however, may not detect declines that occur in very mild dementia, particularly in high-functioning individuals. Informant-based assessments, on the other hand, may reveal early cognitive change because of a longitudinal perspective and having face validity such as the Clinical Dementia Rating (CDR) incorporate information from a collateral source to assess change in the patient's cognitive ability to conduct their accustomed activities. These informant-based examinations, intra-individual comparisons, are more sensitive than cognitive function tests, inter-individual comparison, in detecting early stage of AD. Current informant-based assessments, however, are lengthy and require interpretation by an experienced clinician; therefore, they are difficult to use in community practice and there will likely be some acceptable trade-off to the clinician, sacrificing specificity and sensitivity to detect dementia to keep the clinical tool brief. The AD-8 scale developed by Washington University in St Louis that could be completed in a just in a few minutes with maximally balanced sensitivity and specificity to screen elderly who are already having very mild stage dementia. We test the applicability of AD-8 and examine its sensitivity and specificity in Taiwan as well as other Asian Countries.

**SCREENING EARLY STAGE OF DEMENTIA IN THE COMMUNITY.** AKIRA HOMMA (*Director, Department for Dementia Intervention, Tokyo Metropolitan Institute of Gerontology, President, Japan Society for Geriatric Psychiatry President, Japan Society for Dementia Care President, Asian Society Against Dementia*)

Persons with dementia are cared under the long-term care insurance in Japan. Eight years have passed after the implementation, there are still many issues which to have to be solved, especially regarding to the care for persons with dementia in the community. One of the major issues is how to detect early stage of dementia in the community. According to the results of recent survey, approximately 60% did not do anything when they realized some changes indicating progressive memory loss suspecting dementia in the everyday life of their relatives. Such situation is also true in the recognition and awareness of the care staff working under the long-term care insurance. Although MMS is one of the representative screening instruments to detect dementia, it is often difficult for the care staff to administer it at home in Japan. This is actually the reason why we need an instrument to detect early stage of dementia, which is easily administered by the care staff, especially in the community. Any informant-based screening instrument may be valid in this context, if it could be administered by the care staff. Also, the information collected in the administration of such instruments may be useful to construct a care plan for each person with dementia. However, it should be careful that every informant-based screening instrument will not valid for persons with suspected dementia living alone. The clinical utility and the limitations of informant-based instruments will be commented.

**MODIFIED AD8 – A USEFUL DEMENTIA SCREENING INSTRUMENT FOR CROSS-CULTURAL STUDIES IN ASIA.** ASITA DE SILVA (*Clinical Pharmacologist & Director, Clinical Trials Unit, Department of Pharmacology, Faculty of Medicine, University of Kelaniya, Ragama, SRI LANKA*)

The Mini Mental State Examination (MMSE), is the best known and most widely used cognitive screening instrument. This test, however, has been criticized both for its lack of sensitivity and specificity as well as the influence that education has on performance. Moreover, the MMSE lacks sensitivity in identifying patients with early symptoms of AD and mild cognitive impairment (MCI), and may not be useful as a screening instrument to detect early features of cognitive impairment. Thus, many researchers have tried to develop more sensitive screening tests that could have additional value in making a diagnosis of early dementia as well. The Seven-minute screen (7MS) developed by Solomon et al (1998) consists of four components (enhanced cued recall, temporal orientation, verbal fluency, and clock drawing) that assess memory, visuospatial and visuconstruction, fluency of expression, and orientation to time, cognitive functions typically compromised in AD. This test has shown good diagnostic accuracy in AD and MCI. We assessed the usefulness of the 7-MS as a screening instrument for cognitive impairment in Sri Lankan patients. 53 patients with mild-moderate AD, 34 with other dementias, 36 with mild cognitive impairment (MCI) referred to a memory clinic, and 60 patients with depression with no evidence of dementia and 56 healthy volunteers (controls) were recruited after informed consent. We found that the 7MS is a reliable instrument to screen for AD, MCI. However, it lacked sensitivity and specificity to differentiate AD from other dementias. In this context, the modified AD8 developed by Prof Yang and colleagues in Taiwan is a significant advance in dementia research in Asia. The brief instrument is simple, easy to understand, assesses important cognitive domains affected by dementia and seems 'culture friendly', and probably not affected by the level of education of the subject. As such, AD8 should be a reliable tool in cross-cultural harmonized studies in Asia to screen for early dementia, and when used with a brief cognitive assessment a useful test battery for clinical trials.

**COMMENT ABOUT POSSIBILITY OF USE OF AD8 IN INDONESIA.** PAULUS ANAM ONG (*Department of Neurology, Hasan Sadikin Hospital, Padjadjaran University, Indonesia Head, Memory Clinic of Hasan Sadikin Hospital Bandung Indonesia*)

Informant-based assessment CDR has been used as gold standard tool for early diagnosis and staging of dementia. As it is developed from CDR, AD-8 can be valid in Indonesia if all questions are culturally sensitive. In Indonesia, retirees usually do not make financial decisions directly or giving tips though they are still asked for opinion. The majority of them do not have hobbies and taking care of grandchildren are the most frequent activity they engaged. Majority of them may operate TV remote control, but not for VCR or microwaves. Some of them pay water and electricity bills, but majority of them do not handle checkbook balancing or income taxes. Considering its brevity and simple administration (can be done by clerical staff) and reported validity, it is encouraging to conduct a preliminary study to evaluate its validity in detecting dementia cases in Community Health Care Center, the widely scattered health care unit in all regions in Indonesia, where a team of health care provider included doctor(s), nurses and clerical staffs carry out health care programs.

## VASCULAR DEMENTIA

**THE RELATIONSHIP BETWEEN ALZHEIMER'S DISEASE AND VASCULAR DEMENTIA.** RACHELLE S. DOODY (*Professor, Department of Neurology, Baylor College of Medicine*)

Objectives: to discuss the areas of overlap in the clinical presentations of these two forms of dementia, as well as the differences in diagnostic criteria and prognosis, and the interactions between the two disorders. Design: review of published diagnostic criteria, natural history data, radiographic features, and studies suggesting that minor vascular lesions can unmask the presence of underlying AD. Setting: cohort studies and controlled clinical trials in academic and/or clinical trials settings. Participants: subjects with AD or VD diagnosed by standardized criteria. Intervention: clinical trials data will be included. Measurement: psychometric, radiologic, neuropathologic. Results: VD is overdiagnosed on the basis of radiographic changes. Diagnostic criteria improve specificity at the expense of sensitivity. AD patients have radiographic features that overlap with those of VD. Conclusion: Most cases thought to have VD likely have AD alone or in combination with VD.

**VASCULAR DEMENTIA: CONCEPTS, EPIDEMIOLOGY, AND NEUROPSYCHOLOGY.** KENICHI MEGURO (*Professor, Department of Geriatric Behavioral Neurology Tohoku University Graduate School of Medicine, Sendai, Japan Head of Office Against Dementia, The Osaki-Tajiri SKIP Center, Osaki, Japan*)

Vascular dementia (VaD) is the second most common cause of dementia after Alzheimer disease (AD). In contrast to AD, there is no gold standard of pathologic findings. Clinically we can use the most strict and specific NINDS-AIREN criteria, or broader term Vascular Cognitive Impairment (VCI) to avoid 'Alzheimerization' bias and promote early therapeutic intervention. The concept for subcortical VaD (SVD) has also been proposed to clarify the controversies. According to the Osaki-Tajiri Project, the

prevalence of VaD was found to be different based on the diagnostic criteria (DSM-IV, ADDTC, and NINDS-AIREN). Regarding VCI-No Dementia (vascular MCI), we identified the CDR 0.5 population who had strategic cerebrovascular disease in the thalamus, caudate head, etc. We also investigated the incidence of VaD in the same population and found two patterns: some patients met the NINDS-AIREN criteria as a result of developing cerebral infarction in the cortex, and the other pattern was the CDR 0.5 patients with cerebrovascular disorder who met the diagnosis criteria of SVD and subsequently progressed to dementia based on mal-control of risk factors. Regarding neuropsychological findings, VaD subjects showed executive dysfunction as well as memory impairment, so did the VCI-ND population. There were no effects of cerebrovascular diseases on general cognitive function or depressive state. The executive dysfunction was found to be predictive for progression to VaD, together with higher age and MRI findings such as white matter lesions and cerebrovascular diseases. A comprehensive medical and welfare system including the CDR, cognitive tests, and MRI, is recommended in community-based health policy planning for dementia.

#### **THE ROLE OF CHOLESTEROL-LOWERING AGENTS IN TREATMENT AND PREVENTION OF DEMENTIA.** CHAUR-JONG HU (*Chief, Assistant Professor, Department of Neurology, Shuang-Ho Hospital, Taipei Medical University, Taiwan*)

Although it is still not totally clear, whether the beneficial effect of cholesterol-lowering agents directly targets brain metabolism or it is an indirect effect caused by a reduction of the cardiovascular risks, the cholesterol-lowering agents could be a potential choice for treatment and prevention of dementia. In the basic researches, many proteins involved in the cholesterol homeostasis also participate the metabolism of amyloid- $\beta$  (A $\beta$ ) and repair of brain injury. Apolipoprotein E is the major cholesterol transporter in brain and it is the most important genetic risk factor for sporadic Alzheimer's disease (AD). Enhancement of ApoE expression showed both promotion of reinnervation and amyloid clearance in the brain. Elevation of cholesterol in cell membrane tends to favor the  $\beta$ -site cleavage of amyloid precursor protein (APP) and results in A $\beta$  formation. In animal models, high cholesterol diet induced A $\beta$  formation and deposition in the brain. Pharmacological depletion of neuronal cholesterol by methyl- $\beta$ -cyclodextrin or statin might switch the balance toward the non-amyloidogenic pathway. In the epidemiological researches, some longitudinal studies support the association between high midlife serum cholesterol and subsequent development of dementia. Contradictorily, it is still controversial but that high late-life serum cholesterol confers a protective effect on dementia in few studies. There are at least three waves regarding to the effects of cholesterol-lowering agents, statin in dementia. The initial wave of cross-sectional, observational studies favored a protective role for statins. The second waves, mainly consisted of two large clinical trials, which contains cognitive function as the secondary endpoint, failed to identify the same conclusion as the first wave researches. The third wave consisting of the clinical trials which focus on the treatment of dementia as the primary endpoint is still ongoing. The Alzheimer's disease cholesterol-lowering treatment (ADCLT) is a double-blind, placebo-controlled, randomized trial with accompany of cholinesterase inhibitors for mild to moderate AD (MMSE=12-28). A significant positive effect on ADAS-cog performance occurred after 6 months of atorvastatin therapy compared with placebo. The positive effect was more prominent in the patients with higher MMSE score, higher cholesterol levels (>200 mg/dl) or ApoE4 allele. In ADCLT trial, atorvastatin 80mg/day was also associated with highly significant reduction in right hippocampal volume. Another large-scaled trial of combination of atorvastatin 80mg/day and donepezil 10mg/day, the atorvastatin/donepezil in Alzheimer's disease study (LEADe) is ongoing. LEADs will report soon and is expected to provide a more definitive evaluation of the potential for statins in the treatment of AD.

Based on the basic researches, epidemiology data, clinical observation and the clinical trials, the cholesterol-lowering therapy could be a potential strategy for treatment and prevention of dementia. It warrants further investigation.

## **DEMENTIA LONG-TERM CARE MODEL**

#### **SETTING UP THE DAY TO PROMOTE HEALTH AND WELL-BEING IN LONG-TERM CARE.** MARY EGAN, LYNDIA WOLF (*Associate Professor, School of Rehabilitation Sciences, University of Ottawa, Ottawa, Ontario, Canada*)

Objectives: Daytime activity is related to well-being in individuals with dementia yet studies consistently demonstrate low levels of activity among individuals with dementia in long-term care. The objective of this presentation is to discuss facility-based decisions that, while seeming to lead to good care, actually discourage daytime activity. Approach: From the literature and clinical experience, 6 institutional factors that discourage activity were identified. These are 1. standards of care that emphasize efficient completion of activities of daily living, rather than using these tasks as opportunities for activity; 2. safety concerns leading to immobilization of individuals, which paradoxically can actually contribute to injuries; 3. emphasis on treatment of behavioural symptoms, rather than on maintenance of activity; 4. preference for large group activities which allow participation among only the most fit; 5. therapeutic intervention that favours "expert" development of programs to be carried out by rehabilitation staff, rather than training of care staff to recognize remaining abilities and interests that could support enhanced physical activity and; 6. lack of access to the patient's story by members of the care team. The impact of these practices will be discussed as well suggestions for alternative policies that encourage activity. Implications for practice: Administrators and other long-term care decision-makers play an important

role in encouraging activity to promote health and well-being among residents by ensuring that policies which encourage activity are developed and implemented. Conclusions: Many factors designed to protect the health and well-being of patients in long-term care likely contribute to inactivity and related consequences. Knowledge of these factors may be helpful in proactive development of policies and procedures that favour activity and well-being.

#### **DEMENTIA: HOW A CONSENSUS WAS REACHED BETWEEN FAMILY DOCTORS AND SPECIALISTS TOWARDS DIAGNOSIS AND TREATMENT.** SERGE GAUTHIER (*McGill Center for Studies in Aging, Douglas Mental Health Institute, Montreal, Canada, Professor, Department of Departments of Psychiatry, Neurology & Neurosurgery, Medicine McGill University, Director, Alzheimer Disease and Related Disorders Unit, McGill Centre for Studies in Aging, Douglas Mental Health University Institute*)

Objective: to update existing guidelines for the diagnosis and treatment of dementia by all interested clinicians across Canada. Design: consensus conference after review of evidence in the medical literature, complemented by expert opinion from family doctors and specialists in the field of geriatric medicine, neurology, neuropsychology and psychiatry. Results: consensus conferences implicated all disciplines interested in the care of persons with dementia in Canada have taken place in 1989 (CMAJ 1991, 144: 851-853) and in 1998 (CMAJ 1999, 160: 1738-1742; Can J Neurol Sci 2001, 28 [Suppl 1]: S1-S121). The Third Canadian Consensus Conference on the Diagnosis and Treatment of Dementia took place in March 2006 in Montreal. The main topics included: (1) concept of Mild Cognitive Impairment; (2) diagnostic criteria for dementia and mixed dementia; (3) differential diagnosis of dementia; (4) assessment and management of risk factors towards dementia; (5) management of mild to moderate Alzheimer's disease; (6) management of severe Alzheimer's disease; (7) management of dementia with a cerebrovascular component; (8) ethical issues in dementia care; (9) genetics aspects of dementia. The conclusions were published in the specialty journal *Alzheimer's & Dementia* 2007, 3: 262-440, with commentaries from world opinion leaders. Dissemination of the conclusions to family doctors is under way in the CMAJ using case studies as illustrations of the relevance of evidence-based treatment guidelines for clinical practice. Conclusions: the involvement of family doctors in consensus conferences towards the diagnosis and treatment of dementia since 1989 has facilitated access to care across Canada. Dissemination of diagnosis and treatment guidelines through medical journals read by family doctors and using case studies will facilitate dissemination of conclusions from the consensus conference. It is predicted that family doctors will play a key role in the identification of persons at risk of progression to dementia and in the use of prevention strategies.

#### **MODELS OF LONG-TERM CARE OF DEMENTIA IN THE PHILIPPINES.** SIMEON M. MARASIGAN (*Professor, Department of Neurology and Psychiatry, Faculty of Medicine and Surgery, University of Santo Tomas, Chairman, Department of Neurology & Psychiatry University of Santo Tomas Hospital*)

Characteristically, because of the close family ties, parents, grandparents live with their nuclear family usually with an unmarried child or if all are married, either with the family of the eldest or youngest child. Another common arrangement is the child who inherits the house stays with the surviving parent/s in health or in disease. These arrangements are the norm within the traditional Filipino family. One unwritten rule, no old individual lives alone or lives with "strangers" (like nursing homes) even through the early, mild or moderate stages of dementing disorders.

Long term care of patients with dementia or care of patients with moderate to severe dementia alters the family structure mildly (almost unnoticed). Because of the increasing number of people with dementia several models of care have evolved in the Philippine setting. 1. Traditional home care: patient is assimilated in a son's/daughter's family with other family members frequently visiting. Family members go on rotation at caregiving. 2. In house care: with children establishing their own family elsewhere, patient stays in his original house with house help maintained by well-off children. 3. Home extension care: family members (abroad or in the country) buy/rent/borrow a residential abode (a small house, apartment or condo unit) within the city or town where a member lives. Patient is provided with at least two helpers: one maid and one helper who accompany him for check up, for a walk or for church visit. 4. Western style care (nursing homes, assisted living): this type is not yet as popular as in the US or Europe and only available in the metropolis; usually patronized mostly by children who are working abroad for their parent. Within these models, the elements of long term care in the Philippines will be considered in the discussion: 1. Patients; 2. Carers; 3. Type of care provided; 4. The environment; 5. Finances

#### **LONG-TERM CARE FOR THE OLDER PEOPLE WITH DEMENTIA IN KOREA: PAST, PRESENT, AND FUTURE.** GUK-HEE SUH (*Professor of psychiatry, Hallym University College of Medicine, Seoul, Korea*)

Treatment of older people with dementia appears to vary in many cases with the level of affluence a society enjoys. In very poor societies, older people with dementia may be left to die. In nomadic societies, they may be seen as a burden. In peasant societies, little may be expected of them, with consequences for the identification and care of the older people with dementia. It is generally believed that in relational or sociocentric societies where the self is defined in relation to others (i.e. Confucian tradition in East Asian society), older people remain an integral part of their family and community structure. But, this is not always the case and certainly does not always mean their situation is exclusively

happier than in the West. Since the 20th century, almost all countries around the world went through or have been under their own form of “modernization” with the drastic economic, political and social changes to various extents and at varying rates. This modernization involved industrialization, urbanization, family nuclearization and “westernization”. Globalization is a new challenge of the 21st century. The current trends of changes and transformations in social structures, cultural values and behavioral patterns will continue throughout the 21st century. While, in most developing countries, modernization progresses in varying degree, the postmodern high tech revolution will continue to change the developed countries as well. Phenomenal advances of internet or web-based technology will inevitably tie whole globe as one nation. Nowadays, highest value is a global standard. In Confucian tradition, filial piety is one of the virtues to be cultivated; a love and respect for one’s parents. Filial piety is a social value which has greatly influenced the parent care and parent-child relationship of East Asian peoples – Koreans along with Chinese and Japanese. The practice of filial piety has traditionally been the natural duty and norm of adult children. In Korea, filial piety is now conceptualized and practiced more expansively over the boundary of family such as free lunch, free transportation, elderly seats in public transportation, free counseling, continuing education, sightseeing tours, elderly discount, and the long-term care insurance for the elderly. Traditionally, in East Asia, the oldest son and his wife are socially expected to assume the caregiver role for parents. But, now all offspring – husband and wife and brothers and sisters – tend to share this role. In order to adapt to new social requirement in the changing society, modification of filial piety is necessary. Authoritarian and patriarchal relationships should be changed into egalitarian and reciprocal patterns of mutual help and respect between generations. Filial piety should be re-emphasized and firstly adopted as a global standard of the 21st century. In Korea, universal nationwide long-term care insurance scheme was implemented in July 1, 2008. Ministry of Health, Welfare and Family is responsible for the maintenance and promotion of national health and social welfare, but the 3rd party payer for the long-term care insurance is the National Health Insurance Corporation (NHIC). All insurers should pay 5.04% more on top of NHI premium in 2008. Beneficiaries are older people aged 65 and older, or people with dementia or stroke whose age is under 65. Criteria to assess level of care include activity of daily living, nursing care need, rehabilitation need, cognition, and behavioral problem, which will be divided into 5 different levels. For them, a variety of comprehensive care services are provided, including community care, institutional care, cash allowance, and allowance in kind. Some problems has been observed during 2 months; exclusion of mild or ambulatory older people with dementia (PWD), relocation of PWD from geriatric hospitals to nursing homes to get benefits of long-term care insurance, complaints of insurers who should pay about 10% more premium, lack of medical treatment, lack of prevention and rehabilitation, mismatched geographical distribution of PWD and nursing homes, protests of employees of nursing homes, and so on. Future direction for dementia care should integrate medical, care, and welfare services to harmonize long-term care for older people with dementia and to optimize their quality of life as human beings with dignity.

**THE LONG-TERM CARE SYSTEM FOR THE ELDERLY IN TAIWAN: A DOMESTIC MODEL.** CHING-KUAN WU<sup>1</sup>, HUI-CHING WU<sup>2</sup>, YIN-YIN CHENG<sup>3</sup> (1. Tsy-Huey Mental Hospital, Kaohsiung Jen-Ai’s Home; 2. Department of Social Work, National Taiwan University; 3. Nursing Home of Jing-Ho Mental Hospital Yen-Chau Branch)

Purpose: For the increasing elderly population and the changing of family style and illness chronicity, the study of long-term care system becomes an important issue in Taiwan. This study tried to establish a domestic model of long-term care for the needy population. Method: This is a descriptive study to explore the related issue and current condition of development of long-term care system for the elderly in Taiwan. The data collection from literature review, the elderly services institution interview, and anecdotal evidence at Jing-Ho Mental Hospital Yen-Chau Branch were employed. Depending on collected data, we established a domestic model of long-term care system for the elderly. Result: Before Oct., 2005, there is 2,200,000 elderly, 9.7% of all population, living in Taiwan. There are 915 long-term care institutions that provide 45,926 beds for the elderly. Only 71% of beds put to use. The study found there is an inadequate comprehensive health care system to provide consistent services for the elderly in Taiwan. Based on the concept of “Aging in the place” for establishing a community long-term care system, Jing-Ho Mental Hospital Yen-Chau Branch has tried to connect diverse institutions and integrate their caring models for providing a comprehensive and consistent long-term care services. Conclusion: The study suggests it is important to build a localized long-term care network based on the living county for the elderly should be noted.

**DEMENTIA CARE MODEL IN TAIWAN: THE EXPERIENCE OF CFAD (THE CATHOLIC FOUNDATION OF ALZHEIMER’S DISEASE AND RELATED DEMENTIA).** BOW-YIN WANG (Director of St. Joseph Home For Alzheimer’s Disease and Related Dementia)

55,000 to 110,000 people suffer from dementia in Taiwan. Most of these patients are given home care by their families. Caring for a demented member is a superb burden for any family. Considering the increase of aging people in our society, demented people will also increase. How to care for them is a big challenge. The current long term care policy from government is constructing community care system to reach the goal of aging in place. The settings are: home services, home care, day care center, respite care and institution services. Dementia care is a multiple team work, the issues expect directly care services, also include education and training, research, publication and raising of public awareness program. Follow the four steps of dementia care, through the process to understand, to find out, to be concerned about and to look after for demented people, the

aim is for us to work together and dedicate ourselves for the creation of a loving world for Alzheimer’s Disease and Related patients.

## POSTERS

**FAMILY CAREGIVERS’ BURDEN IN INDIVIDUALS WITH COGNITIVE IMPAIRMENT IN TAIWAN.** LINEN LIN<sup>1,2</sup>, SHWU-CHONG WU<sup>2</sup>, MING-BEEN LEE<sup>3</sup>, RONG-CHI CHEN<sup>4</sup> (1. Department of Psychiatry, En Chu Kong Hospital, Taiwan; 2. National Institute of Health and Policy Management, National Taiwan University, Taiwan; 3. Department of Psychiatry, National Taiwan University Hospital and College of Medicine, National Taiwan University, Taiwan; 4. Department of Neurology, En Chu Kong Hospital, Taiwan)

Objective: To provide information on burdens experienced by family caregivers who took care of care-recipients with cognitive impairment in Taiwan. Design: Cross-sectional study. Setting: Community in Taiwan. Participants: 7,630 pairs of care recipients and family caregivers. Measurements: Care givers’ burdens are conceptualized as physical burden, emotional burden, relational burden, burden of time, and financial burden. Results: A multinomial logistic regression analysis of the influence of care recipients’ cognitive impairment on the family caregivers’ burden reveals statistically significant results across all dimensions. For males aged 65–69 years with cognitive impairment, a monthly household income between NTD 100,000 to 199,999, more than 5 chronic illnesses, more than mild ADL impairment, and exhibiting disturbing behaviors, and their family caregivers who are typically female, involved in a relationship of spouse, with poor health status, occupational conflicts, poor support systems, and care conflicts, with a total care period of less than 1 year, daily care period of more than 8 hours, and an additional monthly expenditure of more than NTD 1,000, relieving the family caregivers of their physical burden is mandatory. In the case of males aged 65–69 years with cognitive impairment, moderate to severe ADL impairment, and disturbing behaviors, and their family caregivers who have poor health status, occupational conflicts, poor support systems, and an additional monthly expenditure of NTD 5,000 to 100,000, relieving the family caregivers of their emotional burden is mandatory. For males aged 65–69 years with cognitive impairment, a monthly household income of less than NTD 9,999, moderate to severe ADL impairment, and disturbing behaviors, and their family caregivers who are married, involved in a relationship of non-spouse, with poor health status, occupational conflicts, poor support systems, and daily care period of more than 8 hours, relieving the family caregivers of their relational burden is mandatory. In the case of those aged 65–69 years, who are graduates from junior or senior high school, with cognitive impairment, more than 5 chronic illnesses, more than mild ADL impairment, and disturbing behaviors, and their family caregivers are jobless, with more than 6 years of education, poor health status, occupational conflicts, poor support systems, care conflicts, a total care period of less than 1 year, daily care period of more than 8 hours, and an additional monthly expenditure of more than NTD 1,000, relieving the family caregivers’ burden of time is mandatory. For males aged 65–74 years, with cognitive impairment, a monthly household income of less than NTD 10,000, more than 3–4 chronic illnesses, more than mild ADL impairment, and disturbing behaviors, and their family caregivers who are illiterate, without couple, jobless, with poor health status, occupational conflicts, poor support systems, daily care period of more than 8 hours, and an additional monthly expenditure of more than NTD 1,000, relieving the family caregivers of financial burden is mandatory. Conclusion: Policy makers should consider care-recipients’ cognitive impairment and care givers’ needs to provide appropriate support for various dimensions of family caregivers’ burdens. Keywords: family caregiver, caregiver burden, dementia, cognitive impairment

**ALZHEIMER’S DISEASE RADIOPHARMACEUTICALS: [18F]FDDNP AND [123I]IMPY.** K.W. CHANG<sup>1,2</sup>, S.H. LEE<sup>2</sup>, C.C. CHEN<sup>2</sup>, L.H. SHEN<sup>2</sup>, H.E. WANG<sup>1</sup> (1. Department of Biomedical Imaging and Radiological Sciences, National Yang-Ming University, Taiwan; 2. Division of Isotope Application, Institute of Nuclear Energy Research Atomic Energy Council, Taiwan)

Objective: Alzheimer’s disease (AD) is one of the epidemic neurodegeneration disease in older. In AD, much number of dystrophic neurites has been shown to correlate with the clinical severity of dementia, and neuronal dystrophy is associated with synaptic loss in cortical cultures exposed to fibrillar A $\beta$  ( $\beta$ -amyloid). Senile plaques (SPs) and neurofibrillary tangles (NFTs) are hallmarks in AD. Histological dye Thioflavin-S analogs had many kinds of biomarker for mapping A $\beta$ . [18F]FDDNP (2-(1-{6-[2-[18F]fluoroethyl}(methyl)amino]-2-naphthyl}ethylidene)malononitrile) and [123I]IMPY (6-iodo-2-(4-(dimethylamino)phenylimidazo[1,2-a]pyridine), also showed the superiority characteristics in binding with SPs and NFTs. In the article, we modified the protocol on an auto-synthesizer and wish to use those radiopharmaceuticals in vitro study. Material & Method: In-house-labeling [18F]FDDNP by an auto-synthesizer and [123I]IMPY was also synthesized from in-house kit. Partition coefficient was measure the ratio between the aqueous buffer (PBS) and organic buffer (octanol). In vitro study used transgenic mice (Tg2576, Tg) and human patient brain section for the assay. Sagittal brain sections from Tg mice and human for the in vitro autoradiography assay. Competition assay used 40uCi/40mL labeled-radiotracer and incubated together with 2.5mg non-radiation compound with same brain section. Results: High quality of [18F] FDDNP and [123I]IMPY (Radiochemical purity >90%) were synthesized. Partition coefficient value were 1.93  $\pm$  0.10 and 1.82  $\pm$  0.35, means lipophilic ability to penetrate the blood brain barrier (BBB). In vitro assay in, whatever in Tg mice or human brain, A $\beta$  rich regions

showed high retention ratio. Competition with non-radiation compound, showed the similar results of control. In vitro competitive assay showed that high selectivity and specificity in Tg2576 brain region. Discussion/Conclusion: In those results, we show that synthesis of [18F]FDDNP and [123I]IMPY were success. Higher quality product and in those experiments were showed the superiority results. In vitro competitive assays showed that [18F]FDDNP and [123I]IMPY is available for tracing A $\beta$  in AD research. Our future plan was using transgenic mice in vivo imaging by microPET or microSPECT. Wish to exploitative the platform for diagnosis AD.

**MANAGEMENT OF PATIENTS WITH COGNITIVE IMPAIRMENT AFTER STROKE: A SURVEY OF AUSTRALIAN OCCUPATIONAL THERAPISTS.** CHIA-LIN KOH<sup>1</sup>, TAMMY HOFFMANN<sup>2</sup>, SALLY BENNETT<sup>2</sup>, KRYSS MCKENNA<sup>2</sup> (1. School of Occupational Therapy, College of Medicine, National Taiwan University, Taipei, Taiwan; 2. Division of Occupational Therapy, School of Health and Rehabilitation Sciences, The University of Queensland, Brisbane, AUS)

**Background/Objective:** Cognitive impairment is a common and often debilitating consequence of stroke. The current practice patterns of Australian occupational therapists who work in this area are not clearly known. The aim of this study was to investigate the theoretical approaches, assessments, interventions and research evidence used by Australian occupational therapists who work with patients who have cognitive impairment post-stroke. **Design:** A self-administered, purpose-designed online survey was used. **Participants:** Australian occupational therapists who worked with stroke patients with cognitive impairment during the survey period. **Results:** Survey responses were received from 102 occupational therapists. The client-centred approach was the most commonly used theoretical approach, with 81.3% and 72% using it often or all of the time with inpatients and outpatients, respectively. Assessments that were most frequently used were the Mini-Mental State Examination (63.7% of participants), the Lowenstein Occupational Therapy Cognitive Assessment (45.1%), the Functional Independence Measure (57.8%), and the Assessment of Living Skills and Resources (10.0%). Interventions involving functional activities were used more frequently than compensatory techniques, such as diaries, alarms, or other electronic devices, and paper and pencil remedial exercises. Few (16%) participants used computer programs specifically designed for cognitive rehabilitation. Although 60.8% of the participants reported using research literature when making decisions about interventions, a higher percentage reported relying on their past experience (88.3%) and colleagues' opinions (77.4%). **Conclusion:** This study provides an insight into the current practices of Australian occupational therapists who work with people who have cognitive impairment after stroke. Some frequently used assessments were suggested to inform current occupational therapists when choosing assessments for stroke patients with cognitive impairment. Client-centredness is emphasised in current practice, however, the use of research evidence to inform practice appears to be limited. Further education is necessary to facilitate evidence-based practice in this area. **Key words:** stroke, cognition, occupational therapy, health surveys

**COMPARISON OF PET, SPECT AND MR IMAGES IN EARLY DIAGNOSIS OF CREUTZFELDT-JAKOB DISEASE.** DAIKI TAKANO, TETSUYA MAEDA, MIO MIYATA, YUICHI SATOH, KEN NAGATA (Department of Neurology, Research Institute for Brain and Blood Vessels Akita, Japan)

**Objectives:** Magnetic resonance imaging (MR), especially diffusion weighted images (DWI) is known to be useful in the early diagnosis of Creutzfeldt-Jakob disease (CJD) On the other hand, positron emission tomography (PET) and single photon emission computerized tomography (SPECT) which can detect hypoperfusion and hypometabolism are also widely used in the early diagnosis of dementias. We compare the MR-DWI and SPECT/PET findings in patients with CJD in the early stage. **Subjects and Methods:** The present study was based on 7 consecutive patients who were admitted to our hospital and diagnosed as having CJD between Jan 2000 and Jun 2008. All patients underwent CT, MRI and SPECT or PET, and we compared SPECT or PET findings with MR-DWI findings over time. **Results:** All cases showed decreased uptake of tracer in various regions on SPECT in the early stage of CJD in whom no significant cerebral atrophy was detected on CT or MR images. The hypoperfusion or hypometabolic areas were more extensive than the high-intensity lesions on MR-DWI in 4 of 7 patients and both functional imaging and MR were carried out within one month from their onset in 3 of these 4 patients. Furthermore, as the disease progresses, the high-intensity lesions on MR-DWI expanded to the areas which were shown as hypoperfusion on SPECT. **Case Reports:** Case1: was a 72-year-old woman who complained of a discomfortable feeling in her left upper extremity 2 months before her first visit to our hospital. Upon the first neurological exam, she was restless, and unable to follow the verbal orders properly. Her cognitive function was impaired. She also displayed a truncal and limb ataxia, lead-pipe rigidity and joint contracture in left upper extremity. She showed rapid deterioration after admission, and was received a tube-feeding because of severe dysphasia. Thereafter she rapidly became apallic state, and showed snout reflex and forced grasping. The first MR-DWI demonstrated high intensity lesions in the right cingulate gyrus, middle frontal gyrus and frontal operculum, whereas a hypoperfusion was detected in the right frontal and basal ganglionic areas on IMP-SPECT. One month later, high intensity lesions on MR-DWI expanded to basal ganglionic areas. She died 9 months after her first visit, and was diagnosed as a CJD by the neuropathological investigation. Case2 was a 72 year-old man who showed a word-finding difficulty 4 months before his first visit, and a weakness and tremor in his right upper extremity 2 months before his first visit. Upon the first neurological exam, he was aphasic and showed a mild right hemiparesis. Thereafter he had been showing a gradual deterioration including the right hemiparesis and myoclonus in a bed-ridden state. The first MR-DWI showed high intensity lesions in the left frontal, temporal lobe and basal

ganglia, and 99mTc-HMPAO-SPECT demonstrated a hypoperfusion in those brain regions. There was no significant change on the follow-up MR, whereas an additional hypoperfusion was detected in the right cerebral cortex. One month later, high intensity areas on DWI expanded to the hypoperfusion regions as shown by SPECT. He died 7 months after his first visit and was diagnosed as a CJD by the neuropathological investigation. **Discussion:** Shih and colleagues (1987) reported that the hypoperfusion on 123I-HIPDM SPECT appeared before the morphologic abnormalities on CT or MR in the early diagnosis of CJD patients. Matsuda and colleagues (2001) showed a decreased CBF on 123I-IMP SPECT when no atrophy was seen on CT or MR, and no periodic synchronous discharge (PSD) was detected on EEG in 7 cases with early CJD. Similar to these results, all of our cases showed a decreased tracer uptake on SPECT in the early stage of CJD. These data suggest hypoperfusion and hypometabolism may precede neuronal death. Since Bahn and colleagues (1997) demonstrated high intensity signals on MR-DWI in patients with early CJD, MR-DWI has been widely used in the early diagnosis of CJD. Although the exact mechanisms underlying the high intensity of MR-DWI remains to be clarified, spongy degeneration or accumulation of prion protein can be a candidate for the explanation of the high intensity of MR-DWI. However, there are only a few reports which compared the decrease in CBF with high intensity on MR-DWI in CJD patients. Our data suggest that the hypoperfusion may precede the appearance of the high-intensity lesions on MR-DWI in the early stage of CJD. We can also observe a hypoperfusion on SPECT in the early stage of Alzheimer disease when there is no significant cortical atrophy on either CT or MR. Hypoperfusion reflects a hypometabolism in the lesions. It is well known that there is a peculiar parieto-temporal hypoperfusion pattern on SPECT or PET in patients with early Alzheimer disease, whereas CJD patients show hypoperfusion in various brain regions including frontal lobes from the early stage of the disease. It will be useful for the differential diagnosis of CJD from other cause of dementias to compare the hypoperfusion patterns on SPECT. **Conclusion:** Patients with CJD show hypoperfusion and hypometabolism on SPECT or PET from their early stage. A combination of MR-DWI with SPECT or PET may strengthen the early diagnosis of CJD. **Keywords:** Creutzfeldt-Jakob disease, early diagnosis, MRI, SPECT

**NEUROIMAGING PREDICTORS FOR COGNITIVE IMPAIRMENT IN CONFLUENT WHITE MATTER LESION.** VINCENT MOK, KELVIN WONG, ADRIAN WONG, CAROL XIONG, XIANG YAN CHEN, YANGKUN CHEN, REINHOLD SCHMIDT, WINNIE CHU, LAWRENCE WONG, STEPHEN WONG (Department of Medicine and Therapeutics (V.M., A.W., C.X., X.Y.C., Y.K.C., L.W.) and Department of Radiology and Organ Imaging (W.C.), The Chinese University of Hong Kong, Shatin, Hong Kong SAR, China; Department of Neurology, Medical University of Graz, Austria (R.S.) Methodist Hospital Research Institute, Texas, USA, and Cornell Weill Medical College (K.W., S.W.))

**Objectives:** Although confluent white matter lesion (WML) may associate with cognitive impairment, some patients with confluent WML may have normal cognition. We hypothesized that atrophy at frontal sub-regions and cortical gray matter (cGM) may also impair cognition. **Design:** Cross-sectional study. **Setting:** Stroke clinic of a university affiliated hospital. **Participants:** We recruited 100 ischemic stroke patients (mean age 75 $\pm$ 7.6; 48% female) with confluent WML on MRI having varying severity levels of cognitive impairment. **Measurements:** We used automated method to quantify volume of WML and regional brain volumes. We performed separate univariate regression by entering volume of various frontal sub-regions (superior, middle, and inferior frontal gyrus and lateral and medial fronto-orbital gyrus) to identify predictor(s) for executive function as measured by Mattis dementia rating scale - initiation/perservation subscale (MDRS I/P) and global cognition as measured by mini-mental state examination (MMSE). We then determined independent predictors for MDRS I/P and MMSE separately by entering volume of significant frontal sub-region(s) and following variables into multivariate regression: age, education, and volume of WML, total infarct, hippocampus, lateral ventricle, and cGM. **Results:** Univariate regression identified that only volume of left lateral fronto-orbital gyrus ( $\beta$ =-0.30,  $p$ =0.02) predicted MDRS I/P. Multivariate regression showed that only education ( $\beta$ =0.28,  $p$ <0.001) and volume of left lateral fronto-orbital gyrus ( $\beta$ =-0.30,  $p$ =0.02) predicted MDRS I/P. Univariate regression failed to identify any frontal sub-regions in predicting MMSE. Multivariate regression without entering data of frontal sub-regions showed that education predicted MMSE ( $\beta$ =0.49,  $p$ <0.001) and volume of cGM had borderline significance ( $\beta$ =-0.21,  $p$ =0.06) in affecting MMSE. **Conclusion:** Atrophy of the left lateral fronto-orbital gyrus predicts executive dysfunction and cGM atrophy probably impairs global cognition in patients with confluent WML. **Keywords:** neuroimaging predictors, confluent white matter lesion

**THE CLINICAL USE OF P300 EVENT-RELATED POTENTIALS FOR THE EVALUATION OF DONEPEZIL TREATMENT FOR ALZHEIMER'S DISEASE.** YU-SAN CHANG., MEEI-YUEH CHEN, CHAI-FAN CHIU, SHU-HUI TANG (Kai-Suan Psychiatric Hospital, Kaohsiung, Taiwan)

**Objective:** To evaluate the effect of donepezil (5mg/day) treatment upon auditory P300 event-related potentials (ERPs) and cognitive change amongst patients afflicted with Alzheimer's disease (AD). **Methods:** Sixty patients (29 men, 31 women, average age 77.1 $\pm$ 5.8 yr) suffering from AD, according to DSM-IV and NINC-ADRDA criteria, underwent evaluation of their cognitive function (defined by Cognitive Ability Screening Instrument, CASI and Mini-Mental State Examination, MMSE) and P300 ERPs at the commencement of, and during, a 20-to-22-week study period. During this period study participants were administered donepezil at 5mg/day. Paired Student's t-testing and application of Pearson's correlation were used for statistical analysis of study data. **Result:** All patients completed the study in full. Reduction of P300 latency ( $p$ =0.001) over time,

associated with a parallel improvement as regards cognitive performances (CASI scores,  $p=0.015$ ; MMSE scores,  $p=0.003$ ) were observed for the study group patients being administered donepezil. The P300 latency for these individuals was significantly positively correlated with the mean CSAI scores and the mean MMSE score at baseline ( $p=0.034$ ,  $p=0.005$ ) and at end-point ( $p=0.005$ ,  $p=0.000$ ). Conclusion: Donepezil treatment revealed both a cognitive improvement for study participants, and also a P300-latency reduction subsequent to the drug's administration for a period of 20-22 weeks. P300 latency would appear to be a reliable objective instrument for the assessment of cognitive response to donepezil for patients afflicted with AD. Keywords: Alzheimer's disease, cognitive function, donepezil, P300

**THE PROCESSING OF VERBAL WORKING MEMORY IN NORMAL AGEING AND PRECLINICAL DAT PATIENTS.** HSIAO-TING HO<sup>1</sup>, JULIA-HSIN TSU<sup>2</sup>, NELWEN GUO<sup>3</sup>, MING-CHYI PAI<sup>3,4</sup> (1. Potz General Hospital; 2. Department of Clinical Psychology, Jianan Mental Hospital; 3. Institute of Behavioral Medicine, National Cheng Kung University; 4. Division of Behavioral Neurology, Department of Neurology, National Cheng Kung University Hospital)

Objective: Many studies have shown that normal aging and Dementia of Alzheimer's type (DAT) performed less well in verbal short-term memory tasks. However, the cognitive processes responsible for this verbal short-term storage impairment are still unclear for both populations. Since the deterioration of working memory functions has been suggested as an explanation of cognitive decay, besides, verbal processing originates from auditory and visual perception; the study used a task that includes auditory and visual stimuli to assess the participants' verbal working memory to determine the underlying cognitive processes. Design: Case-control study. Setting: Neurological clinic in a teaching hospital and community. Participant: 38 healthy younger individuals, 32 healthy older individuals, and 31 preclinical DAT patients were enrolled. All participants have normal or corrected visual and auditory acuity. Measurement: Information about the participants' cognitive state was obtained from Mini-Mental State Examination (MMSE). The Scale of Instrumental Verbal Working Memory of Daily Life was used to measure the participants' verbal working memory. Result: Healthy younger individuals performed superior in visual subtest while participants with normal aging and preclinical DAT were doing better in auditory subtest. Furthermore, healthy older individuals demonstrated a simultaneous performance with healthy younger adults in auditory subtest, whereas patients with preclinical DAT performed significantly lower as compared to healthy younger and older adults. Moreover, there was a degenerative tendency in visual subtest from healthy younger individuals to healthy older individuals to preclinical DAT patients. Conclusion: It was assumed that healthy elderly individuals and preclinical DAT patients have limited working memory capacity. Thus, they cannot benefit from dual perceptions but suffer from information with dual codes. Although it was suggested that these inefficiencies could be compensated by some support, the result in the present study showed that not all supplements would be useful. Instead, the clinical practitioners should find an appropriate support for different type of subjects. The finding of this study provided a perspective that may relate to the verbal short-term storage impairment. In addition, the finding would be helpful in designing individualized cognitive rehabilitation program for normal aging and patients with preclinical DAT. Keywords: verbal short-term storage impairment, verbal working memory, normal aging, preclinical DAT

**INOS AND PER1 EXPRESSION IN DIFFERENT SLEEP STAGES AMONG COGNITIVE IMPAIRMENT PATIENTS.** ING-JY TSENG<sup>1</sup>, HSING-CHENG LIU<sup>2,3</sup>, REY-YUE YUAN<sup>4</sup>, JAU-JIUAN SHEU<sup>4</sup>, JIA-MING YU<sup>4</sup>, CHAUR-JONG HU<sup>4,5,6</sup> (1. College of Nursing, Taipei Medical University, 2. Department of Psychosomatic Medicine, Taipei City Psychiatric Center, Taipei City Hospital, 3. Department of Psychiatry, School of Medicine, Taipei Medical University, 4. Department of Neurology and The Topnotch Stroke Research Center, Taipei Medical University, 5. Sleep Center, Taipei Medical University Hospital, 6. School of Medical Technology, Taipei Medical University, all in Taipei, Taiwan)

Objectives: Circadian and sleep disturbances are common behavioral and psychological symptoms of dementia. The circadian rhythm-related molecules might be altered in dementia patients. This study was to explore the PER1 (one of the circadian genes) and inducible nitric oxide synthase (iNOS, could generate nitric oxide which is important in sleep regulation) expression difference between cognitive impairment subjects and controls. Design, Participants and Measurements: We surveyed the iNOS and PER1 mRNA expression in the peripheral leukocytes by real-time PCR during rapid eye movement (REM) sleep, non-REM sleep and wake stages respectively among the patients with Alzheimer's disease (AD, N=5), mild cognitive impairment (MCI, N=8) and controls (N=9) under polysomnography examination. Results: We found iNOS expression significantly increased during REM sleep in AD patients by comparison to MCI patients and controls. There were no significant differences of PER1 expression between these three groups but an increase of PER1 expression in the wake stage was observed among all participants. Conclusion: The possible cause of increase of iNOS expression in REM sleep in AD patients might be a compensation to maintain REM sleep. However, the real role of nocturnal expression of iNOS in AD requires further investigation.

**NO EVIDENCE OF ASSOCIATION BETWEEN METABOLIC SYNDROME AND EVENT-RELATED POTENTIALS.** CHIOU-LIAN LAI, HSIN-YI HSIEH, CHING-KUAN LIU (Department of Neurology, Kaohsiung Medical University Hospital, Kaohsiung Medical University)

Background: The metabolic syndrome, a clustering of several commonly disorders that include hyperlipidemia, may be a risk factor for cognitive decline in the elderly. The

diagnosis of dementia largely depends on neuropsychological assessment that is heavily influenced by cultural background and educational level. Event-related potentials (ERPs; P300) are free from cultural and educational influence and provide an objective method to evaluate cerebral function related to cognitive processes. Objectives: The aim of this study was to clarify the relationship between metabolic syndrome and ERPs in middle-aged and older adults without dementia. Methods: Using cross-section design, we recruited 145 cognitively intact participants (M/F: 68/77; mean age: 67.72±6.33 y/o; mean educational level: 11.38± 3.61 years) from community and health examination center in Kaohsiung Medical University Hospital. Each subject underwent 1) the fasting plasma glucose, 2) the serum levels of HDL-cholesterol and triglyceride, 3) the waist circumference, body weight, and body length, 4) the blood pressure, 5) P300. The metabolic syndrome (MS) was based on the National Cholesterol Education Program's Adult Treatment Panel III (NCEP: ATP III) criteria. Results: There was no difference in demographic characteristics, including mean age (MS, 68.39±6.45 y/o vs. non-MS, 67.45±6.30 y/o), sex (M/F: MS, 19/22 vs. non-MS, 49/55), and level of education (MS, 11.07±3.54 years vs. non-MS, 11.50±3.65 years) between participants with and without metabolic syndrome. After adjustment for age, gender, and level of education, there was no significant difference between those with and without metabolic syndrome in latencies (Fz: MS, 406.68±39.42 ms vs. non-MS, 408.99±39.40 ms, Cz: MS, 411.23±45.89 ms vs. non-MS, 415.17±42.02 ms, Pz: MS, 417.45±45.49 ms vs. non-MS, 421.95±39.27 ms), and amplitude (Fz: MS, 7.98±3.78  $\mu$ V vs. non-MS, 8.12±7.99  $\mu$ V, Cz: MS, 8.16±3.71  $\mu$ V vs. non-MS, 8.05±5.81  $\mu$ V, Pz: MS, 8.81±4.45  $\mu$ V vs. non-MS, 9.17±5.18  $\mu$ V) of the P300. Conclusion: The metabolic syndrome has no effect on ERPs in middle-aged and older adults without dementia. Keywords: metabolic syndrome, event-related potentials, elderly

**SLEEP DISTURBANCES IN PATIENTS WITH ALZHEIMER'S DISEASE AND SUBCORTICAL ISCHEMIC VASCULAR DEMENTIA.** JONG-LING FUH, SHU-JIUN WANG (Neurological Institute, Veterans General Hospital-Taipei and National Yang-Ming University Schools of Medicine, Taipei, Taiwan)

Background: Subcortical ischemic vascular dementia (SIVD), due to small-artery disease and hypoperfusion, is clinically homogeneous and a major cause of vascular cognitive impairment and dementia. Our previous study showed that in patients with SIVD or Alzheimer's Disease (AD) behavioral disturbances did not differ. Less is known about the sleep disturbance symptoms in patients with these disorders. Objective: To explore sleep disturbances in patients with SIVD and AD. Method: We conducted a case-control study in a dementia clinic. All the participants received brain imaging studies. The diagnosis of SIVD was made according to the criteria proposed by Erkinjuntti et al. and the diagnosis of probable AD to the criteria of the National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer's Disease and Related Disorders Association. The Mini Mental State Examination (MMSE) was used to evaluate global cognitive function and the Sleep Disturbance Symptom Questionnaire (SDSQ) was used to assess 20 symptoms of sleep disturbance. Two measures were calculated based on the SDSQ symptom response. The "sleep disturbance score" (sum of 20 frequency ratings) and the number of items rated as having occurred at least once per month. The behavioral disturbance was evaluated by the Neuropsychiatric Inventory (NPI-10) and Cohen-Mansfield Agitation Inventory (CMAI). Results: We enrolled 103 patients (63 males and 40 females, mean age 80.4±5.6) with SIVD and matched with 103 patients with AD by age ( $\pm 3$  years), gender and MMSE score ( $\pm 3$ ). Their MMSE scores (16.6±5.9 SIVD vs. 17.1±5.9 AD), educational years (8.4±5.5 SIVD vs. 8.5±5.2 AD) and the scores of NPI-10 (11.3±14.7 SIVD vs. 13.5±20.9 AD) and CMAI (41.0±18.0 SIVD vs. 42.3±20.0) were similar between the patients with SIVD and AD. The time in bed did not differ between the patients with SIVD and AD (9.1±2.3 vs. 9.0±2.3 hours) but the patients with SIVD had significantly higher SDSQ scores compared with AD patients (28.0±13.2 vs. 22.9±13.5,  $p=0.007$ ). SIVD patients had higher frequencies of two day-time behaviors when compared to those with AD (drowsiness during the day: 85.4% vs. 66.0%,  $p=0.001$ ; and, taking naps during the day: 91.3% vs. 76.7%,  $p=0.004$ ). The night time behavior did not differ between these two patient groups. Conclusions: Manifestations of sleep disturbance differ between patients with AD and SIVD. The patients with SIVD had a more disturbed circadian rhythm compared to patients with AD, which might be due to different underlying mechanisms.

**MENTAL SPATIAL ROTATION ABILITY AND GETTING LOST EXPERIENCES IN PATIENTS WITH MILD ALZHEIMER'S DISEASE.** KUANG-CHI CHEN<sup>1</sup>, MING-CHYI PAI<sup>2</sup> (1. Institute of Behavioral Medicine; 2. Division of Behavioral Neurology, Department of Neurology, National Cheng Kung University, Tainan, Taiwan)

Objectives: Alzheimer's disease (AD) is a common degenerative disease among older adults. Many AD patients exhibit way-finding difficulties in the very early stage of the disease, and about half of them had the experiences of getting lost. The reasons why AD patients would get lost are still not entirely understood. Mental spatial rotation is an ability to rotate mental representation from one perspective to another, and has shown to be impaired in AD patients. This research aimed at analyzing the relationship between the ability of mental spatial rotation and the getting lost experience in the very mild AD patients who are residing in southern Taiwan. Participants: Twenty-nine AD participants, including 17 male, were invited to take part in this study, from Medical Center of Chen Kung University. The diagnosis of AD was made by a behavioral neurologist according to NINCDS-ADRDA and DSM-IV criteria. Thirteen normal controls (NC), including 4 male, are healthy volunteers without neurological or psychiatric disorders. Two groups were matched in educational years. Design and Measurements: We divided AD patients into two groups by Questionnaire for Everyday Navigational Ability (QENA), one with getting

lost experiences (AD-GL, n = 15) and the other without (AD-NGL, n = 14). The cognitive and daily living functions of the participants were assessed by CASI and CERAD, and their mental spatial rotation ability by Right-left Orientation Test of Examiner's Body (RLOT/EB), Figure Rotation Test (FRT) and Money Road-map Test (MRMT). We also administered Right-left Orientation Test of Own Body (RLOT/OB) and Judgment of Line Orientation Test (JLOT) to eliminate other factors that would affect the performance of mental spatial rotation such as right-left discrimination and visual-spatial perception. We used Virtual Environment Test (VE) to see if the mental rotation ability would affect the sense of direction of these participants in the 3-D environment. Sitting in front of the computer with 17-inch LCD monitor, each participant was provided with a map of the VE with five landmarks on it. They were requested to point each of the landmarks by using joy stick at three perspectives, namely 0°, 90° and 180°, when the map direction was kept unchanged. One of the three perspectives was congruent with the map direction, while for the other two perspectives, the participants had to perform 90° and 180° mental spatial rotation. Pointing error between the pointing direction and the correct direction was calculated automatically. We hypothesized that AD-GL would perform worse at 90° and 180° perspectives than AD-NGL and NC did. Results: The mean age of the AD was 70.9 years old and that of the NC 61.5. AD patients performed worse than NC in MMSE (24.9 vs. 28.9, p=0.000), CASI (82.2 vs 94.6, p=0.000), and Word List (p=0.027), Registration (p=0.000), Recall (p=0.000), Recognition (p=0.001), Spatial Recall (p=0.000), and Trail-making in the CERAD. No difference, however, was detected between AD-GL and AD-NGL in CASI and CERAD. No difference was found between AD and NC in all mental rotation tests: RLOT/EB (p=0.134), FRT (p=0.327), MRMT (p=0.796). AD-GL performed better than AD-NGL did in MRMT (p=0.041) but difference was not detected between AD-GL and AD-NGL in RLOT/EB (p=0.089), FRT (p=0.243). In VE Test, three AD-GL and four AD-NGL participants failed because of an inability to understand the instructions. Those who complete the VE study produced more pointing errors at 90° and 180° than at 0° perspective (p=0.002), and AD patients made more errors than NC (p=0.022) did, but no interaction was found between the three perspectives and the two groups (p=0.538). There was neither difference of pointing error between AD-GL and AD-NGL (p=0.088), nor was an interaction between perspectives and groups (p=0.895). Conclusions: Although the AD patients were in the very early stage, they showed deficits in many cognitive domains, especially in the domain of memory. Half of them reported having getting lost experiences, indicating that way-finding problem is one of the most important issues for such patients. That no difference was detected in the tests requiring mental spatial rotation ability between AD and NC as well as between AD-GL and AD-NGL may suggest that deficit in mental spatial rotation ability alone is not a key factor causing AD patients to be lost. The more pointing errors in VE test produced by AD may be unrelated to mental spatial rotation. Further study is needed to answer this question. Keywords: Alzheimer's disease, getting-lost, mental spatial rotation, virtual environment

**PATIENT-CENTERED GROUP HOME: A NEW DEMENTIA CARE MODEL.** CHIA-YING LIN<sup>1</sup>, MIAO-YU LIAO<sup>1</sup>, KOW-TING FANG<sup>2</sup> (1. Taichung Hospital, Department of Health (Taiwan); 2. National Yunlin University of Science & Technology (Taiwan))

Objective: Currently, people, with age over 65 years old, is over two millions, about 10.2% in the whole populations in Taiwan. The emergence of incidences came from dementia patients are increasing and will continuously dominate the entire hospital setting in the near future. Armed with the memory loss, thinking problem, and bazaar behavior of Dementia patients, their family and themselves suffer from a variety of pains, including finance, care burden, time spend, social perspectives. Taichung Hospital initiated a new patient-centered group home care model for dementia patients in Mar, 2008 and aimed to make these patients feel like at home, and receive professional medical care. Design & Settings: Patient-centered Group Home consists of the following components: 1. Tailor-made hardware, Patient-centered group home design, in terms of nine people in a small unit with living room, restaurant, multi-functional sensor room and hidden nurse station, is likely to help patients to bridge the perception gap between hospital and home. 2. Integrated team work. Patient-centered group home incorporate with a team work who have family physicians, neuro doctors, psychiatrics, rehabilitation doctors, nurses, nurse aids, social workers, pharmacists, and dieticians to make the integrated care plans in terms of short, mediate, long term, from medical, psychological, social aspects, for the Dementia patients. Measurements: At the beginning, Standard evaluation form (Clinical Dementia Rating score,CDR) was measured for Dementia patients and then, Geriatric depression score and satisfaction questionnaire were given every 6 months for monitoring the change of their situations and perceptions. Results: Our Integrated team plan for every resident is 100%. CDR results showed that 88% dementia patients are mild to moderate and 12% are severe type. Based on GDS (Geriatrics Depression Score), there is two-third with normal situation and 33% in mild depression field. Eighty-three percent of residents satisfied with our group home. Conclusion: The results revealed that group home care model is good for mild to moderate dementia patients associated with maintaining their origin life model, keeping their function, dignity and privacy. Due to group home is a new care model in Taiwan, it is hopeful that this model provides a rough direction for its exploration.

**USING TWO KIND OF TRANSGENIC MICE TO ESTIMATE ALZHEIMER'S DISEASE RADIOPHARMACEUTICALS.** K.W. CHANG<sup>1,2</sup>, S.H. LEE<sup>2</sup>, C.C. CHEN<sup>2</sup>, L.H. SHEN<sup>2</sup>, H.E. WANG<sup>1</sup> (1. Department of Biomedical Imaging and Radiological Sciences, National Yang-Ming University, Taiwan; 2. Division of Isotope Application, Institute of Nuclear Energy Research Atomic Energy Council, Taiwan)

Objective(s): Alzheimer's disease (AD) is the most common neurodegenerative disorder-affecting millions of elders with two hallmark: senile plaques (SPs) and

neurofibrillary tangles (NFTs). Transgenic mice (Tg mice) have proven as modeling of AD neuropathology. In the article, we used Tg2576, APP protein and dE9, APP and PS1 protein, as the model to estimate with AD radiopharmaceuticals. Material & Method(s): In-house-labeling [18F]FDDNP and 123I-IMPY. In vitro study used transgenic mice brain section with radiopharmaceuticals. Ex vivo study, postinjected for 30min, sacrificed and take the brain section for imaging. Protein quantitatively used the western blotting with mouse serum. Result(s): High quality of [18F] FDDNP and [123I]IMPY were synthesized. In vitro and ex vivo study, we measure different sections by brain and Tg2576 mice showed higher accumulation than dE9 mice. Protein quantitative, Tg2576 mice showed more Aβ 1-40 than dE9 mice (155 pg/mL and 55 pg/mL, separately). Discussion/Conclusion(s): In those results, we could observed Tg2576 had higher Aβ 1-40 than dE9 mice (although two kinds mice will grow more than 20 months). Maybe it causes the distinct results in in vitro and ex vivo study. So in developing of radiopharmaceuticals maybe used Tg2576 mice is between than dE9 mice.

**EFFECTS AND RELATIVE FACTORS OF MAINTAINING AChEIS TREATMENT ON ALZHEIMER DISEASE IN A 4-YEARS FOLLOW-UP STUDY IN TAIWAN.** WEN-CHEN OUYANG<sup>1,2,3</sup>, YUN-CHAN CHI<sup>4</sup>, CHIEH-NAN LIN<sup>1</sup>, WAN-TING HSU<sup>1</sup>, SHUN-CHIN LIANG<sup>1</sup>, HSIEN-JANE CHIU<sup>1</sup> (1. Jianan Mental Hospital, Taiwan; 2. Griffith University, Australia; 3. Chang Jung Christian University, Taiwan ; 4. National Cheng Kung University, Taiwan)

Objectives: This study is meant to explore the treatment efficacies of the three AChEIs used in Alzheimer's dementia patients, to compare the differences in the maintenance treatment time for the three AChEIs and to find related factors affecting maintenance treatment time during 4-year follow-up. Design, setting, and participants: A retrospective, observational hospital-based study in 140 male and 212 female patients with Alzheimer's dementia using AChEIs had a mean age of 76.2+ 7.6 and were followed up for a mean of 1.66 + 1.39 years. Intervention: 3 AChEIs such as Aricept, Exelon, and Reminyl. Methods: There are 352 patients using three types of AChEIs, 160 patients using Exelon, 158 patients using Reminyl, 34 patients using Aricept, between 31, Jan, 2001 and 01, Jul, 2008. The information is input and analyzed by means of the SPSS 14.0 statistics software and the statistics are done with Chi-square test, ANOVA, Log-rank test, and Cox-Hazard regression. Main outcome measures & variables: We collected gender, physical disease, CDR at first visit and before stopping AChEIs, side effect after 1st use of AChEIs, years of using AChEIs, years of education, duration between disease onset and using AChEIs(years), age for the first doctor's visit by medical chart review. Results: There is no difference among the three AChEIs group's age by ANOVA, (p=0.428). No statistical differences are found in terms of gender, years of education, duration between disease onset and using AChEIs. (P > 0.05, Chi-square test or ANOVA) Each of the three groups, namely Exelon, Reminyl, and Aricept, has 76.9%, 65.2%, and 73.5% cases, respectively, with concurrent physical diseases. (P = 0.067, Chi-square test). There are 230 patients collected the first and latest (before stopping AChEIs) CDR. The first and latest CDR = 0.5 for these sample are 12.2% vs. 12.6%. The CDR =1 are 44.8% vs. 29.6%. The CDR=2 are 36.5% vs. 27.8%. The CDR =3 & 4 are 6.6% vs. 30.0%. (p < 0.001, by McNemar's Chi-square test).The ratio of deterioration during AChEIs treatment is 32.6% (75/230), and the ratio of improvement is 11.3%. There are 56% of AD patient using AChEI whose CDR did not deteriorated or improved. 31.5% of dementia patients experience overall side effects during the first 6 months after using AChEIs. There are statistically different between 3 groups by Chi-square test ( p=0.025). 57.1% of the dementia patients have used the AChEIs for over 6 months. There is no statistical difference among the three groups by Chi-square test. The average numbers of months for using Exelon, Reminyl, and Aricept are 14.6 ± 15.2, 13.9 ± 14.2, and 17.4 ± 16.9, respectively. There is no difference among the three groups. (P=0.475, ANOVA) The long-rank test finds no significant statistical differences in the maintenance treatment time when using these three AChEIs (p = 0.482). The median survival for Exelon is 7.57 months. That for Reminyl is 7.37 months. That for Aricept is 8.7 months. The ratios for using AChEIs in six months, one year, two years and three years among the 352 patients are 57.1%, 38.1%, 21.0%, and 11.4%. In addition, Cox-Hazard regression shows there is no different risk of discontinuation between the three types of drugs. (p= 0.39 & 0.28, HR of Aricept=1). The male had 1.29 higher risk of stopping AChEIs than female(p=0.036). The hazard rate (HR) is 1.93 in the patients whose duration between disease onset and using AChEIs were below one year than the patients who suffered from AD over 3 years before using AChEIs (p=0.040). The third relative factor of maintaining using AChEIs is education level. The patient who has no education has shorter maintenance time than the others (HR=1.497, p= 0.015). Conclusion: This study shows no significant differences in the maintenance treatment times among patients using 3 AChEIs to treat their Alzheimer's disease. The ratio for continually using AChEIs in Alzheimer's dementia patients decrease from 57.1% to 11.4% after 6 month to 3-year follow-up. This study also finds the patients whose gender are male, whose duration between disease onset and using AChEIs is below one year and patients without receiving any education have higher risk of discontinuation of AChEIs. Keywords: Alzheimer's disease, AChEIs, elderly dementia, adherence, maintenance treatment

**THE EFFECT OF CUE MANIPULATION ON RECOGNITION OF SCENES IN PATIENTS WITH EARLY ALZHEIMER'S DISEASE.** YEN-TI LEE<sup>1</sup>, MING-CHYI PAI<sup>2</sup> (1. Institute of Behavioral Medicine; 2. Division of Behavioral Neurology, Department of Neurology, National Cheng Kung University, Tainan, Taiwan)

Objectives: Previous studies have shown that patients with Alzheimer's disease (AD) would exhibit impairment to detect changes in the visual environment and deficits in spatial contrast sensitivity. These impairments may affect their everyday navigation, particularly in the scene recognition. The aim of this study was to evaluate AD patients

their ability to recognize street views by manipulation of various visual cues. Participants: The study was carried out in the Medical Center of National Cheng Kung University located in southern Taiwan. Twelve AD patients, including four males who were diagnosed as having early stage of AD according to NINCDS-ADRDA and CDR were invited to participate in the study. Seven normal controls (NC), including three males, are healthy older adults without neurological or psychiatric disorders. Two groups were matched in age, gender and educational years. Design and Measurement: The basic cognitive and daily living functions of the participants were evaluated by CASI and CERAD and their basic visual acuity by Rey Complex Figure Test and Visual Form Discrimination test. After an elaborate work, we obtained the personal information of each participant and prepared 8 personally familiar and 8 novel pictures of scenes, which were divided into two categories, namely Blurred and Dark. The pictures in Blurred category are manipulated by clearness and those in Dark category by illumination. The presentation of each picture began from level 10, representing the most difficult. The participants were requested to make a judgment whether the picture was familiar or not. If they could not make sure, next level was given until they made a judgment or the level 1 representing the easiest was given. We recorded accuracy, strategy used, confidence level, cue demands and the times of correction. Finally, we also assessed their distance judgment by asking which of the two scenes is closer from the third scene and recorded the reaction time and accuracy. Results: No difference was detected between AD and NC in age (68 vs. 65 years) or in educational years (10.6 vs. 11.8 years). AD group performed worse than NC in MMSE (24.6 vs. 28.7,  $p=0.042$ ), CASI (82.2 vs. 94.7,  $p=0.009$ ) and the item of Spatial Recall in CERAD (6.4 vs. 9.3,  $p=0.031$ ). AD and NC had equally normal visual acuity. There were no difference between AD and NC in Rey Complex Figure Copy Test (AD 34.0 vs. NC 34.4) and in Visual Form Discrimination Test (AD 12.8 vs. NC 14.7). As compared with NC, AD needed easier level to recognize the scenes (AD 3.6 vs. NC 4.9,  $p=0.115$ ), indicating AD patients tended to have a poor recognition ability when the street views are becoming blurred or darker. AD had a lower accuracy (AD 12.1 vs. NC 15.0,  $p=0.022$ ). Most importantly, AD patients had more times to misidentify novel scenes as familiar (AD 1.4 vs. NC 0.3,  $p=0.048$ ). Regarding the strategy used, AD patients relied more on specific local cues while NC on whole views when scenes were becoming blurred and darker. As for the distance judgment, AD patients made less accuracy (AD 7.9 vs. NC 9.8,  $p=0.006$ ) even semantic cues such as street names were given. This reveals that although having recognized scenes adequately or got semantic information, AD patients still could not connect the relative position among scenes. It might also reflect that for AD patients merely recognizing the scenes or semantic information does not guarantee an intact ability to use the spatial relationship. The poor ability of AD patients to differentiate familiarity from novelty of a street view also prevents them from utilizing these scenes efficiently. Conclusions: When a specific environment is not clear or bright enough, AD patients may need more cognitive resources to recognize it. This also explains in part why AD patients sometimes did not know where they were in a place they had been familiar with for a long time, especially in the night time or when it is cloudy. Keywords: Alzheimer's disease, scene recognition, spatial perception, contrast sensitivity

#### QUESTIONNAIRE FOR EVERYDAY NAVIGATIONAL ABILITY (QUENA) IN PATIENTS WITH ALZHEIMER'S DISEASE: THE PRELIMINARY REPORT.

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Objectives: Many patients with Alzheimer's disease (AD) have way finding difficulties (WFD), and a certain proportion of them had been lost even in the familiar environments. The aim of this study was to know the navigational impairment in a group of patients with AD. Setting: This study was conducted in a dementia special clinic of a national university medical center located in southern Taiwan. Participants: The participants are the patients and their main care givers. A diagnosis of AD was made by a senior behavioral neurologist, according to the NINCDS-ADRDA (National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association) criteria. This study was approved by the IRB of hospital and an informed consent was signed by each participant. Design and measurements: This was a prospective, cross-sectional study by using a semi-structural questionnaire (Questionnaire for Everyday Navigational Ability, QuENA). The information was obtained from the patients and their major caregivers. Here, WFD was defined as having problems to navigate freely from a place to another in a familiar environment. Getting lost behavior (GLB) refers to topographical disorientation in familiar places, which usually makes the navigator unable to reach a destination or return home without help from others. GLB can be an event (GLE) having occurred already or a potential to be lost (GLP). Although having never been lost, patients with GLP would be expected to be lost and worried by their family if they navigate alone. In order to analyze the correlation between variables, the function was categorized as Level 0 (normal), Level 1 (WFD only), Level 2 (GLP only), Level 3 (GLE with awareness) and Level 4 (GLE without awareness). Results: A total of 329 AD patients completed the study, including 116 males and with mean age of 76 years old. Among them, 279 (85%) had WFD. Two hundred and sixty one patients (79%) were defined as GLB, which included 44% GLE and 35% GLP. No relationship was detected between AD with GLB and those without on demographic data except for age ( $r=0.16$ ,  $p=0.016$ ). As compared with non-GLB, the GLB group got worse score on CASI ( $p<0.001$ ). In the same way, GLE was worse on CASI score than non-GLE ( $p<0.001$ ). Regarding the GLE group ( $n=144$ ), 68% of the them had ever been wandering in familiar places near to their home before their GLE and 32% of them experienced the first time GLE in the first year of clinical AD. The level of the navigational ability did not predict the recurrence of GLE ( $r=0.056$ ,  $p=0.512$ ). Only 239 patients can be analyzed regarding the consistence of level

rating between patients and their care givers. Among them, only 96 were consistent, 121 patients overestimated and 22 underestimated. Conclusion: GLB is prevalent in patients with AD, even in the early stage of the disease. This is dangerous because half of the patients overestimate their navigational ability and are highly at risk to be lost sooner or later. Keywords: Alzheimer's disease; getting lost behaviors; questionnaire

#### PREVALENCE OF EXECUTIVE DYSFUNCTION IN KOREAN ELDERLY PEOPLE. DONG-WOO LEE<sup>1</sup>, SEUNG-HO RYU<sup>2</sup> (1. Inje University Sanggye Paik Hospital, Seoul, Korea; 2. Konkuk University Hospital, Seoul, Korea)

Objectives: To study the prevalence of executive dysfunction and its impact on the daily function of the elderly people living in the community. Design: Elderly people living in the community were randomly sampled, and were assessed by the following procedures. Executive function was measured by initiation-perseveration scores of Mattis dementia rating scale. Instrumental activities of daily living(IADL) were measured by Lawton IADL scores. Setting: Assessments were done by home visits in the community setting. Participants: 600 Elderly people living in a community in Seoul, capital of Korea, were assessed. Measurements: The prevalence of the executive dysfunction was calculated. Multiple regression analysis was performed to see the impact of the executive dysfunction on the instrumental activities of daily living. Results : The prevalence of the executive dysfunction was 13.7%. Executive dysfunction predicted impairment of instrumental activities of daily living better than the global cognitive function. Conclusion: Executive dysfunction is highly prevalent in the community. Executive dysfunction is more closely associated with impaired daily function. Keywords: executive dysfunction, prevalence, IADL

#### DISRUPTED SLEEP AND POOR DAYTIME ACTIVITY IN RELATION TO COGNITIVE FUNCTION IN PATIENTS WITH ALZHEIMER'S DEMENTIA. CHIEN-JUNG LU, YU SUN (Department of Neurology, En Chu Kong Hospital)

Objectives: Disturbed sleep cycles are the principle cause of institutionalization in dementia and represent a major clinical problem. We aimed to evaluate the association between sleep-and-daytime movement parameters and cognitive function; compare the differences of sleep pattern and daytime activities between patients with mild and moderate Alzheimer's dementia. Design and Setting: Cross-sectional observational study design. Participants: Patients with mild to moderate Alzheimer's dementia with CDR score 1 or 2. Intervention: All participants underwent body movements monitor by wrist-worn actometer (Actiwatch) for 7 days. Measurements: Daytime wake-up activity and maintenance of nighttime sleep were measured by actigraphy. Sleep diary was also recorded by patients and family. The parameters in daytime activity included total activity time, activity score, number of immobile phases, mean length of immobility, immobility phases of 1 minute, and index of restlessness. The sleep parameters included total bed time, actual sleep time, sleep latency, sleep efficiency, wake bouts in sleep, and activity score in sleep. Multiple regressions were performed to evaluate the association between these actigraphy parameters and cognitive function scored by MMSE and CDR adjusted for possible confounding factors including age, sex, education, medical history of hypertension, diabetes mellitus, Parkinson's disease, hyperlipidemia, sleep apnea syndrome and drug history of hypnotics, tranquilizer, antidepressant, antipsychotic and acetylcholine esterase inhibitor and NMDA agonists. Results: Fifty-two patients (age 79.2 ± 6.8 years, 60% women) with CDR score 1 or 2 were enrolled. After adjusting for age, sex, education, medical history of Parkinson's disease, and concurrent use of hypnotic medicine, the patients with moderate dementia (MMSE<20) had lower sleep bouts (continuous sleep blocks)( $p=0.029$ ), higher wake bouts in sleep ( $p=0.0005$ ) than those with mild dementia (MMSE > 20). In daytime activities, those with better cognitive function had higher wake-up time ( $p=0.0005$ ), wake-up percentage ( $p=0.0038$ ), period of time where the movement occurs ( $p=0.008$ ), and total activity score ( $p=0.025$ ). Conclusions: This study provided quantitative evidences of sleep pattern and daytime activity in patients with mild to moderate Alzheimer's dementia. The severity of disrupted sleep and poor daytime activity were associated with declined cognitive function. Keywords: Alzheimer's dementia, actigraphy, circadian rhythm, sleep pattern, activity

#### INSIGHT IN SEMANTIC DEMENTIA. KEIICHIRO KANEDA, MAMORU HASHIMOTO, YUSUKE YATABE, SHIHO MATSUZAKI, MANABU IKEDA (Department of Neuropsychiatry, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan)

Objectives: Semantic dementia (SD), included in the frontotemporal lobar degeneration (FTLD), is a neurodegenerative disease characterized by progressive loss of semantic knowledge. Early loss of insight remains one of the core diagnostic features of FTLD. Therefore, SD patients have been thought just like the lack of insight. However, patients are aware of, although frequently unperturbed by, failures in word comprehension and visual recognition. There are few systematic studies for insight in SD. The aim of this study is to examine the presence of insight in SD. Design: Case series study. Setting: This study was conducted at Department of Neuropsychiatry, Kumamoto University Hospital, Japan. Participants: All procedures strictly followed the clinical study guidelines of the Ethical Committee, Kumamoto University Hospital, 2007. Before entering this study, written informed consent was obtained for all patients or their caregivers. The requirements of SD group for inclusion in the current study were meeting the criteria of the clinical diagnostic features of semantic dementia (Neary et al. 1998). Ten patients who fulfilled the criteria were selected from consecutive outpatients with a medical examination at our hospital between April 2007 and August 2008. All patients were examined comprehensively by senior psychiatrists and were given routine laboratory tests and

standardized neuropsychological examinations including the Mini-Mental State Examination (MMSE), and MRI or CT of the brain. In addition, Neuropsychiatric Inventory (NPI) and the Stereotypy Rating Inventory (SRI) were done in their caregivers. All results were incorporated in the diagnosis. The clinical and investigative data collected prospectively in a standardized fashion were entered into the Kumamoto Dementia Follow-up Registry. To compare with insight of SD patients, 10 probable AD patients (NINCDS-ADRDA, 1984) were selected from the registry. They were matched one to one to the SD patients on the basis of age (within 6 years), sex, and severity of cognitive disturbances as shown by their MMSE score (within 1 point). Measurements: All the data were obtained from the registry and clinical records. The requirements of full insight in the current study were 1) same degree of evaluation for their disturbance of language, amnesia, psychiatric symptoms, behavioral abnormalities as their family's evaluation, 2) usually appeal that they were inferior to the person of same age group, 3) consultation to the hospital by own intention. Stereotyped behavior, decline in social interpersonal conduct, and emotional blunting were evaluated by the NPI and SRI to compare between the presence of insight and behavioral abnormality. Case description: One SD case with enough insight is described below. A 71-yr-old, right-handed man, retired teacher presented with a 1-yr history of progressive difficulty in understanding speech and in naming. When asked, 'Which is your handedness?', he replied 'What's handedness?'. He went out to the same place at the same time everyday, and lived with a strictly fixed daily rhythm that looks like a timetable. He had consultation to the hospital alone and appealed repeatedly 'The name of the thing doesn't come out', and 'I want some medicines that improve my brain'. MRI scan demonstrated focal atrophy of the left temporal region. Results: There were consecutive 10 SD patients who fulfilled the criteria. Six patients were female. All of them were right-handed. The mean age was  $73.0 \pm 6.6$  years (values are mean  $\pm$  SD). The mean disease duration was  $3.0 \pm 1.9$  years. The mean MMSE score was  $12.5 \pm 6.4$ . Eight patients revealed focal temporal atrophy that was predominantly left. Two patients, more marked focal atrophy in right temporal lobe, revealed Prosopagnosia. Seven SD patients showed the insight. They appealed, 'The name of the thing doesn't come out', 'I got a dementia', and 'I became foolish recently'. Two of them came to the hospital alone. In SD patients with insight ( $n = 7$ ), all of them showed stereotyped behavior. Among this group, 1 patient showed decline in social interpersonal conduct, 4 patients showed emotional blunting, and 1 patient showed more marked focal atrophy in right temporal lobe. In SD patients without insight ( $n = 3$ ), all of them showed stereotyped behavior and emotional blunting. Two patients showed the decline in social interpersonal conduct, and 1 patient showed more marked focal atrophy in right temporal lobe. In AD group ( $n = 10$ ), only 2 patients showed the insight and 1 of them consulted by himself. Eight AD patients without insight said 'I have no problem', and 'I have amnesia by age, not by illness'. Comparison of the insight between SD group and AD group revealed a statistically significant tendency ( $p = 0.0697$ , Fisher's exact test). Conclusion: In the present study, surprisingly, 7 of 10 patients with SD showed insight. They repeatedly appealed their disturbance. Two of them came to the hospital alone. One of them strongly requested some medicines that improve his brain. Compared with AD patients who had matched severity of cognitive disturbance, it is noteworthy that SD patients were more likely to have insight than AD patients. These results suggest that insight in SD patients is relatively maintained. Although patients with insight seem to be more mild behavioral abnormalities, there was no relation between insight and behavioral abnormalities in this study. The relation between anosognosia and right hemisphere damage has been reported, but in this study, the laterality of focal atrophy did not relate to the presence or the absence of insight. SD patients may complain of their disturbance because of their normal episodic memory. SD patients mainly present a language disturbance. On the other hand, AD patients mainly present a memory disturbance. A development of insight may be more likely to occur in the language disturbance than the memory disturbance. Furthermore, there are SD patients who stereotypically complain their disturbance, therefore, they may only maintains superficial insight. Keywords: semantic dementia, insight, case series study

**PRESCRIPTION OF POTENTIALLY INAPPROPRIATE MEDICATIONS IN DEMENTED PATIENTS.** YUSUKE YATABE<sup>1</sup>, MAMORU HASHIMOTO<sup>1</sup>, KAZUKI HONDA<sup>1</sup>, KEIICHIRO KANEDA<sup>1</sup>, SHIHO MATUZAKI<sup>1</sup>, KUNIO ARAKI<sup>2</sup>, MANABU IKEDA<sup>1</sup> (1. Department of Neuropsychiatry, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan; 2. Kumamoto Shinryo Hospital, Kumamoto, Japan)

Objectives: Prescription of potentially inappropriate medications (PIM) in the elderly people has been well documented, but little is known about the impact on demented patients. The purpose of the present study is to investigate the prevalence of PIM on demented patients, and to evaluate whether PIM impact on cognitive function and behavioral and psychological symptoms of dementia (BPSD) of patients with Alzheimer's disease (AD). Design: A prospective cohort study from database. Setting: The memory clinic located in Kumamoto, Japan. Participants: All procedures strictly followed the clinical study guidelines of the Ethical Committee, Kumamoto Shinryo Hospital, 2007, and were approved by the institutional review board. Before entering this study, written informed consent was obtained for all patients or their caregivers. According to the following criteria, 137 patients who had a medical examination to our clinic between May 2007 and April 2008 were selected. All patients were examined comprehensively by senior neuropsychiatrists and were given routine laboratory tests and standardized neuropsychological examinations including the Mini-Mental State Examination (MMSE), digit span tasks, and word fluency tasks. In addition, neuropsychiatric inventory (NPI) and Zarit's caregiver burden scale (ZBI) was done in their caregivers. All patients underwent brain computed tomography (CT). All results were incorporated in the diagnosis. The clinical and investigative data collected prospectively in a standardized fashion were entered into the Kumamoto Dementia Follow-up Registry. Among the requirements for

inclusion in the current study were 1) 65 or older on the point of examination, 2) those who fulfilled the criteria of dementia (DSM-IV-TR, 2000), 3) those who had no past history of psychosis. Further, 78 probable AD patients (NINCDS-ADRDA, 1984) were divided into two groups by PIM prescribed or not, and evaluated the impact of PIM on their cognitive functions and BPSD. Measurements: All the data were obtained from the registry. In this study, we considered the following medications from Beers Criteria Japanese version (Imai et al., 2007) as PIM which might deteriorate cognitive function; benzodiazepine, barbiturates, amitriptyline, conventional antipsychotics for dementia with Lewy bodies (DLB), CNS stimulants, indomethacin, pentazocine, MAO inhibitor, amantadine, anticholinergics, antispasmodics, H2-blocker, digoxin (should not exceed  $>0.125$  mg/d except when treating atrial arrhythmias), disopyramide, clonidine, muscle relaxants, and antihistamine. MMSE (general cognitive function), digit span tasks (attention), word fluency tasks (executive function), NPI (BPSD), and ZBI (caregivers' burden) were compared between two AD groups. A significant level of 0.05 (two tailed) was set for all analyses. Results: There were consecutive 137 patients who fulfilled the inclusion criteria. Ninety-one (65.4%) were female. The mean age was  $80.7 \pm 7.1$  (values are mean  $\pm$  SD). The mean disease duration was  $3.6 \pm 2.7$ . The mean MMSE score was  $14.2 \pm 6.2$ . The largest presenting disease was AD,  $n = 78$  (56.9%), followed by vascular dementia,  $n = 33$  (24.1%), and DLB,  $n = 13$  (9.5%). The average number of medications was  $4.3 \pm 3.3$  (range 0-15). Fifty five patients (41.7%) were prescribed one or more PIM. The most frequent PIM was benzodiazepine ( $N = 33$ ), followed by H2-blocker ( $N = 18$ ), anticholinergics ( $N = 8$ ). All of anticholinergics were urinary organ affecting agent. Thirty (38.5%) of 78 patients with AD had PIM. Comparison between AD patients with PIM (PIM (+) group,  $n = 30$ ) and those without PIM (PIM (-) group,  $n = 48$ ) was revealed that the mean age and the average number of medications were significant higher in PIM (+) group than PIM (-) group ( $83.6 \pm 5.8$  versus  $79.7 \pm 7.4$ ;  $p = 0.016$ ,  $5.7 \pm 2.1$  versus  $2.4 \pm 2.8$ ;  $p = 0.00001$ , respectively). There were no differences in gender, educational level, and disease duration between two groups. In cognitive function, the MMSE score was significantly lower in PIM (+) group than PIM (-) group ( $12.3 \pm 5.7$  versus  $15.7 \pm 5.8$ ;  $p = 0.016$ ). In an ANCOVA, where age was entered into the model as covariate, the effect of PIM on the MMSE score remained significant ( $p = 0.005$ ). The significant differences in digit span tasks and word fluency tasks were not shown between two groups. In NPI, PIM (+) group was the higher frequency of apathy and irritability than PIM (-) group (88.5% versus 63.8%;  $p = 0.024$ , 65.4% versus 34.0%;  $p = 0.010$ , respectively). The possibility remains that the antipsychotics affected the result, as the ratio of the patients with antipsychotics was significantly higher in PIM (+) group than PIM (-) group (26.7% versus 4.2%;  $p = 0.004$ ). Even if the patients with antipsychotics were excluded from the analysis, the result remained unchanged; PIM (+) group was the higher frequency of apathy, irritability, and euphoria than PIM (-) group (94.7% versus 62.2%;  $p = 0.008$ , 73.7% versus 31.1%;  $p = 0.002$ , 21.2% versus 4.4%;  $p = 0.037$ , respectively). There was no difference in ZBI score between two groups. Conclusion: It is surprising that 40 % of the demented patients prescribed PIM when they consulted to our memory clinic. In PIM (+) group, the mean age and the number of medications were significantly higher than PIM (-) group. This result corresponds with a previous study which focused on the residents in nursing home. PIM (+) group showed a significantly lower MMSE score than PIM (-) group, and even after we controlled for age, the effect of PIM on the MMSE score remained unchanged. This result suggests PIM may deteriorate cognitive functions in demented patients. It is noteworthy that most of AD patients who prescribed PIM were presenting apathy. In demented patients, apathy often causes disuse syndrome that deteriorates cognitive function. There is a possible explanation that the low MMSE score is caused by apathy. Moreover, compared with other psychiatric symptoms such as delusion, hallucination, and agitation, we have a tendency to miss apathy. Therefore, prescription of PIM might have continued surprisingly high rate in demented patients. Keywords: potentially inappropriate medications (PIM), memory clinic, Alzheimer disease, cognitive function, behavioral and psychological symptoms of dementia (BPSD)

**THE EFFECT OF LIFESTYLE INTERVENTION ON THE COGNITIVE FUNCTION OF GENERAL POPULATION: A COMMUNITY-BASED COHORT STUDY.** SONG-YEN TSAI<sup>1</sup>, JIUNN-RONG CHEN<sup>2</sup>, CHYI-HUEY BAI<sup>3</sup>, HSING-YU HWANG<sup>4</sup> (Department of Neurology 1,2, Tzu-Ai General Hospital, Shin Kong WHS memorial hospital<sup>3</sup>, Stroke center<sup>4</sup>, Tzu-Ai General Hospital)

Objectives: We aim to evaluate the effect of lifestyle modification on the cognitive function of adult. Design: Prospective, randomized, longitudinal trial. Setting: Community-based, randomized trial in general population with age larger than 40 years old in a rural area. The follow-up duration were 1 year, 2.5 year and 3.5 year. Participants: This cohort enrolled 1178 residents (543 men and 635 women, mean age  $57.5 \pm 10.3$  yrs). Sixty three percents of the cohort had educational level equal to or below primary school. Intervention: After randomization, these participants received one of the two lifestyle intervention programs: standard consultation (SC) group and patient participation (PP) group for the first year. Then the two groups were followed up under the same program of standard consultation. Measurements: The demographic data and information of lifestyle such as smoking, drinking and exercise etc, were collected. Biochemical items including blood pressure, fasting glucose, HbA1c, total cholesterol, triglyceride, LDL and HDL, the Mini-Mental Status Examination (MMSE), depression score (Center for Epidemiological Studies-Depression; CES-D), were measured before and after the intervention. Results: Age, gender, education levels and depression are possible covariates of MMSE score, and they could explain the half of variance of MMSE score. By using GEE model analysis, the mean MMSE score were significantly higher in men with high education levels, and negatively associated with age and depression score. After adjusting the possible covariates, the mean MMSE score and depression score had no difference between SC and PP group. The mean MMSE score of SC and PP groups increased (0.89% and 1.11%)



slightly at the follow up of 1 yr as compared with baseline data, and then declined gradually. The mean depression scores of the participants were improved 12 months later, in both groups, and then increased significantly at the follow-up of 2.5 yrs, and the tendency remained at 3.5 yrs follow-up. The lifestyle intervention in either SC or PP group can significantly ameliorate the depression status, and slightly increase the mean MMSE score, but there is no statistical significance for the latter. However, the mean MMSE score and depression score gradually deteriorated from the 2nd year. Conclusion: Lifestyle interventions in either SC or PP group can ameliorate the MMSE score and depression score, temporarily. The long-term effect of lifestyle intervention needs to be investigated in the future. Keywords: MMSE, cognitive function, community-based

**TRANSIENT TOPOGRAPHICAL DISORIENTATION: A CASE REPORT.** YA-CHI YANG<sup>1</sup>, YEN-TI LEE<sup>1</sup>, MING-CHYI PAI<sup>1,2</sup> (1. Institute of Behavioral Medicine; 2. Division of Behavioral Neurology, Department of Neurology, National Cheng Kung University)

**Introduction:** Patients with transient topographical disorientation (TTD) usually have a sudden, short-lasting difficulty in finding the correct way in very familiar areas without loss of consciousness or amnesia to the episode. The patients may have landmark agnosia or loss of directional sense. The cause of TTD, which mainly occurs in the subjects of their 6th or 7th decade, is still unknown. Some authors had linked TTD to early dementia, especially Alzheimer disease. **Case report:** A 47-year-old, right-handed woman visited our clinic because of more than 10 episodes of transient inability to recognize the scenes in which she was. On mid June 2008, she experienced her first episode of such symptom when driving through an area of downtown Tainan where she had been familiar with. In fact, she had been an insurance saleswoman and visited her clients living in these areas regularly. At the time, from her recollection, she suddenly had a feeling that she was thrown into a foreign country which she assured impossible. She did not stop driving, only slowed down, until arrived at a crossroad where she resumed the orientation. During the period of disorientation, she lost cognitive map, as well as the familiarity to scenes, but she did not lose the ability to recognize people, as her one or two of her sons were in the car, or to recognize objects. In the following several weeks, she continued to experience such attacks, with a duration from several seconds to eight minutes. No aura or discomforts had occurred before each episode and she recovered completely. She has an education of 15 years and scored 28/30 on the Mini-Mental State Examination (MMSE) and 94/100 on the Cognitive Abilities Screening Instrument (CASI). The results of visuo-spatial attention, language, spatial cognition, facial recognition, left-right orientation abilities were normal. Although the scores of the WMS-III (Wechsler Memory Scale-III) were above cut-off on all tasks, her performance on visual memory was worse than that on verbal memory. The score of the Rey-Osterreith Complex Figure test was abnormal. Meanwhile, the patient performed well on a series of tests for topographical orientation, including verbal route description, familiar and novel scenes discrimination, scenes recognition and a sketch map drawing. A cerebral magnetic resonance (MR) imaging studies were done on 24 June and 28 August 2008; the second one revealed a choroids cysts. EEG done on 11 August 2008 showed mild cortical dysfunction over right temporal area. A cerebral single photon-emission computed tomography (SPECT) on 14 July 2008 showed an increased radioactivity in the right lingual gyrus. A follow-up SPECT examination was done on 12 August 2008, 9 day after the longest episode, with duration of 8 minutes, and showed mildly decreased radioactivity in the bilateral temporal areas.

She was placed on oxcarbamazepine at a dose of 300 mg per day. She had took for one week and quitted because of severe dizziness. She had never experienced similar attack, however. **Conclusions:** The patient did not have visual perception or other cognitive decline except TTD. The results of neuroradiological examination found abnormality in right lingual gyrus, which was responsible for recognizing familiar landmark in previous research. (555) **Keywords:** transient topographical disorientation, lingual gyrus, case report

**LURIA'S HAND SEQUENCING MANEUVER AS A SCREENING TEST FOR DEMENTIA.** CHING-HSIUNG LIU, CHUN-LIANG LIN, HUNG-CHIH LIN (Department of Neurology, Lo-Tung Poh-Ai Hospital, Ilan, Taiwan)

**Introduction:** In clinical practice, we often use the Luria's hand sequencing test (LHST) to detect frontal lobe dysfunction. Recently, several neuroimaging studies of cognitive aging have found that age-related deficits in working memory and episodic memory abilities are related to changes in prefrontal cortex function. However, there is few study discuss about the relation between Luria's hand sequencing test and dementia. **Objective:** The aim of our study is to evaluate the sensitivity and specificity of this test to screen for dementia and, to clarify the relationship between the hand sequencing performance and other neuropsychological examination. **Methods:** We enroll all consecutive patients visiting to dementia OPD for memory complaints. All patient performing Luria's hand sequencing (slap-fist-cut maneuver) test, mini-mental state examination (MMSE), clinical dementia rating scale (CDR) and global deterioration scale (GDS). Using DSM-IV criteria for diagnosis of dementia. **Outcome Management:** The sensitivity and specificity of the LHS test for screen of demented patient was evaluated. We also study the correlation between LHS test and other neuropsychological examination and we prospect the LHS test is a most simple, less educated affect and least time consuming for screen of dementia. **Result:** Total 178 subjects age 50 or older were included the studies. 42% of them failed to performing LHS test, 114 (64.0%) individuals suspected demented by MMSE, 58.9% examiner with CDR > 0.5 and 53.9% with GDS score >3. The number of diagnosed dementia by DSM VI criteria were 113 (63.4%). Compare to MMSE, the suspect demented patients screen by LHST with sensitivity and specificity were 71.9% and 48.4%; and poor sensitivity and specificity when compare to DSM IV criteria (42.4% vs. 47.7%). However,

the difference of LHS test results with traditional evaluation tools (MMSE, CDR and GDS) was significant ( $p < 0.005$ ). **Conclusion:** In screen of demented patients, mini-mental state examination is an unsubstituted method. Low specificity and sensitivity of Luria's hand sequencing test when used in screen for demented persons. However, Luria's hand sequencing test maybe a quick maneuver for detected the status people who complaining poor memory requiring further investigation. **Keywords:** Luria's hand sequencing test, MMSE, dementia

**THE IDENTIFICATION OF FAMILIAR SCENES AND FACES IN PATIENTS WITH VERY MILD ALZHEIMER DISEASE: AN EVENT-RELATED POTENTIAL STUDY.**

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**Objective:** In addition to episodic amnesia, topographical disorientation or getting lost is also a common symptom in patients with Alzheimer disease (AD), even in the early part of the disease. As the disease progresses, patients with AD would gradually lose the ability to recognize the faces of familiar people, including their own, as well as familiar scenes. Based on the fact that the brain regions responsible for face and scene recognition are overlapped, we were interested to study whether there is a dissimilar cognitive architecture to identify faces and scenes in patients with very mild AD. We used event-related potential (ERP) to examine whether the deterioration in the recognition of familiar faces and scenes is unparallel in patients with very mild AD. **Participants:** Total 20 very mild AD (CDR 0.5) (8 female, mean age 71 years old, education 10 years, CASI 76 and MMSE 21) and 17 normal subjects (8 female, mean age 69 years old, education 9 years, CASI 90 and MMSE 28) finished the study and brought into data analysis. An informed consent form was signed. All participants were right-handed, had normal vision and audition; moreover, none had other neurological, psychological or serious medical disorders. **Design, Setting, and Measurements:** All participants received the Mini-Mental State Examination (MMSE), the Cognitive Ability Screening Instrument (CASI), Consortium to Establish a Registry for Alzheimer's Disease Assessment Packet (CERAD) and the Neuropsychiatric Inventory (NPI). Two TYPES of stimuli were used, FACES and SCENES, and two versions of each type were presented, namely FAMILIAR and NOVEL. The electrophysiological signals were recorded when participants determined if the pictures displayed was familiar or not. Average amplitudes of P100, N170 (structural encoding process) and N250r (familiar effect) were measured. **Results:** A prominent N170 was elicited by face in P8 and largest N170 in P3 and P4 by scenes [ $F(3,35)=40.18, P=.000$ ]. In addition, participants had more errors when judging pictures of SCENES as familiar or not than those of FACES. Interestingly, we failed to be detected the familiarity effect in AD patients from the N250r when familiar scenes were provided [ $F(1,35)=4.83, P=.035$ ]. **Conclusions:** The study clearly demonstrates that different neural regions are responsible for early visual process in the structure encoding of scenes and faces. For very mild Alzheimer Disease patients, the conflict between behavior and physiological responses may play a pivotal role in their risk to be lost. As compared with face recognition, the process of scene recognition has more difference between patients with very mild Alzheimer Disease and control elders. **Keywords:** Alzheimer disease, face, scene, event-related potential, topographical disorientation

**COGNITIVE MAP IN PATIENTS WITH MILD ALZHEIMER'S DISEASE: A COMPUTER-GENERATED ARENA STUDY.** SHENG-SIANG JHENG<sup>1</sup>, MING-CHYI PAI<sup>1,2</sup> (1. Institute of Behavioral Medicine, School of Medicine, National Cheng Kung University; 2. Division of Behavioral Neurology, Department of Neurology, Medical College and Hospital, National Cheng Kung University, Tainan, Taiwan)

**Objective :** In addition to memory impairment, getting lost is among initial symptoms in patients with early Alzheimer disease (AD). At least two kinds of wayfinding strategies, egocentric and allocentric, had been proposed. It is believed that people may form a cognitive map after having navigated a specific environment for several times, and are able to use it as an aid for navigation. We investigate the cognitive maps in early AD patients and their application in a computer-generated arena (CGA). **Measurements:** We invited very mild AD (CDR 0.5) patients and normal controls (NC) to participate in the current study. We used pencil-paper tests to assessed their supposedly previously formed cognitive maps of familiar environments, and performance of target finding in CGA to measure their new environment learning as well as the application of the old map. **Results:** Nineteen patients (female 8, mean age 67.6 years old, education 9.7 years, and MMSE 24) and eighteen NCs (female 10, mean age 66.4 years old, education 8.8 years, and MMSE 27) completed the study. In the hand-drawing map part, both groups did as well. In the new environment learning, NCs did better than AD group in the third trial. As for old environment navigation experiment, AD group performed worse than the NCs did in finding target, but they had no difference in percentage of path on target quadrant. **Conclusion** Early AD patients are still able to use cognitive map and keep pretty good allocentric representation of their familiar environments as well as NC, but perhaps both of them do not routinely use cognitive map to navigate in the everyday life. **Keywords:** Alzheimer's disease, cognitive map, allocentric, navigation, hippocampus

**PREVALENCE OF BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS IN PATIENTS WITH ALZHEIMER'S DISEASE – A COMPARATIVE STUDY ON COMMUNITY AND INSTITUTION PATIENTS.** Ting-Wen Cheng<sup>1</sup>, Ta-Fu Chen<sup>1</sup>, Ping-Keung Yip<sup>2,4</sup>, Mau-Sun Hua<sup>3</sup>, Chi-Cheng Yang<sup>3,5</sup>, Ming-Jang Chiu<sup>1,3</sup> (1. *Department of Neurology, National Taiwan University Hospital, College of Medicine*; 2. *Neurological Center, Cardinal Tien Hospital, Taipei, Taiwan*; 3. *Department of Psychology, National Taiwan University, Taiwan*; 4. *College of Medicine, Fu-Jen Catholic University, Taipei, Taiwan*; 5. *Division of Neurosurgery, Department of Surgery, National Taiwan University Hospital*)

Objectives: Behavioral and psychological symptoms of dementia (BPSD) increase caregiver burden and are the major reason for institutionalizing patients with dementia. We aimed to compare the prevalence and characteristics of BPSD between community-dwelling and institution patients with Alzheimer's disease (AD). Design: We assessed BPSD by interviewing their principal caregivers, either family or professional caregivers, with Behavioral Pathology in Alzheimer's disease Rating Scale. Participants: In total 138 patients diagnosed as probable AD from the memory clinic and 173 patients diagnosed as possible AD living in the long-term care units were recruited. The diagnoses followed the NINCDS-ADRDA criteria. Results: The prevalence of at-least-one BPSD was high in both groups (community 81.9%, institution 74.9%). The BPSD profile of either group was

similar but not identical that activity disturbance led in both groups (community 52.2%, institution 38.7%). Community patients had a higher prevalence than their institution counterpart. The community patients had more severity in the delusion/ paranoid ideation and affective disturbance than the institution patients adjusting age, gender and education years. The global rating of severity was also higher on the community side. Conclusion: Institution effect and family caregiver factor were possible accounts for the higher prevalence and more severity of BPSD in the community AD patients. Institutions provide a stable care-giving routine which helps reduce BPSD. Family caregivers may report more BPSD from their caregiver distress. High levels of antipsychotic prescriptions for dementia in the long-term care units and hesitation of the family caregivers towards using of psychotropics may be contributory. Keywords: Alzheimer's disease, long-term care units, behavioral and psychological symptoms, prevalence