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### 5<sup>th</sup> International Conference on **Alzheimer's Disease & Dementia** September 29-October 01, 2016 London, UK

# **Posters**



September 29-October 01, 2016 London, UK

#### Primary and secondary prevention interventions for cognitive decline and dementia - An overview

Flodgren Gerd National Institute of Public Health, Norway

**Background:** The prevalence of dementia, including Alzheimer's Disease (AD), is increasing due to the aging of the world's population. As there is no cure for dementia, there is a great need to identify effective interventions to delay or prevent its onset.

**Methods:** We searched eight databases from inception and up to January 2016. We included high quality systematic reviews of any intervention that included people who were either cognitively healthy or had mild cognitive impairment, We used standard review methods with independent screening, assessment and data extraction.

**Results:** We identified eight eligible reviews. Five reviews involved interventions (blood pressure or cholesterol lowering drugs, Omega 3 FAs, cognitive training, and aerobic training) targeting cognitively healthy people. Three reviews concerned interventions (cholinesterase inhibitors, Omega 3 FAs, and vitamin E) targeting people with mild cognitive impairment. High to moderate certainty of evidence from seven of these reviews suggest that neither the pharmacological interventions, nor any of the nutritional supplements evaluated are effective in delaying or preventing cognitive decline, dementia or AD. The effects of aerobic training on cognition are uncertain, due to low to very low quality of evidence from one review. Moderate evidence from one review suggest that computerised cognitive training may lead to a small short-term improvement in cognitive function.

We found no reviews of interventions to promote other healthy lifestyle changes, e.g. conversion to a healthy diet, decreased alcohol intake, smoking cessation, etc., or addressing other risk factors for dementia, e.g. depression, lack of social interaction, and low educational attainment.

**Conclusion:** Evidence from systematic reviews of effective interventions to prevent cognitive decline, AD and dementia are lacking. Only single faceted interventions have been evaluated in systematic reviews. Due to the multifactorial aetiology of dementia, interventions addressing more than one modifiable risk factor may be needed.

#### **Biography**

Flodgren has a PhD in Sports Medicine from Umeå University, Sweden. He has for the last eight years worked in the Cochrane Effective Practice and Organisation of care group, first at the University of Newcastle, and the last five years at Oxford University. She is the first author of a number of Cochrane systematic reviews.

gerdmonika.flodgren@fhi.no

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#### Cognitive impairment is correlated with and unstable mental health profile

Etindele Sosso Faustin Armel and Molotchnikoff Stéphane University of Montreal, Canada

Gerebral function is mainly reorganized during years between adolescence and midlife. This important period is characterised by creation of synapses, fine-tuning of excitatory and inhibitory neurotransmitter systems, improvement of brain structures, and development of nervous connections. Indeed most of brain diseases result due to variance or damage to any of these events. Variances or imbalances in timing of neuronal maturity process strongly increase the risk for cognitive impairments and certainly leads to the development of neurodegenerative diseases, dementia, anxiety and psychiatric disorders in unknown rate in the groups of young adults (aged between eighteen years old until midlife). Moreover, these changes also influenced the risk for Alzheimer disease, Dementia and other associated diseases. The aim of this study is to explore how detection of cognitive impairments is link with a combined effect of sociodemographic items we choose, on a healthy young adult's population. This epidemiological study was leaded with a questionnaire incorporating the short fifteen items version of cognitive complaints detection's Mc Nair Test which is used for detect cognitive complains. The questionnaire also included ten socio-demographic items and fourty seven others questions divided in seven sections: quality of sleep, level of stress, depression, anxiety, general health, physical skills, and dependences. Our results suggested a strong link between increasing in memory deficit and the combination of at least two bad score to each section, with a significant correlation with unstable mental health profile.

#### **Biography**

Etindele Sosso Faustin Armel is PhD student of Neurophysiology in university of Montreal. He has completed a Master degree in Microbiology in university of Yaounde I in Cameroon, and A master degree in anesthesiology in University Central of Tunis in Tunisia. His research concerns cerebral plasticity and his interactions with neuronal memory. His objective is to develop a model of prediction for cognitive impairments related to neurodegenerative diseases.

faustin.armel.etindele.sosso@umontreal.ca

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## Effect of non-pharmacological interventions on functional performance in mild cognitive impairment (MCI): A scoping review

Navaldeep Kaur, Patricia Belchior and Isabelle Gelinas McGill University, Canada

ild Cognitive Impairment (MCI) is one of the most recognized risk factors for dementia. It affects approximately 19% Mof the individuals over 65 years of age (Lopez et al., 2003) It is now recognized that these individuals are independent in performing everyday activities, but "take more time, are less efficient and make more errors" (Albert et at., 2011). Few studies have investigated the effects of non-pharmacological interventions in improving functional performance in this population. Thus, the aims of this study were to identify the non-pharmacological interventions which have been targeted at improving functional performance in individuals with MCI. To conduct a scoping review, a systematic electronic search was executed in following bibliographic databases: Ovid Medline (1999-2014), CINAHL (1999-2014), PsychINFO (1987-2014). Publications which estimated the effect of any non-pharmacological approaches in MCI and had instrumental activities of daily living (IADLs) as one of their outcomes of interest, were deemed eligible. Data were extracted on the author, publication year, target population, study design, MCI diagnostic criteria, nature of the intervention, functional outcome measure and the outcome. Ten studies fulfilled the eligibility criteria. Four studies focussed on exercise training, five evaluated behavioural interventions and one combined both exercise and cognitive stimulation. Overall, exercise interventions reported improvements in functional abilities. The effect of behavioural interventions varied across studies. Combined aerobic training and cognitive stimulation did not yield any benefits in improving IADLs. Exercise studies seem promising, whereas the behavioural interventions illustrated mixed results. The findings of the review highlight more rigorous research is required in this area with specific considerations to methodology, follow-up duration, MCI criteria and IADL measures.

#### **Biography**

Navaldeep is a doctoral student in Rehabilitation Science at the McGill University, Canada. She completed her MSc in Exercise Science from the University of East London in the year 2010. Her research interests are focussed on individuals with Alzheimer's disease (AD) and mild cognitive impairment (MCI).

naval.ndp@gmail.com

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#### A Multifaceted rehabilitation model in Alzheimer's Disease maintains brain speed over 60 Months: A case report

Valentin Bragin<sup>1</sup> and Ilya Bragin<sup>1,2</sup> <sup>1</sup>Stress Relief and Memory Training Center, USA <sup>2</sup>Upstate Medical University, USA

**Objective:** A multifaceted rehabilitation approach (MRA) in the treatment of Alzheimer's dementia (AD) patients is aimed at achieving optimum levels of physical, psychological and behavioral functioning in the presence of neurodegenerative processes, aging, and the progression of chronic medical illnesses. We hypothesize that the simultaneous implementation of multiple therapeutic modalities could delay the progression of dementia in mild and moderate stages including chronometric changes. Here we describe an individual with multiple medical problems with dementia depression successfully treated with a MRA.

Methods: Case Report.

**Results:** The MRA consisted of standard pharmacotherapy, physical and mental exercises, and other interventions. It was initiated in the office and maintained in the patient's home indefinitely, as would any other program for chronic disease.

Finger taping speed, simple, and complex (go/no go) reaction time was used as a proxy for brain speed.

The patient is a 80 y.o. male, engineer, with a long history of memory loss, and depression, on memantine and venlafaxine . He has hypertension, cardiovascular disease and dyslipidemia. At age 80, his finger taping speed, simple and complex reaction time were  $202 \pm 12$  ms,  $239 \pm 72$  ms and  $431 \pm 100$  ms, respectively. After 60 months of the treatment his finger typing speed, simple and complex reaction time were  $186 \pm 14$ ms,

302±110 ms and 490±102 ms, respectively. Traditional cognitive testing results (MMSE) remained stable through this time period

**Conclusion:** An MRA can been an effective intervention strategy to prevent decrease of brain speed in the setting of dementia and depression.

#### Biography

Bragin, M.D., Ph.D. completed his MD and then PhD in biochemistry from the Medical Military Academy in St. Petersburg, Russia, where he studied the effects of stress on organ function and ATP synthesis. He is the director of the Stress Relief and Memory Training Center in Brooklyn, NY. His interests include stress and stress-related disorders. For many years he has focused on the rehabilitation of cognitive functioning in the elderly who suffer from memory loss and depression.

val11235@gmail.com

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## Systematic review of positive psychology outcome measures for family carers of people with dementia

**Jacki Stansfeld** University College London, UK

**Introduction:** The importance of positive psychology in understanding the wellbeing and experiences of family carers of people with dementia is increasingly being recognised. Despite this, outcome measures used in research with family carers of those with dementia are often centered on concepts such as burden and depression. There is a scarcity of positive psychology measures developed for or validated in this population

**Aim:** By employing standardised criteria, this review aimed to assess the quality of positive psychology measures developed for or already in use with family carers of people with dementia and to determine their potential utility in future interventional studies.

**Methods:** We performed a systematic review of positive psychology measures for family carers of people with dementia. The databases searched were PsychINFO, CINHAL, MEDLINE, EMBASE and PubMed. Two reviewers independently assessed full-texts for inclusion and performed a quality assessment of each of the scale development studies identified to examine the psychometric properties reported.

**Results:** This review identified 10 positive psychology outcome measures (and 6 validation papers of these scales) within the constructs of self-efficacy, spirituality, resilience, gain, and meaning.

**Conclusion:** Several outcome measures were identified that may have potential utility for future interventional studies, but it is clear that there is still work to be done to develop and refine more positive psychology measures for this population. A lack of reporting of the psychometric properties by development authors limited the conclusions that could be drawn. It is recommended that authors aim to report this in the future.

#### **Biography**

Jacki Stansfeld is currently completing her PhD at University College London in the Division of Psychiatry. She works as a Research Assistant on the Valuing Active Life in Dementia (VALID) research programme.

j.rutherford@ucl.ac.uk

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#### Trends of successful exelon (Rivastigmine) patch in geriatric patients with Dementia

Janice Hoffman Western University of Health Sciences, USA

Skin reactions are one reason for termination of rivastigmine patch. The study goal was to identify factors associated with skin reactions from rivastigmine patch in older adults. A retrospective chart review with prospective skin assessment observational study was performed on all outpatients with Alzheimer's dementia at a specialized ambulatory geriatric evaluation clinic.

Demographic, clinical, and outcome variables were compared between the two groups (i.e., those with versus without skin reactions) using  $\chi 2$  or Fisher's exact test for cross-tabulations of nominal variables and independent samples and Student t-test, for continuous variables. Statistical differences between groups were considered significant when p-values were  $\leq 0.05$ .

A total of 33 patients were included with 24.2% males, 75.8% females and a mean age of 83 years. Race included Caucasian (90.9%) and Hispanic (9.09%). Patients lived at home with a spouse (39.39%), home with caregiver (24.24%) or in an assisted-living facility (6.06%).

A statistically significant finding was MMSE score of 17 (p<0.01) and a skin reaction. Comorbidities included, 15.2% had diabetes and 66.7% had hypertension. On average sodium plus potassium values were 139 mEq/L and 4 mEq/L respectively. Bathing was on average 3 baths weekly. Concomitant medications included: memantine (39.4%), antidepressant (51.5%), antipsychotic (12.1%) with 24.2% not taking any medications.

Two statistically significant skin reactions seen were erythema where the patch was applied and pruritis (p<0.01). There were no significant skin reactions resulting in rivastigmine patch discontinuation.

This small cohort showed one statistically significant trend: the lower MMSE score the increase risk of a skin reaction.

#### Biography

Hoffman has completed her Pharm.D. from the University of Southern California, School of Pharmacy in Los Angeles, CA, USA and postdoctoral studies from University of Maryland at Baltimore Mental Health System. She is the director of PGY-1 pharmacy residency in Geriatrics at the los Angeles Jewish Home for the Aginig, and an Associate Professor at Western University of Health Sciences where she is the expert in nuerology. She has published more than 25 papers in reputed journals and has been serving as an Associate Editor of the *California Pharmacist* Journal.

jhoffman@westernu.edu

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#### Oxidative modification of $\gamma$ -secretase enhances amyloidogenic pathway

Harkkyun Kim

Sungkyunkwan University School of Pharmacy, Republic of Korea

The cause of elevated level of amyloid beta-peptide ( $A\beta42$ ) in common late-onset sporadic Alzheimer's disease (AD] has not been established. Here, we show that the membrane lipid peroxidation product 4-hydroxynonenal (HNE) is associated with amyloid and neurodegenerative pathologies in AD and that it enhances gamma-secretase activity and  $A\beta42$  production in neurons. The gamma-secretase substrate receptor, nicastrin, was found to be modified by HNE in cultured neurons and in brain specimens from patients with AD, in which HNE-nicastrin levels were found to be correlated with increased gammasecretase activity and Abeta plaque burden. Furthermore, HNE modification of nicastrin enhanced its binding to the gammasecretase substrate, amyloid precursor protein (APP) C99. In addition, the stimulation of gamma-secretase activity and  $A\beta42$ production by HNE were blocked by an HNE-scavenging histidine analog in a 3xTg-AD mouse model of AD. These findings suggest a specific molecular mechanism by which oxidative stress increases  $A\beta42$  production in AD and identify HNE as a novel therapeutic target upstream of the gamma-secretase cleavage of APP.

#### Biography

Harkkyun Kim has completed his BS degree at the age of 26 years and is studying Molecular Cellular Biology from Sungkyunkwan University School of Pharmacy. Now he is Ph.D candidiate studying molecular pathogenesis of Alzheimer's disease, especially about the relationship between adiponectin and Alzheimer's disease.

kimhak114@naver.com

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#### Neurocognitive markers in early diagnosis of Alzheimer's disease

Pooja Rai, I L Singh and Tara Singh Banaras Hindu University, India

A lzheimer Disease (AD) is a neurodegenerative disorder in which proteins build up in the brain to form structures called 'plaques' and 'tangles' resulting in an increase in cognitive decline. Attention is the first cognitive domain affected in AD because disconnection between frontal and posterior parietal areas may mediate the selective disruption of attentional function of AD (Parasuraman & Haxby, 1993). The early diagnosis of AD has been the major concern in present era. Although past research focused on memory deficits in AD, recent studies show that attention functions deteriorate earlier than memory and visuospatial deficits. Recent brain imaging studies have provided strong support for the anatomical and neuropsychological bases of attentional network, which may be dysfunctional in Alzheimer's disease. In this research, published research papers on neuropsychological markers of AD were collected and reviewed.

The aim was to examine the current status of research on neuropsychological markers for the identification of AD. Many studies have focused on neuropsychological and cognitive markers which may be more relevant for early identification of AD. Available evidence show that in AD, attention is the first cognitive domain, which is affected. Although, very few neuropsychological markers of AD have been identified to-date, the results of studies identifying neuropsychological markers of AD have been promising in the field. Among several tests, which measure the attention function, Attention Network Task (ANT) stands out for its comprehensiveness. The neuropsychological markers, therefore, have an edge over other markers in terms of feasibility and specificity. These markers can also help in screening of community residing older adults who remain undiagnosed, as they do not understand the difference between normal signs of aging and dementia. The neuropsychological markers have far greater importance in comparison to neurophysiological and biological markers. Thus, neuropsychology of attention along with the visuospatial and memory function may provide a better understanding of the early diagnosis of AD.

#### Biography

Pooja Rai, a post graduate in Psychology with specialization in Clinical Psychology from Banaras Hindu University. At present, she is pursuing her second year of Ph.D. from Department of Psychology, Banaras Hindu University under the supervision of Prof. I. L. Singh on the topic Attention Networks in Alzheimer's disease (AD) and Healthy Aging. Her research interests include psychodiagnositics and neuropsychology of Alzheimer's disease. During the course of her Ph.D. she aspire to explore the tenets underlying the attentional deficits in Alzheimer's patients and finding objective and reliable neuropsychological markers of Alzheimer's disease especially attentional, memory and visuospatial markers. She is a hardworking student and acheive B.H.U. Gold medal in her graduation and postgraduation. She has presented over dozens of papers in several national and international conferences. She has published 2 papers in her postgraduation itself.

pooja.rai.138@gmail.com

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#### Role of presenilin-1 mutations in Mitochondrial dynamics

Heejin Park

Sungkyunkwan University, Republic of Korea

E arly stage of Alzheimer's disease reveals mitochondrial deficit and dysfunction. Mitochondrial dysfunction in Alzheimer's disease causes synaptic alteration, imbalance of lipid homeostasis, calcium homeostasis, and lack of ATP production. Familial Alzheimer's disease-linked Presenilin-1, catalytic subunit of  $\gamma$ -secretase, mutations cause early onset Alzheimer's disease. All mutation types have different pathological mechanism and ultimately break down cellular homeostasis. Our research shows more details about relationship between Presenilin-1 mutations (PS1A431E, PS1E280A, PS1H163R, PS1M146V, PS1 $\Delta$ E9) and mitochondrial dysfunctions. All of PS1 mutants-expressing cells exhibited mitochondrial dysfunctions and reduced levels of proteins involved in mitochondrial dynamics without alteration of total mitochondrial biogenesis.

#### **Biography**

Heejin Park is studying at Molecular Cell Biology laboratory, from Sungkyunkwan University School of Pharmacy, South Korea, for her M.S. Course. She completed her bachelor degree from the Department of Genetic engineering of Sungkyunkwan University and decided to transfer to School of Pharmacy because she was interested in neurodegenerative diseases and Alzheimer's Disease. Now she is investigaing for the relationship between mitochondrial dysfunction and Alzheimer's Disease.

pania994@naver.com

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## Vitamin D and resveratrol prevents cognitive decline via reduces APP amyloidogenic processing in the SAMP8 mice

Lili Xin, Jinbo Cheng, Jian Tong and Zhongxiao Wan Soochow University, China

A lzheimer's disease is the most prevalent cause of progressive dementia in the elderly. Vitamin D (VD) and resveratrol (RSV) are two nutritional factors that have known neuroprotective effects. We aimed to explore whether the combination of VD with RSV might be more effective for reversing memory impairments shown by SAMP8 mice than intervention independently, as well as the underlying mechanisms. SAMP8 mice and SAMR1 were randomized into 5 groups: SAMR1, SAMP8, SAMP8 with VD (VD), SAMP8 with RSV (RSV) and SAMP8 with both VD and RSV (VDRSV). At the end of 24 weeks intervention, Morris water maze test was performed to assess the cognitive function; hippocampus and parietal cortex were dissected for further analysis. The combination of VD and RSV (VDRSV) is more effective for reversing cognitive impairment than intervention independently as demonstrated by the increased time spent in target quadrant and number of crossing. In the hippocampus, SAMP8 mice has elevated APP and BACE1 protein expression compared to SAMR1 mice; VDRSV has significant reduced expression of BACE1 compared to SAMP8 group. In the cortex, SAMP8 group has elevated APP, BACE1 and cathepsin B protein expression compared to SAMP8 group. Meanwhile, VD+RSV significantly reduced elevated AP<sub>42</sub> levels in SAMP8 mice. In conclusion, the combination of VD with RSV is more effective for reversing cognitive impairment in SAMP8 mice, this might be associated that the combination might positively affect APP amyloidogenic processing, consequently A<sub>42</sub> burden.

#### **Biography**

Lili Xin has completed her PhD at the age of 25 years from Huazhong University of Science & Technology and postdoctoral studies from Soochow University. She is now working at Soochow University as an associated professor. She has published approximately 6 papers in reputed journals.

llxin@suda.edu.cn

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## The Role of Mental and Physical Activities against Development of Alzheimer's disease in Socialized and Isolated Rats

Azza A Ali<sup>1</sup>, Mona G Khalil<sup>2</sup>, Hemat A Elariny<sup>1</sup> and karema Abu-Elfotuh<sup>1</sup> <sup>1</sup>Al-Azhar University, Egypt <sup>2</sup>Modern University for Technology and Information, Egypt

**Background:** Alzheimer's disease (AD) is a progressive neurodegenerative disorder; lifestyle changes may slow its onset and progression. Mental and physical activities have been associated with better cognitive function in healthy older adults. Cognitive engagement and physical activities have been associated with decreased risk of AD. Social isolation refers to a complete absence of or insufficient contact with other members of society and can exacerbate memory deficits.

**Objective:** To study the influence of mental and physical activities in normal socialized conditions as well as to evaluate their role in social isolated conditions on normal and AD rat models.

**Methods:** Rats were divided into two main groups; Group I socialized and Group II isolated. Both socialized and isolated groups were subdivided into four subgroups; two received saline and served as control, while two served as AD subgroups and received ALCl3 (70mg/kg IP) every day for four weeks. One of the control and AD subgroups was exposed to mental and physical activities but the other not exposed. Mental and physical activities were performed using Swimming test and Y-maze (each for one time/week) during four weeks. Isolated rats were housed individually in cages covered with black plastic while socialized rats randomly paired and housed in transparent covered cages. Histopathological changes in different brain regions and biochemical changes in A $\beta$ , ACHE, brain monoamins (DA, NE, 5-HT), inflammatory mediators (TNF- $\alpha$ , IL-1 $\beta$ ), oxidative parameters; (MDA, SOD, TAC) as well as brain derived neurotrophic factor (BDNF) were also measured for all groups.

**Results:** Brain neurological damage characterizing isolation was more pronounced in isolation-associated AD rats. Mental and physical activities significantly decreased A $\beta$ , ACHE, MDA, TNF- $\alpha$ , IL-1 $\beta$  together with increased SOD, TAC, DA, NE, 5-HT and BDNF. The protective effect of mental and physical activities against brain neuronal degenerations was more marked in isolated rats especially in isolated-associated AD rats. These results were confirmed by histopathological examinations of different brain regions.

**Conclusion:** Mental and physical activities can protect from brain neuronal degenerations either induced by isolation or that associated with AD in both socialized and isolated rat models. The protection using mental and physical activities is more pronounced in isolation-associated AD model.

#### Biography

Azza A Ali has completed her PhD from Faculty of Pharmacy, Cairo University and postdoctoral studies from Faculty of Pharmacy, Al-Azhar University. She is the Head of Pharmacology and Toxicology Department, Al-Azhar University, Egypt. She has published more than 35 papers in reputed journals and developed research line in behavioral pharmacology in Egypt. She is member of many scientific societies in Egypt and of (AAPS) American Association of Pharmaceutical Scientists (2002). She is interested in CNS degenerations and disorders especially AD and dementia and has many researches and publications on its causes, prevention and risk factors especially stress and malnutrition. She is an Editorial Board Member at journal of Acta Psychopathologica.

azzamoro@gmail.com

## 5<sup>th</sup> International Conference on Alzheimer's Disease & Dementia

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#### Study on Social Isolation as a Risk Factor in Alzheimer's disease

Azza A Ali<sup>1</sup>, Mona G Khalil<sup>2</sup>, Hemat A Elariny<sup>1</sup> and karema Abu-Elfotuh<sup>1</sup> <sup>1</sup>Al-Azhar University, Egypt <sup>2</sup>Modern University for Technology and Information, Egypt

**Background:** Alzheimer's disease (AD) is a neurodegenerative disease that leads to memory loss. It is characterized by deposition of Beta-amyloid peptides (A $\beta$ ), accumulation of neurofibrillary tangles and cell loss. Social isolation may exacerbate memory deficits. The risk of cognitive decline and the onset of AD may be lower by maintaining social connections and keeping mentally active. Relationship between frequent social activity and enhancing cognitive functions has been established.

**Objective:** To study the influence of complete social isolation for a long period on biochemical & histopathological changes and DNA fragmentation in the brain of normal rats as well as investigate the possible interaction between social isolation and development of AD using isolation-associated AD rat model.

**Methods:** Four groups of rats were used; 2 groups socialized and 2 isolated for four weeks. One of each socialized and isolated groups were served as control and the other (AD group) injected by ALCl3 (70mg/kg, IP) every day during four weeks of isolation or socialization. Isolated rats were housed individually in cages covered with black plastic while socialized rats were randomly paired and housed in transparent covered cages. Biochemical changes in the brain as acetyl cholinesterase (ACHE), A $\beta$ , brain derived neurotrophic factor (BDNF), brain monoamins (Dopamine, Serotonin, Norepinephrine), inflammatory mediators (TNF- $\alpha$ , IL-1 $\beta$ ), oxidative parameters (MDA, SOD, TAC) and DNA fragmentation were estimated for all groups. Histopathological changes in the brain were also evaluated.

**Results:** Complete social isolation for a long period resulted in brain neurological damage indicated by significant increase in A $\beta$ , ACHE, MDA, TNF- $\alpha$ , IL-1 $\beta$  as well as decreases in SOD, TAC, BDNF, brain monoamins and confirmed by histopathological changes in different brain regions. In addition, isolation enhanced the DNA fragmentation induced by AD. Brain neurological damage was more severe in isolation-associated AD than in socialized condition.

**Conclusion:** Complete social isolation for a long period induces brain neuronal degenerations. It represents a risk factor especially when associated with AD; it increases DNA fragmentation and enhances the severity and progression of AD. Thus, socialization is advised especially with AD to avoid worsen or deterioration of the disease.

#### **Biography**

Azza A Ali has completed her PhD from Faculty of Pharmacy, Cairo University and postdoctoral studies from Faculty of Pharmacy, Al-Azhar University. She is the Head of Pharmacology and Toxicology Department, Al-Azhar University, Egypt. She has published more than 35 papers in reputed journals and developed research line in behavioral pharmacology in Egypt. She is member of many scientific societies in Egypt and of (AAPS) American Association of Pharmaceutical Scientists (2002). She is interested in CNS degenerations and disorders especially AD and dementia and has many researches and publications on its causes, prevention and risk factors especially stress and malnutrition. She is an Editorial Board Member at journal of Acta Psychopathologica.

azzamoro@gmail.com

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#### Inhibition of mitochondrial fission ameliorates the pathogenesis of Alzheimer's disease

Heejin Park

Sungkyunkwan University, Republic of Korea

Excessive mitochondrial fission is a prominent early event, and contributes to mitochondrial dysfunction, synaptic failure and neuronal cell death in the progression of Alzheimer's disease (AD). In the present study, we examine the role of Drp1, a key regulator of mitochondrial fragmentation, in mitochondrial and synaptic dysfunction-induced by A $\beta$ , and ADlike neuropathology and cognitive functions in AD mice. Our results demonstrate that the inhibition of Drp1 alleviates mitochondrial fragmentation, loss of mitochondrial membrane potential, ROS production, and ATP reduction in neurons treated with A $\beta$  oligomers. An inhibitor of Drp1 also significantly restores A $\beta$ -mediated depression of synaptic vesicle exocytosis. Furthermore, Drp1 inhibition significantly improves learning and memory, synaptic density, and prevents mitochondrial fission, lipid peroxidation, BACE1 expression and A $\beta$  deposition in an AD mouse model. These results provide evidence that Drp1 plays an important role in A $\beta$ -mediated and AD-related neuropathology, and in cognitive function in an AD animal model. Thus, inhibiting excessive Drp1-mediated mitochondrial fission may be an efficient therapeutic avenue for AD.

#### Biography

Heejin Park is studying at Molecular Cell Biology laboratory, from Sungkyunkwan University School of Pharmacy, South Korea, for her M.S. Course. She completed her bachelor degree from the Department of Genetic engineering of Sungkyunkwan University and decided to transfer to School of Pharmacy because she was interested in neurodegenerative diseases and Alzheimer's Disease. Now she is investigaing for the relationship between mitochondrial dysfunction and Alzheimer's Disease.

pania994@naver.com

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## XHC restores cognition of Alzheimer's disease mice and reduces amyloid beta burden via repressing BACE1 promoter activity

#### Gun Young Jung

Sungkyunkwan University School of Pharmacy, Republic of Korea

A lzheimer's disease (AD) is a chronic neurodegenerative disease. In developed countries, AD is one of the most financially costly diseases however, the cause of AD is still unclear. Among the many hypotheses, Amyloid hypothesis postulated that exceed extracellular amyloid beta (A $\beta$ ) deposits are the fundamental cause of the disease. A $\beta$  is produced by sequential proteolysis to amyloid beta precursor protein (APP) by  $\beta$ -secretase (BACE1) and  $\gamma$ -secretase. Another important phenomenon in AD patient is increased BACE1 expression. Many big pharmaceutical companies have been focused on developing direct inhibitors for BACE1. However, direct and complete blocking of enzymatic activity of BACE1 can cause unpredictable side effects because of numerous physiological substrates of BACE1. Therefore, our strategy is to find specific drugs reducing BACE1 expression rather than direct inhibition of BACE1. Using USA FDA approved drug library (Prestwick Chemical Library), we could discover putative therapeutic chemicals by cell based assay. Among those candidates, XHC reduced the levels of BACE1 protein and mRNA in SH-SY5Y cells. A soluble APP $\beta$  and C99 which are the products of BACE1 protease, were also decreased by treatment of XHC. We also confirmed that XHC could improve cognitive functions of 3xTg-AD mice. Decreased level of A $\beta$  deposition and BACE1 expression also observed in XHC-treated AD mice.

#### **Biography**

Gun Young has completed his B.S. from Sungkyunkwan University School of Pharmacy in 2015. He is doing his master's degree at Sungkyunkwan University School of Pharmacy. His major expertise is molecular cell biology.

chocobi119@hanmail.net

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## RA improves cognitive function of Alzheimer's disease mouse model through inhibition of BACE1 expression and neuroinflammation

#### Gun Young Jung

Sungkyunkwan University School of Pharmacy, Republic of Korea

A lzheimer's disease (AD) is the most common dementing illness, and the peptide amyloid- $\beta$  (A $\beta$ ) has a chief function in the pathogenesis of AD. Sequential proteolysis of amyloid precursor protein (APP) by BACE1 and  $\gamma$ -secretase produces A $\beta$  which drives cerebral neuroinflammation. Recent findings have provided insight into a newly discovered inflammatory mechanism that contributes to the pathogenesis of Alzheimer's disease mediated by multi-protein complexes called NLRP inflammasomes. In the present study, we orally administered the brain penetrant, natural compound isolated from compound RA to the transgenic APP/PS1 (bearing mutant human APP and presenilin-1 transgenes) and 3xTg-AD (bearing mutant human APP, presenilin-1, and tau transgenes) mice models of Alzheimer's disease. Oral treatment of natural compound reversed transgene-associated behavioral deficits, but did not alter wild-type mouse behaviors. Furthermore, brain A $\beta$  depositions as well as abundance of various A $\beta$  species were decreased in natural compound-treated AD mice. These effects occurred with decreased cleavage of  $\beta$ -carboxy-terminal APP fragment, reduced BACE1 expression, attenuated neuroinflammation, and reduced expression of NLRP inflammasome proteins. As *in vitro* validation, we treated neuronal and microglial cells with this compound and found that the levels of NLRP inflammasome proteins, A $\beta$  production, BACE1 expression, and oxidative stress were significantly decreased. Collectively, our findings reveal this compound as a potential therapeutic modality for targeting A $\beta$  production and A $\beta$ -induced NLRP inflammasomes.

#### **Biography**

Gun Young has completed his B.S. from Sungkyunkwan University School of Pharmacy in 2015. He is doing his master's degree at Sungkyunkwan University School of Pharmacy. His major expertise is molecular cell biology.

chocobi119@hanmail.net

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The combination of  $1\alpha$ ,25dihydroxyvitaminD3 with resveratrol prevents endoplasmic reticulum stress-mediated neuronal degeneration by improving insulin signaling and inhibiting tau hyperphosphorylation in SH-SY5Y cells

Zhongxiao Wan, Jinbo Cheng and Liqiang Qin Soochow University, China

**E** ndoplasmic reticulum stress (ER stress) is a critical factor involved in the pathogenesis of AD. Vitamin D and resveratrol are two nutritional factors that have reported neuroprotective effects, and findings from cellular model suggest that resveratrol could potentiate vitamin D's effects. We aimed to determine the effects of vitamin D & resveratrol on ER stress mediated neurodegeneration and whether synergistic effects existed. Tunicamycin ( $2\mu$ M) was utilized to induce ER stress in SH-SY5Y cells, cells were then incubated with vitamin D ( $10^{-7}$ ,  $10^{-8}$  and  $10^{-9}$  M) and resveratrol ( $25\mu$ M). The combination of vitamin D & resveratrol completely reversed tunicamycin induced cytotoxicity in SH-SY5Y cells, as well as elevation in ER stress markers (i.e.GRP78, p-eIF2 $\alpha$  and CHOP), insulin signaling disruption (i.e. elevation in p-IRS-1serine307 and reduction in p-Akt serine473) and tau phosphorylation (i.e. reduction in p-GSK3 $\beta$ serine9, and elevation in p-Tau serine396 &404). Further studies are required to clarify whether the observed synergistic effects in the present study would also existed *in vivo*, this will lay scientific foundation whether the combination of vitamin D with resveratrol might be an effective maneuver in the prevention and treatment of AD in human subjects.

#### Biography

Zhongxiao Wan has completed her PhD at the age of 29 years from University of Alberta and postdoctoral studies from University of British Columbia. She is now working at Soochow University as a research fellow. She has published approximately 16 papers in reputed journals in obesity and Alzheimer's disease related fields.

zhxwan@suda.edu.cn

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#### SH2B1 is involved in the accumulation of Aβ42 in Alzheimer's disease model

Wen-An Wang<sup>1,3</sup>, Fu-De Huang<sup>2</sup>, Yijun Shen<sup>1,2</sup>, Yiling Xia<sup>1,2</sup>, Shiquan Meng<sup>2</sup> and Nastasia K H Lim<sup>2</sup>

<sup>1</sup>Xin Hua Hospital Affiliated to Shanghai Jiaotong University School of Medicine, China

<sup>2</sup>Chinese Academy of Sciences, China

<sup>3</sup>Shanghai Jiaotong University School of Medicine, China

Insulin has been identified as a modulator of the neuronal pathways involved in learning and memory, and is also implicated as a modulator of A $\beta$  and tau metabolism toxicity. Disrupted insulin signaling pathways are evident in Alzheimer's disease (AD) patients and it is understood that type II diabetes can increase the risk of developing AD, suggesting a possible link between metabolic disorders and neurodegeneration. SH2B1 is a key protein in the insulin signaling involved in regulating the activity of the insulin receptor. To further identify the role of the insulin signaling in the pathology of AD, SH2B (*Drosophila* SH2B1 homologue) in neurons was partially knocked out or overexpressed in an AD *Drosophila* model expressing A $\beta_{42}$ . Partial knockout of SH2B had a detrimental effect on mobility and neurotransmission, and increased levels and intraneuronal accumulation of A $\beta_{42}$  in the A $\beta_{42}$ -expressing flies as assessed by ELISA and immunostaining, while, overexpression of SH2B produced the opposite effect. Thus, SH2B1 may be an upstream modulator of A $\beta$  metabolism, acting to inhibit A $\beta$  accumulation, and has a role in the pathogenesis of AD. SH2B1 may therefore have potential as a therapeutic target for this common form of dementia.

13611641232@163.com

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#### Clinical Usefulness of [18F]FC119S PET as an Auxiliary Diagnostic Methods for Dementia

Sang Moo Lim

Korea Institute of Radiological and Medical Sciences (KIRAMS), Republic of Korea

The newly developed <sup>18</sup>F-labeled amyloid tracer, 2-[2-(N-monomethyl)aminopyridine-6-yl]-6-[(S)-3-[<sup>18</sup>F]fluoro-2hydroxypropoxy]benzothiazole ([<sup>18</sup>F]FC119S) was recently introduced. We assessed the usefulness of [<sup>18</sup>F]FC119S PET as an auxiliary diagnostic methods for dementia. 1) For the comparison of [11C]PiB PET and [<sup>18</sup>F]FC119S PET, a total of 48 subjects-clinically diagnosed Alzheimer's disease (AD) in 10, mild cognitive impairment (MCI) in 10, and congnitive normal subjects (CN) in 28-underwent both [<sup>11</sup>C]PiB PET and [<sup>18</sup>F]FC119S PET. 2) To assess the diagnostic performance of [<sup>18</sup>F] FC119S, a total of 100 subjects-AD in 50, non-Alzheimer's dementia (NAD) in 15, and CN in 35-underwent brain [<sup>18</sup>F]FC119S PET. 1) The concordance rate of visual analysis of [<sup>11</sup>C]PiB PET and [<sup>18</sup>F]FC119S PET was 98% (44 of 45 cases) and the SUVR of [<sup>11</sup>C]PiB PET and [<sup>18</sup>F]FC119S PET significantly correlated (r = 0.844, p < 0.001). 2) Based on visual analysis, 45 of 50 cases with AD (90%), 6 of 15 cases (40%) with NAD (40%), and 1 of 35 CN cases (3%) were read as positive scans, respectively. Therefore, visual assessment of [<sup>18</sup>F]FC119S PET yielded a sensitivity of 90% and a specificity of 86%. The mean values of SUVR were 1.22±0.16 in AD, 1.05±0.06 in NAD, and 1.02±0.06 in CN subjects, respectively. SUVR yielded a sensitivity of 84% at the criterion of SUVR > 1.07. There were no clinically significant adverse effects during trial periods. [<sup>18</sup>F] FC119S PET yields high sensitivity and specificity for identifying AD and therefore may be an auxiliary diagnostic methods for dementia, especially to exclude AD.

#### Biography

Sang Moo Lim is the director of the department of nuclear medicine, Korea Institute of Radiological and Medical Sciences (KIRAMS), Seoul, Republic of Korea.

nmbbh@hanmail.net



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## e-Posters



# 5<sup>th</sup> International Conference on Alzheimer's Disease & Dementia

September 29-October 01, 2016 London, UK

## Morphologic substantiation of Alzheimer's disease stages by using Tomography Dementia Rating Scale (TDR)

#### Ivan V Maksimovich

Clinic of Cardiovascular Diseases named after Most Holy John Tobolsky, Russia

**Background:** To determine dementia stages, "The Clinical Dementia Rating scale" proposed by J.C. Morris is widely used in the world clinical practice. Alzheimer's disease (AD) development is accompanied by temporal and fronto-parietal brain regions atrophy increase which in turn causes dementia development. To determine AD dementia stages, we propose to complement the scale by objective CT and MRI morphological data showing atrophy severity in accordance with the clinical stage. Since fronto-parietal regions allocation is difficult, we calculated temporal regions atrophy, focusing on bone formations. The resulting scale was named The Tomography Dementia Rating scale (TDR).

Methods: The research included 108 patients:

- 49 aged 34-80 with AD various stages Test Group;
- 59 aged 28-78 with various kinds of brain lesions with dementia but without AD (moderate and severe vascular dementia, Parkinson's atherosclerosis, Binswanger's disease, Parkinson's disease) Control Group.

All patients underwent MRI, CT with subsequent temporal lobes atrophy degree calculation, brain scintigraphy (SG), rheoencephalography (REG), cerebral angiography (MUGA).

**Results:** CT and MRI among all patients with AD revealed that brain characteristic objective morphological features were temporal lobes atrophic changes of 4-62% at various AD stages. These data made it possible to make a scale allowing certain atrophic changes determination at each AD stage:

- Preclinical AD stage (those with high probability of AD inheritance, growing memory disorders, immediate relatives suffering from AD, without dementia or cognitive impairment) TDR-0: temporal lobes atrophy with 4-8% tissue mass decrease.
- Early AD stage mild dementia TDR-1: temporal lobes atrophy with 9-18% tissue mass decrease (corresponds to CDR-1).
- Average AD stage mild dementia TDR-2: temporal lobes atrophy with 19-32% tissue mass decrease (corresponds to CDR-2).
- Late AD stage severe dementia TDR-3: temporal lobes atrophy with 33-62% tissue mass decrease (corresponds to CDR-3).

These atrophic changes are not observed among patients with other cerebral lesions.

**Conclusions:** The morphologically determined scale of AD-TDR stages is an effective method for objectively determining AD stage by means of widespread CT and MRI. At the same time, this scale allows to differentiate AD from other diseases that are accompanied by the development of cerebral neurodegenerative changes complicated by dementia and cognitive impairment. The scale is easily applicable to medical institutions allowing correct and objective AD stage determination in clinical practice.

#### Biography

Ivan V. Maksimovich, MD, Head Physician of Clinic of Cardiovascular Diseases named after Most Holy John Tobolsky (Moscow, Russia) since 1993. One of the major problems the clinic deals with is the diagnosis and treatment of various brain lesions including Alzheimer's disease. For a long time I have fully concerned myself with the diagnosis and treatment of Alzheimer's disease. Over the past 15 years I have published over 60 scientific works on this subject. ISTAART member, ESC member, EAPCI member, WSO member, ESO member, EPA member.

carvasc@yandex.ru

# 5<sup>th</sup> International Conference on Alzheimer's Disease & Dementia

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#### Monitoring the Effectiveness of Treatment of Alzheimer's Disease with Morphologically Substantiated Dementia Scale - The Tomography Dementia Rating Scale (TDR)

#### Ivan V Maksimovich

Clinic of Cardiovascular Diseases named after Most Holy John Tobolsky, Russia

**Background:** Morphologically determined, objective assessment of disease stage and dementia severity plays an important role in Alzheimer's disease (AD) treatment. Consequently, the Tomography Dementia Rating scale (TDR scale) based on tomographic assessment of brain atrophic changes severity was developed and compared to the Clinical Dementia Rating scale.

The research presents results of AD stage evaluation by means of TDR scale before and after treatment.

**Materials and Methods:** 172 patients with different AD stages were examined. The examination included: CDR, MMSE evaluation, cerebral scintigraphy (SG), rheoencephalography (REG), cerebral CT and MRI, morphometric definition of AD stages (TDR), cerebral multi-gated angiography (MUGA).

For the treatment, we selected 89 patients aged 34-79 (mean age 67), 31 (34.83%) men and 58 (65.17%) women. According to AD stages, the patients were divided:

- TDR-0 (preclinical stage) 10 (11.24%) patients;
- TDR-1 (early stage with mild dementia, mild cognitive impairment) 28 (31.46%) patients;
- TDR-2 (middle stage with moderate dementia, cognitive impairment sufficiently resistant) 34 (38.20%) patients;
- TDR-3 (late stage with fairly severe dementia, severe cognitive impairment) 17 (19.10%) patients.

**Test Group** - 46 (51.68%) patients - transcatheter treatment using low-energy lasers.

Control Group - 43 (48.31%) patients - conservative treatment with Memantin Rivastigmine.

**Results:** All 46 (100%) Test Group patients showed improvement of cerebral microcirculation, which resulted in persistent reduction of dementia and restoring cognitive functions and allowed to transfer patients to an earlier TDR group or to withdraw from TDR stages. Patients with TDR-1 and TDR-2 stages have shown positive effect for over 10 years. Patients with TDR-2 stage demonstrated positive effect within 4-5 years. Patients with TDR-3 stage displayed positive effect within 2-2.5 years.

Control Group patients with earlier AD stages (TDR-0, TDR-1, TDR-2) had stabilization of their condition for the period of 6 months - 2 years, with subsequent increase of dementia and cognitive impairment. Patients with late AD stage (TDR-3) had further increase in dementia and cognitive impairment.

**Conclusions:** Using morphologically, CT and MRI justified tomography dementia rating scale allows to more easily and objectively assess the level of dementia during AD, by taking into account the severity of cerebral atrophy changes. It can be done before, during and after treatment, regardless of the chosen treatment method; besides, the scale makes it possible to evaluate the effectiveness of the treatment.

#### Biography

Ivan V. Maksimovich, MD, Head Physician of Clinic of Cardiovascular Diseases named after Most Holy John Tobolsky (Moscow, Russia) since 1993. One of the major problems the clinic deals with is the diagnosis and treatment of various brain lesions including Alzheimer's disease. For a long time I have fully concerned myself with the diagnosis and treatment of Alzheimer's disease. Over the past 15 years I have published over 60 scientific works on this subject. ISTAART member, ESC member, EAPCI member, ESO member, EPA member.

carvasc@yandex.ru



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# **Accepted Abstracts**



September 29-October 01, 2016 London, UK

#### Genetics and Molecular Pathology Laboratory, Faculty of Medicine and Pharmacy

Nadia El Kadmiri Hassan li University of Casablanca, Morocco

 $\mathbf{N}$  europroteomics studies conducted in recent years have highlighted the potential involvement of the oxidoreductase, glyceraldehyde-3-phosphate dehydrogenase (GAPDH), in Alzheimer Disease (AD) associated proteins, including the  $\beta$ -amyloid,  $\beta$ -amyloid precursor. In our previous study we elucidated the critical role of GAPDH and its interaction with  $\beta$ -amyloid in the blood of Moroccan patients with familial AD (FAD) carrying presenilin mutations.

The aim of this current study was to assess the mechanism responsible of decreased expression of GAPDH protein in the blood of Moroccan FAD cases. Our result revealed a non-significant difference of mRNA expression level of GAPDH from FAD cases carrying mutations as compared to healthy controls and FAD case confirmed at autopsy (P> 0.05). Our finding is consistent with several studies by showing the direct involvement of GAPDH in amyloid aggregation; the GAPDH in AD can undergo many different oxidative post-translational modifications, which affects its chemical structure and biological activity. These Data open prospects to clarify more these mechanisms in blood of AD cases by aiming to use GAPDH as a biomarker for diagnostics and monitoring AD modification.

elkadmiri1979@gmail.com

#### Clathrin endocytic pathway as new player in Amyloid beta pathway

C. Matrone, Poulsen E. Toftgaard, A. Larsen, A. Zollo, A.L. Jørgensen and J.J. Enghild Aarhus University, Denmark

The  $\beta$ -amyloid precursor protein (APP) has been extensively studied for its role as the precursor of the  $\beta$ -amyloid protein (A $\beta$ ) in Alzheimer's disease (AD). However, our understanding of the normal function of APP is still patchy. Emerging evidence indicates that a dysfunction in APP trafficking and degradation can be responsible for neuronal deficits and progressive degeneration in humans.

We recently reported that Y<sub>682</sub> mutation on the <sub>682</sub>.YENPTY<sub>-687</sub> domain of APP, devoted to APP internalization and trafficking (1) affects APP binding to some specific adaptors leading to an anomalous compartmentalization of APP, defects in the autophagy machinery, progressive premature neuronal degeneration and dementia in mice (2-3). A comparative Mass spectrometry analysis between mutated and control mice leaded to the identification of some crucial proteins that might be probably responsible of the phenotype observed in mutated mice (2,3). Two of these proteins, named Clathrin and its adaptor, AP2, are part of a big protein complex controlling APP trafficking inside neurons (4). Notably, the relevance of these proteins in the APP pathway and functions was further demonstrated in neuronal progenitors from Alzheimer's disease patients.

Overall, our results consolidate and refine the importance of APP adaptors in APP normal functions from an animal model of premature aging/dementia and from human differentiated stem cells. Additionally, they open the perspective to consider these adaptors as potential targets for the design and development of new therapeutic strategies.

matrone@biomed.au.dk

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#### Statistical Analysis of 3D Images of Alzheimer's disease

Mohamed M. Dessouky, Mohamed A Elrashidy, Taha E Taha, and Hatem M Abdelkader University of Menoufiya, Egypt

Alzheimer's disease is the most common type of dementia which it has no cure nor imaging test for it. Diagnosis of the Alzheimer's disease (AD) still a challenge and difficult. An early diagnosis for Alzheimer's disease is very important to delay the progression of it. This paper extract and analyze various important features of 3D-MRI brain medical images to provide better analysis and diagnosis of AD. These extracted features had been used for detection of the abnormalities among different demented and non-demented MRI AD images. This paper deals with the statistical analysis to discriminate among the different types of tissue. Also, it investigates and building up an efficient Computer Aided Diagnosis (CAD) system for AD to assist the medical doctors to easily diagnose the disease. Statistical, structural, and textural features had been extracted for different images. These extracted features had been used as an input to the SVM classifier. In addition, all these features had been applied to the proposed algorithm and then had been classified using SVM classifier. The performance of the CAD system based on statistical analysis and the proposed algorithm had been measured using different metric parameters. Also, the proposed algorithm had been applied to the images with intensity level. The obtained results indicate that the metric parameters increase from 60% without using the proposed algorithm to 100% using the proposed algorithm.

Alzheimer's disease is a degenerative brain disease and the most common cause of dementia. The most common initial symptom is a gradually worsening ability to remember new information, planning or solving problems, completing familiar tasks at home or work, Confusion with time or place, and problems with words in speaking or writing. Alzheimer's disease is a progressive disease, which means that it gets worse over time. There is no cure, specific blood or imaging test for Alzheimer's disease. However, some drugs are available which may help slow the progression of Alzheimer's symptoms for a limited time. Diagnosis of the Alzheimer's disease (AD) still a challenge and difficult, especially in the early stages. The early detection will be key to prevent, slow and stop Alzheimer's disease. The last 10 years have seen a tremendous growth in research on early detection. Statistical analysis method is one of the important methods for feature extraction in digital images. There are different previous approaches that depends on extracting statistical, textural, and structural features from digital images in different application.

The statistical analysis of 3D and 2D images of AD had been presented in this paper. Different important statistical, structural and textural features that had been extracted from different AD MRI images (normal, very mild AD and mild AD). The 3D images had been analyzed in three plans and the features had been extracted from each plane. Studying and analyzing these extracted features may help the medical doctors to diagnose the Alzheimer's disease.

This paper presents the proposed algorithm which consists of six stages. These stages are:

- 1. Preprocessing and Normalization for the input images.
- 2. 3D or 2D image to 1D signal conversion.
- 3. Proposed feature selection method.
- 4. Proposed feature extraction method.
- 5. Cross-validation
- 6. Feature matching or Classification process using SVM.

The obtained results represent different extracted features from normal, very mild and mild 3D MRI images. The features had been extracted from the images planes (X-Y, X-Z, and Y-Z). The number of pixels used for calculation was very large this leads to high values for each feature. By studying the three difference types of extracted statistical, structural and textural features it is noted that, the values of these different extracted features for normal, very mild and mild stages may help the medical doctors to diagnose the Alzheimer's disease. The results concluded as follows:

1. The SVM classifier had been used to classify the statistical features of the images into two classes (normal and patient). The obtained values of the metric parameters were about 60%.

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2. The proposed algorithm had been applied to the extracted statistical features before performing the classification step using the SVM. The obtained results of the metric parameters values improved to 70%.

3. The proposed algorithm had been applied to the 2D images with only intensity level of the images. The obtained results of the values of the metric parameters improved to 100% using number of extracted features equal to 500 features.

Finally, the trends of this paper for the Alzheimer's disease is to build up a CAD system used to assist the medical doctors to easly diagnosis it without the need to ask about the symptoms, do physical examinations, check neurological functions, or ask about blood tests and urine samples.

mohamed.moawad@el-eng.menofia.edu.eg

#### More than a century of Alzheimer's disease research... Are we barking up the wrong trees?

Andrew CK Law The University of Hong Kong, China

Decades ago, "senility" was considered a normal part of aging. Scientists and societies have come a long way to understand that cognitive impairments are indeed abnormal. Dementia is a detrimental condition that affects substantial number of individuals worldwide. Despite having ongoing heavyweight research being conducted in prominent laboratories, significant knowledge gaps regarding the pathogenesis remain and that there is not a single convincing therapeutic strategy thus far! The current deficiency of achievement in conquering dementia would prompt many to think... "where have we gone wrong?" This presentation will discuss the possible pitfalls and hopes in our fierce battle with the "mind-robbing demon".

acklaw@hku.hk

#### Explore creative capacity of seniors with dementia - A whole-person approach

Bingyu Li

University of Hong Kong, Hong Kong

In recent years, the goal of dementia care has expanded from maintaining physical health and cognitive functions to achieving holistic wellbeing among seniors with dementia. More and more significance is being attached to whole-person approaches that aim at comprehensively improving the life quality of seniors with dementia. Creativity, as a basis for human life, has been widely proved to be an important factor influencing people's quality of life. Although research has shown that generally dementia impairs people's cognitive functioning, including creativity, it has also been reported that some seniors have developed new forms of creativity after diagnosis of dementia, possibly as a result of disinhibition. Such findings provide a new perspective in dementia care development that empathizes strength rather than symptoms. In the new generation of dementia interventions, seniors should be associated with potentials instead of problems, and they should no longer be considered as passive receivers of caring service but vital participants in creativity of seniors with dementia, as well as effective methods for application and reinforcement of such capacity. Based on current evidence, this paper proposes a practice development model that recognizes, explores and enhances creative capacity of demented seniors, with cultural sensitivity taken into particular consideration.

bingyuli@connect.hku.hk